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EDITORIAL

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Interstitial lung disease associated with idiopathic inflammatory myopathies: the importance of recognizing an early pulmonary phenotype

Enfermedad pulmonar intersticial asociada a miopatías inflamatorias idiopáticas: el valor de reconocer un fenotipo pulmonar temprano

Castro Zorrilla, Liliana[1, 2,3]

"In idiopathic inflammatory myopathies, the lung is not just another organ: it is the one that defines the clinical course."

Idiopathic inflammatory myopathies (IIM) comprise a heterogeneous group of autoimmune diseases in which pulmonary involvement has become a decisive prognostic factor. Interstitial lung disease (ILD) associated with IIM is one of the main determinants of morbidity and mortality[1,2]. In this context, early identification of clinical, immunologic, and radiologic risk patterns is essential to modify the natural course of the disease.

The multicenter study analyzed[3] provides significant data by characterizing a representative cohort of regional clinical practice, with a predominance of women, a high frequency of antisynthetase antibodies –particularly anti-Jo-1– and a dominant pattern of nonspecific interstitial pneumonia (NSIP). These findings are fully consistent with recent international series[4-6], underscoring that accurate identification of the antisynthetase phenotype is a cornerstone of diagnosis, prognosis, and therapeutic decision-making in this context.

Radiologic findings reinforce the importance of expert interpretation of high-resolution computed tomography. The predominance of the NSIP pattern, also observed in contemporary studies[5,7], requires active surveillance, given its potential reversibility when treated promptly. Multidisciplinary collaboration among pulmonology, rheumatology, and radiology is therefore essential to ensure early diagnosis and timely management.

From a functional standpoint, early reduction in diffusing capacity, exercise-induced desaturation, and restrictive ventilatory impairment represent sensitive markers of early pulmonary involvement[1,2]. Systematic assessment with DLCO and walk tests –simple, low-cost tools– plays a central role in detecting subclinical progression and adapting treatment in a timely manner.

Therapeutically, the favorable outcomes observed with mycophenolate and the use of rituximab in refractory cases align with contemporary evidence and recent multicenter studies.[6,8] Early implementation of intensive immunomodulatory therapy has shown benefit in preventing irreversible fibrotic progression and improving long-term survival.

A valuable contribution of the study is the comparison between patients with and without ILD. The higher prevalence of antisynthetase markers among those with ILD, and the greater muscular involvement and ANA positivity in those without pulmonary disease, reflect the phenotypic heterogeneity of IIM.[9] This variability reinforces the need to stratify patients according to distinct clinical and serologic profiles to guide personalized management strategies.

Taken together, this regional study reinforces a key clinical message: active screening for ILD in patients with IIM is essential. Early detection allows intervention before irreversible lung damage occurs, optimizing immunomodulatory therapy and improving long-term outcomes.

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Conflicts of interest

The author declares no conflicts of interest related to this publication.

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EDITORIAL

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Benign Tracheal Stenosis. Therapeutic Response Required for a Disease with High Morbidity Burden

Estenosis traqueal benigna. Respuesta terapéutica necesaria a una patología con alta carga de morbilidad

Carlos Fernando Brescacin[1]

Tracheal stenosis is a dreaded complication in patients who have required prolonged mechanical ventilatory assistance (MVA) or its consequent tracheostomy. It results from ischemic injury to the mucosa caused by contact with the cuff inflated at a pressure exceeding capillary perfusion, leading to prolonged pressure injury. This corresponds to a scarring process of an inflammatory granulomatous type that is generally progressive.[1, 2]

As Ruiz et al highlight in this issue of the journal, this condition is potentially preventable, since the proper use of immediate post-intubation care protocols significantly reduces the occurrence of these lesions, which act as contributing factors to post-MVA comorbidity, leading to a difficult course in airway rehabilitation.

In this study, the authors address the complexity involved in selecting patients who are suitable candidates for the surgical resolution of airway stenosis, emphasizing the importance of having multiprofessional teams with sufficient accumulated experience from case reports in order to achieve better postoperative outcomes.

Tracheal surgery, when performed under strict inclusion criteria, has proven to be an effective therapeutic option, with an acceptable rate of potentially remediable complications. It substantially improves patients' symptom perception and the associated functional limitation, while reducing related complications.

It is also important to highlight the need for appropriate technological support, including the flow–volume loop of computerized spirometry as a first indicator of fixed airway obstruction, flexible as well as rigid endoscopy with complementary therapeutic capability, and access to 3D reconstruction imaging with its potential for virtual endoscopic navigation.

Secondarily, there is the challenge of standardizing follow-up protocols for patients who have required airway instrumentation. This involves using computerized spirometry to objectively measure reduced PEF (peak expiratory flow) and PIF (peak inspiratory flow), suggesting evident fixed obstruction on the box –shaped flow–volume loop, which enables early suspicion and progressive monitoring, especially in oligosymptomatic patients, in primary care settings.[4]

I believe it would be of interest to plan a study comparing 3D tomographic reconstruction with tracheal ultrasound findings, evaluating sensitivity and specificity, as ultrasound is a less costly and more readily accessible practice that could serve as an indicator for referral to a specialized center for definitive management.

The article reflects the importance of collaborative multiprofessional work and interaction among various specialties to provide solutions with a high impact on our patients' quality of life.

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Conflict of interest

The author has no conflicts of interest to declare.

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ORIGINAL ARTICLE

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Multidisciplinary Treatment of Benign Central Airway Stenoses Post Intubation

Tratamiento multidisciplinario de las estenosis benignas de la vía aérea central post intubación

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ABSTRACT

Background: Postintubation laryngotracheal stenoses are lesions of a benign and progressive nature that pose a challenge to the treatment team. The narrowing of the airway lumen is responsible for increasing dyspnea, which requires rapid and effective diagnosis and treatment methods. This is why it is essential to approach this condition by a multidisciplinary team including thoracic surgeons, bronchoscopists and intensivists.
Objective: To evaluate the results obtained with the surgical treatment of patients with laryngotracheal stenosis previously selected according to the algorithm in a specific period and their complications.
Materials and Methods: The medical records of 57 patients with laryngotracheal stenosis were studied observationally and retrospectively between the years 1996 and 2023, and they were included for surgical treatment: 5 were laryngotracheal and 52 were tracheal. Resection and reconstruction were performed according to the Pearson technique in the first group, and resection with tracheotracheal anastomosis was used in the second group.
Results: Of the total 57 operated patients, 48 had a good postoperative evolution and 9 showed complications, which corresponds to 15.7% of the total. 4 air fistulas and 5 restenosis of the anastomosis were observed. There was no mortality in our series of patients.
Conclusions: Surgery is the best therapeutic option in strictly selected patients with laryngotracheal lesion, a fact corroborated by our experience and the literature. The multidisciplinary approach allows for better diagnostic and therapeutic evaluation, since interventional bronchoscopy allows us to dilate and take patients to surgery in better clinical conditions.

Key words: Laryngotracheal stenosis; Benign; Resection; Anastomosis

RESUMEN

Introducción: Las estenosis laringotraqueales postintubación son lesiones de naturaleza benigna y progresiva que plantean un desafío para el equipo tratante. El estrechamiento de la luz de la vía aérea es responsable de la disnea creciente que obliga a utilizar métodos de diagnóstico y tratamiento de manera rápida y efectiva. Es por ello que resulta indispensable el abordaje de esta patología por un equipo multidisciplinario que incluya cirujanos torácicos, broncoscopistas e intensivistas.

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Objetivo: Evaluar los resultados obtenidos con el tratamiento quirúrgico de pacientes con estenosis laringotraqueales previamente seleccionados según algoritmo en un periodo determinado y sus complicaciones.
Materiales y métodos: Se estudiaron las historias clínicas de 57 pacientes con estenosis laringotraqueal en forma, observacional y retrospectiva entre los años 1996 y 2023 a quienes se incluyó para su tratamiento quirúrgico: 5 fueron laringotraqueal y 52 traqueales. Se realizó resección y reconstrucción según técnica de Pearson en el primer grupo y resección con anastomosis traqueotraqueal en el segundo grupo.
Resultados: del total de n=57 pacientes operados, n=48 tuvieron buena evolución postoperatoria y n=9 presentaron complicaciones que corresponde al 15,7% del total. Se reconocieron n=4 fístulas aéreas y n=5 reestenosis de la anastomosis. No hubo mortalidad en nuestra serie de enfermos.
Conclusiones: La cirugía es la mejor opción terapéutica en aquellos pacientes con lesión laringotraqueal estrictamente seleccionados, hecho corroborado con nuestra experiencia y con la literatura. El abordaje multidisciplinario permite una mejor evaluación diagnóstica y terapéutica, ya que la broncoscopía intervencionista nos permite dilatar y llevar a cirugía a pacientes en mejores condiciones clínicas.

Palabras claves: Estenosis laringotraqueal, Benigna; Resección; Anastomosis

INTRODUCTION

Postintubation laryngotracheal stenosis is defined as scar lesions of benign nature, secondary to orotracheal or tracheostomy intubation, with a progressive and irreversible course.[4,6,11]

The subglottic stenosis refers to the narrowing of the airway between the glottis (e.g., vocal cords) and the cricoid cartilage. Tracheal stenosis refers to the narrowing of the airway lumen from the cricoid cartilage to the main carina. Laryngotracheal stenosis involves any obstruction that affects the larynx and/or trachea.[1,2,4]

From a physiopathological standpoint, prolonged or traumatic orotracheal or tracheostomy intubation compromises the laryngotracheal blood supply, causing ischemia and parietal necrosis, followed by a progressive scarring and stenotic process.[3,5,9]

The most common lesions are caused by hyperinflation of the endotracheal tube cuff during prolonged mechanical ventilatory assistance (MVA), or by trauma produced during the performance of a tracheostomy, either from the cuff's traumatic effect or from the tip of the cannula.[2,4,5,6,11,12]

The increasingly frequent occurrence of severe trauma in young patients requiring mechanical ventilatory assistance in the Intensive Care Unit is a major factor in the development of these lesions, since traumatic orotracheal intubation without proper attention to technique or without the use of low-pressure cuffs can injure the tracheal wall. Similarly, lesions occur as a consequence of the improper placement of the tracheostomy or if it is performed by untrained personnel.[4,8,10]

The management of this condition represents a challenge for the medical team due to its complexity, the lack of specialized equipment, and the fact that patients often have high demands, as they present with severe functional limitations. For this reason, a multidisciplinary approach to these patients is essential, requiring trained surgeons in surgical treatment, endoscopists experienced in interventional bronchoscopy, anesthesiologists accustomed to advanced management of difficult airways, radiologists, and trained physical therapists.[3, 7, 8,10]

The objective of this presentation is to share our experience in the surgical management of this complex and challenging condition, emphasizing the need for multidisciplinary collaboration in treatment.

MATERIAL AND METHODS

Between 1996 and 2023, a total of 18,815 fiberoptic bronchoscopies were performed by the Fiberoptic Bronchoscopy Service of our institution, detecting 657 patients with central airway stenosis (CAS). 57 of them were referred to the thoracic surgery service for surgical resolution, and they are the focus of our presentation. Their medical records were reviewed in an observational and retrospective manner. Figure No. 1 shows the diagnostic and therapeutic algorithm used in our population.

The patients selected for surgery met the following preoperative conditions: absence of MVA, good performance status (grade 0, 1, or 2 according to the ECOG [Eastern Cooperative Oncology Group] scale of performance status), and stenosis length less than 6 cm.

Of the 57 surgically treated patients, 31 were men and 26 were women, with a mean age of 25 years (range: 21–30). The main symptom was dyspnea, followed by stridor in 31 patients. The average duration of MVA was 16 days; and 18 patients had a tracheostomy at the time of admission to our service.

The initial diagnosis was made with fiberoptic bronchoscopy in all patients, revealing laryngotracheal lesions in 5 patients and tracheal lesions in 52. 47 of those 52 were cervical, 4 cervicothoracic, and 1 thoracic. Therapeutic bronchoscopies showed grade 4 or 5 stenosis according to the Freitag classification in 90.3% of cases. All patients underwent cervical and thoracic computed tomography. A flow-volume curve was performed in 50 patients, and helical CT of the trachea with 3D reconstruction and virtual bronchoscopy was performed in 42 individuals. This latter imaging study was essential for determining the location of the stenosis, as well as its length and distance from the cricoid cartilage above and the carina below. Due to progressive dyspnea resulting from the stenotic evolution of these lesions, 28 patients underwent dilation prior to surgery, and in 8 of them, a temporary preoperative stent was placed.

The cause of laryngotracheal stenosis in the 5 patients in our series was incorrect tracheostomy placement, which resulted in a lesion to the cricoid cartilage and the first tracheal rings. This led to fibrosis in three patients, while in the other two, the stenosis was caused by prolonged intubation. In two patients, surgery was performed with a stoma located distal to the lesion. The surgery was performed on an outpatient basis.

The Anesthesiology and Fiberoptic Bronchoscopy Service performed intraoperative orotracheal intubation below the lesion and above the carina under fiberoptic bronchoscope guidance. After the surgical incision was made in the trachea, a spiral tube was inserted into the distal end of the trachea, and the previous tube was withdrawn up to the glottis. After resection of the stenotic area and subsequent anastomosis of the posterior tracheal wall, the spiral tube was removed, and the orotracheal tube was advanced distal to the suture line and above the carina, again under fiberoptic bronchoscope guidance.

Laryngotracheal resection was performed in 4 patients using the Pearson technique, with

laryngotracheal anastomosis, while tracheal resection with tracheotracheal anastomosis was

performed in 52 patients. 47 of them were approached through transverse cervicotomy, 4 through cervicomanubriotomy, and 1 through posterolateral thoracotomy. In one patient with laryngotracheal lesion, resection was not feasible because the lesion extended beyond 6 cm, resulting in the patient requiring a tracheostomy (figure 2). The critical moment of the surgical procedure is determining the length to be resected, as it must be sufficient to prevent restenosis if too short, yet not so long as to risk an airway fistula. The average length of stenotic trachea resected was 3 cm. Laryngeal release maneuvers were necessary in only two patients to avoid excessive tension on the suture line. The suture was performed in a single layer with interrupted stitches using either non-absorbable or PDS-type material, whether for laryngotracheal or tracheotracheal anastomosis. There was no need to place a Montgomery T-tube across the anastomosis, nor to create a distal stoma beyond the suture.

The physiotherapy service provided postoperative care to all patients, including breathing exercises, secretion management, and especially monitoring for postoperative complications such as recurrent laryngeal nerve paralysis or swallowing dysfunction. None of these complications occurred in our series.

RESULTS

Of the 57 operated patients, 48 had a good postoperative course, while 9 (15.7%) experienced complications. The highest rate of complications

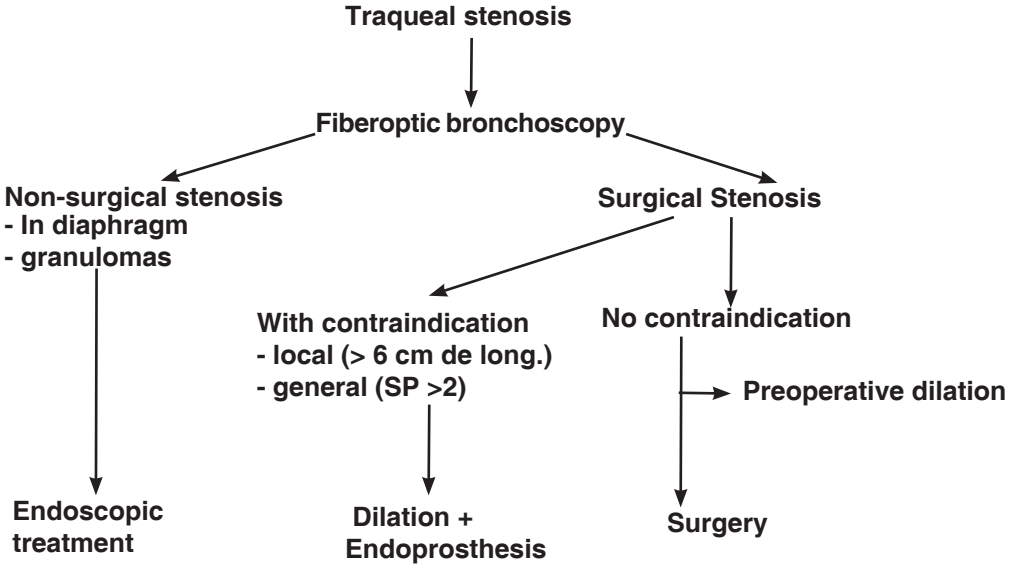
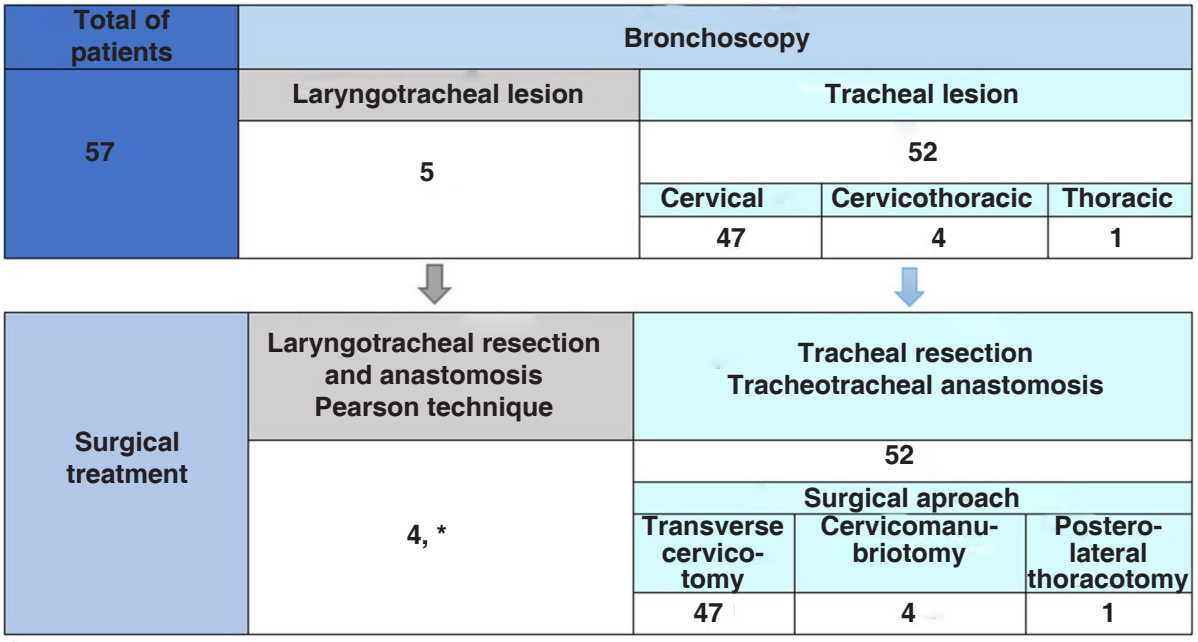


Figure 1. Therapeutic algorithm



* In one patient with laryngotracheal lesion, resection was not feasible because the lesion extended beyond 6 cm, resulting in the patient requiring a tracheostomy.

Figure 2. Localization and surgical approach

was observed in the group of patients with laryngotracheal lesions (2 out of 5). Both patients developed an airway fistula; one required a tracheostomy, and the other underwent stent placement. In the group of patients who underwent tracheal resection, 7 patients out of 52 developed complications. Two of these patients developed an airway fistula: in one case, the fistula closed spontaneously, whereas the other required stent placement. The suture re-stenosed in 5 patients, and was resolved with dilation and stent in 4 subjects, and with distal tracheostomy below the restenosis in 1. Of the total number of patients with tracheal injury complications (7), 6 had undergone preoperative dilation. The unresected patient who underwent tracheostomy had a favorable outcome. There was no mortality in our series of patients.

DISCUSSION

Adequate management of this challenging condition is achievable through strict patient selection criteria and the expertise of a multidisciplinary team. In patients with central airway stenosis who meet the aforementioned selection criteria, surgery is the best therapeutic option –a concept supported by most of the literature and also by our own experience.[3,6,7,8, 10,11]

The optimal timing for performing resective surgery is after the third month, because by this point the lesion progresses to a stage of chronic fibrosis without acute inflammation, which allows for clear delineation of the length of the parietal lesion.[4,6, 9,10,12]

In our series, 84.3% of the operated patients had favorable outcomes (48 out of 57), mostly from the group with tracheal lesions, as patients with laryngotracheal lesions had a higher percentage of postoperative complications (2 out of 5). Interventional bronchoscopy plays a crucial role by enabling treatment of airway stenosis in patients who are not candidates for surgery, as well as managing surgical complications. These complications are typically resolved with stent placement in cases of airway fistula, or with dilation (with or without stent placement) in cases of restenosis.[3,7]

Due to their stenotic and progressive nature, these lesions may also undergo preoperative dilation while awaiting surgery, a procedure performed

in 28 of the 57 patients in our series. However, this preoperative interventional approach carries a higher risk of postoperative complications, as dilation maneuvers are traumatic and cause lesions, parietal hemorrhage, and inflammation. This factor was crucial in the occurrence of complications in our case report, since the 7 patients who developed complications following tracheal resection had all undergone prior dilation while awaiting surgery. Another determining factor in the occurrence of complications was airway infection, as stenosis prevents proper drainage of secretions, which are frequently infected, thereby exerting a deleterious effect on the suture line. [2,8,9]

Laryngotracheal stenoses are complex lesions, difficult to resolve. They usually involve the cricoid cartilage either partially or totally, as well as the first tracheal rings. The technique proposed by Pearson –which includes anterior resection of the cricoid and the affected trachea segment followed by thyrotracheal suture– was the one used in our patients.[10,11,12] Inclusion of the tracheostoma increased the resection length in 2 patients, resulting in postoperative fistula in both.

CONCLUSION

We consider it important to highlight some diagnostic and therapeutic strategies for proper management of this complex condition:

In any patient with a history of prolonged orotracheal or tracheostomy intubation presenting with dyspnea and/or stridor, central airway stenosis (CAS) should be suspected.

Fiberoptic bronchoscopy and helical CT scan of the trachea with reconstruction are two indispensable diagnostic tools. The latter provides information on the length of the stenosis and its relationship to the carina and cricoid. [1,2,4]

Once the diagnosis of stenosis is confirmed, distal tracheostomy should be avoided whenever possible, as it contaminates the airway and increases the length of the trachea requiring resection.[10,11,12]

Surgical treatment is the best therapeutic option in patients who meet the previously described criteria. The psychological state of the patient and their environment must be considered, as performing surgery on an unstable patient can subject the tracheal anastomosis to sudden stress, increasing the risk of early dehiscence, which is the main cause of early mortality. [4,6,10,12]

Preoperative dilation with rigid bronchoscopy provides temporary relief of symptoms and allows surgery to be scheduled. However, repeated dilations cause additional parietal lesion, increasing the rate of complications.

Management of postoperative complications is usually endoscopic, either with dilation or stenting. This aspect, together with its preoperative diagnostic role, makes it indispensable to have access to an interventional bronchoscopy team.

Conflict of interest

The authors have no conflict of interest to declare.

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ORIGINAL ARTICLE

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Interstitial Lung Disease Associated with Idiopathic Inflammatory Myopathies. Multicenter Study Conducted in the Province of Córdoba, Argentina

Enfermedad pulmonar intersticial asociada a miopatías inflamatorias idiopáticas. Estudio multicéntrico en la provincia de Córdoba, Argentina

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ABSTRACT

Introduction: Idiopathic inflammatory myopathies (IIMs) are a group of autoimmune diseases characterized by muscle weakness and extra-muscular manifestations. Diffuse interstitial lung disease (DILD) is a common complication of IIMs, associated with a worse prognosis and higher mortality rates. The objectives of our study were: 1- To describe the clinical, radiological, serological, respiratory functional characteristics, and treatment of patients with DILD associated with IIM. 2- To compare subgroups of IIM patients with and without DILD.

Materials and Methods: An observational, descriptive, multicenter study was conducted, including patients diagnosed with IIM (with and without associated DILD) between 2017 and 2021 from three centers in the city of Córdoba (Hospital Córdoba, Hospital Italiano, and Sanatorio Allende).

Results: The study included a total of 47 patients with IIM, with a mean age of 44.7 years; 74.5% of them were female. DILD was present in 55.3% of patients, most frequently in association with antisynthetase syndrome (46.2%). The Jo-1 antibody was the most prevalent (38.5%), and the most common CT pattern was NSIP (non-specific interstitial pneumonia) (57.79%). The mean baseline FVC (forced vital capacity) was 62.2% of predicted, the mean DLCO (diffusing capacity of the lungs for carbon monoxide) was 52.5%, and 50% of patients showed a drop in oxygen saturation during the six-minute walk test (6MWT). The most frequently used initial treatment regimen was systemic corticosteroids combined with mycophenolate (68%). In refractory cases, Rituximab was administered. When comparing subgroups, patients with DILD showed a higher prevalence of antisynthetase syndrome and respiratory symptoms, whereas those without DILD had more pronounced muscle involvement and ANA-positive antibodies.

Conclusions: In our study of patients with IIM-associated DILD, there was a predominance of middle-aged women, with an autoimmune profile of anti-Jo-1 positivity and an NSIP CT pattern. The treatments used in these patients proved to be effective and safe.

Key words: Diffuse interstitial lung disease; Idiopathic inflammatory myopathies; Antisynthetase syndrome; Jo-1 antibody

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RESUMEN

Introducción: Las miopatías inflamatorias idiopáticas (MII) son un conjunto de enfermedades autoinmunes que se caracterizan por debilidad muscular y manifestaciones extra-musculares. La enfermedad pulmonar intersticial difusa (EPID) es una complicación común de las MII, asociándose a un peor pronóstico y mayor mortalidad. Los objetivos de nuestro estudio fueron 1- Describir las características clínicas, radiológicas, serológicas, funcionales respiratorias y el tratamiento de pacientes con EPID asociada a MII 2- Comparar los subgrupos de pacientes con MII con y sin EPID.

Materiales y métodos: Se realizó un estudio observacional, descriptivo y multicéntrico, incluyendo a pacientes con diagnóstico de MII (con y sin EPID asociada) dentro del periodo 2017 a 2021 de 3 centros de la ciudad de Córdoba (Hospital Córdoba, Hospital Italiano y Sanatorio Allende).

Resultados: Se incluyeron 47 pacientes con MII con una edad promedio de 44,7 años, el 74,5% de sexo femenino. El 55,3% tenía EPID, con el síndrome antisintetasa más frecuentemente (46,2 %), el anticuerpo Jo-1 el más prevalente (38,5%) y el patrón tomográfico de NINE (57,79%). La FVC media inicial fue del 62,2% del predicho, la DLCO media del 52,5% y un 50% presentó caída de la saturación de oxígeno en el test de la marcha. El esquema terapéutico inicial más utilizado fueron los corticoides sistémicos con micofenolato en el 68 % y en los casos refractarios, el Rituximab. Al comparar los subgrupos, los pacientes con EPID presentaron mayor prevalencia de síndrome antisintetasa y síntomas respiratorios, mientras que aquellos sin EPID mostraron mayor compromiso muscular y anticuerpos ANA positivos.

Conclusiones: En nuestro estudio de pacientes con EPID asociada a MII predominaron las mujeres de edad media con perfil autoinmune anti Jo-1 positivo y patrón tomográfico de NINE. Los tratamientos utilizados en estos pacientes demostraron ser efectivos y seguros.

Palabras clave: Enfermedad pulmonar intersticial difusa; Miopatías inflamatorias idiopáticas; Síndrome antisintetasa; Anticuerpo Jo-1

INTRODUCTION

Diffuse interstitial lung diseases (DILDs) are a group of heterogeneous entities with variable behavior, sharing similar clinical, functional, and radiological characteristics.[1]

On the other hand, idiopathic inflammatory myopathies (IIMs) are a group of autoimmune diseases characterized by muscle weakness and other systemic manifestations. Currently, five main types of inflammatory myopathies are recognized: dermatomyositis (DM), polymyositis (PM), immune-mediated necrotizing myopathy (IMNM), overlap myositis (which includes the antisynthetase syndrome), and inclusion body myositis (IBM).[2] Their diagnosis is based on clinical findings, laboratory tests (muscle enzymes and autoantibodies), electromyography, and skeletal muscle histopathology.[3-4] It is estimated that 50-60% of patients present myositis-specific autoantibodies (MSAs) that confirm the diagnosis, define phenotypes, and correlate with clinical manifestations.[5]

DILD is one of the most common complications of IIMs, and its presence is associated with a worse prognosis and higher mortality rates.

The course and severity of IIMs are highly variable, ranging from mild forms to severe, treatment-refractory cases.[6] With the exception of IBM, the cornerstone of treatment for IIMs is the administration of glucocorticoids and immunosuppressive agents such as methotrexate, azathioprine, and mycophenolate. In cases of refractory disease, intravenous immunoglobulin, rituximab, cyclophosphamide, cyclosporine A, and tacrolimus have been used. Currently, knowledge about treatment options is limited because these drugs have not been directly compared in clinical trials.[2,7]

The objectives of our study were: a) To describe the clinical, radiological, serological, respiratory functional characteristics, and treatment of patients with DILD associated with IIM, and b) To compare subgroups of IIM patients with and without DILD.

MATERIALS AND METHODS

Patients and data collection An observational, descriptive, multicenter study was conducted involving patients from three centers in the city of Córdoba (Hospital Córdoba, Hospital Italiano, and Sanatorio Allende) who sought care between 2017 and 2021. The study included individuals over 18 years of age diagnosed with idiopathic inflammatory myopathies (with or without associated DILD). Patients with overlap syndrome involving another autoimmune disease, DILD secondary to another connective tissue disease, or interstitial pneumonia with autoimmune features (IPAF) were excluded. Patients diagnosed with inclusion body myositis (IBM) were also excluded.

Procedures: the medical records of patients with IIM were reviewed, and the following data were collected:

a) *Demographic data*: sex and age at the time of diagnosis.
b) *Type of myopathy*: polymyositis, dermatomyositis, or antisynthetase syndrome, according to the diagnostic criteria published in 2017 by the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR).[8]
c) Clinical manifestations.
d) *Autoimmune serology*: patients were tested using an autoimmune panel that included ANA antibodies and a myositis panel (containing antibodies Jo-1, PM-Scl, PL-7, PL-12, Mi-2, Ku, and SRP).
For the subgroup of patients with associated DILD, the following additional data were collected:
e) Tomographic pattern: high-resolution chest CT scans were performed and evaluated by a specialist in diagnostic imaging. The tomographic patterns were classified according to the American Thoracic Society (ATS) and European Respiratory Society (ERS) guidelines for idiopathic interstitial pneumonias as follows: usual interstitial pneumonia (UIP), nonspecific interstitial pneumonia (NSIP), lymphocytic interstitial pneumonia (LIP), organizing pneumonia (OP), acute interstitial pneumonia (AIP), respiratory bronchiolitis–associated interstitial lung disease (RB-ILD), and desquamative interstitial pneumonia (DIP). Images were evaluated both at the time of diagnosis and during follow-up.[9] Disease status was categorized as stable, improved, or progressive (defined by an increase or appearance of new reticulations, ground-glass opacities, traction bronchiectasis/bronchiolectasis, honeycombing, or loss of lung volume).
f) *Pulmonary function tests (PFTs)*: spirometry, diffusing capacity for carbon monoxide (DLCO), and the six-minute walk test (6MWT) were evaluated at the time of diagnosis. Forced vital capacity (FVC) and DLCO were recorded as percentages (%) of predicted values. In the six-minute walk test, desaturation (oxygen drop) was assessed.
g *Pharmacologic treatment:* systemic glucocorticoids (GCS), methotrexate (MTX), azathioprine (AZA), mycophenolate mofetil (MMF), intravenous immunoglobulin (IVIg), rituximab (RTX), cyclophosphamide (CYC), hydroxychloroquine (HCQ), and leflunomide (LEF). Initial treatment was defined as the initial therapy administered after diagnosis and maintained for at least three months. Second-line treatment was prescribed in cases of lack of initial response.

Statistical methodology The collected data were entered into an Excel-like database, which was later used for statistical analysis. For quantitative variables, measures of central tendency and dispersion (mean and standard deviation) were calculated, while categorical variables were expressed as absolute and percentage distributions. Chi-square tests were applied to compare variables according to treatment response. A significance level of 0.05 was used in all cases. Statistical analyses were performed using InfoStat software (version 2020).

Ethical considerations Approval for this study was obtained from the Institutional Health Research Ethics Committee of Sanatorio Allende. All complementary studies performed were part of the routine follow-up for these patients. Data analysis was conducted using patients' medical records, maintaining participant confidentiality at all times.

RESULTS

General characteristics Information was collected from 47 patients with IIM, with a mean age of 44.7 years. Females represented 74.5% of the cohort. Regarding the type of myopathy, 40.4% of patients were diagnosed with dermatomyositis, 34.1% with polymyositis, and 25.5% with antisynthetase syndrome. 55.3% (26 patients) had DILD (Figure 1). The most prevalent antibodies were: ANA in 40.4%, Jo-1 in 27.7%, Ro in 6.4%, AMA in 6.4%, PL-12 in 4.3%, and Mi-2 in 4.2%. Less fre-

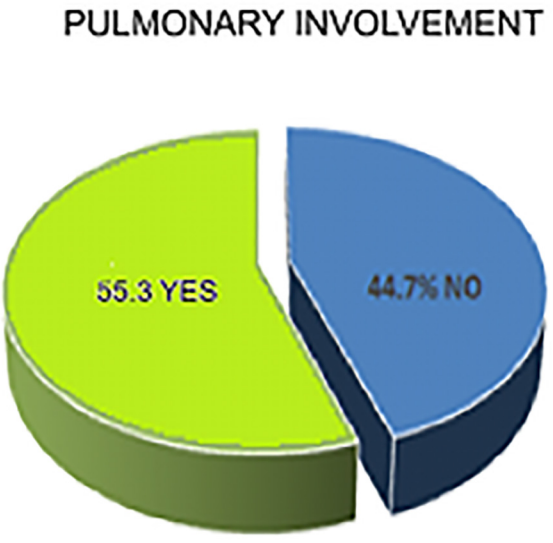

Figure 1. Distribution of the sample according to pulmonary involvement (DILD).

quent antibodies included SRP, Rib P, Pm-Scl100, and RNP, present in 2.1% of patients.

Subgroup with DILD In the group of 26 patients with DILD, the mean age was 48.3 years, and 80.8% were female. Most patients were diagnosed with antisynthetase syndrome (46.2%), followed by polymyositis (30.8%) and dermatomyositis (23.1%).

The most frequently reported symptoms were: dyspnea (84.6%), cough (50%), muscle weakness (50%), joint involvement (42.3%), symptoms meeting the SICCA (Sjögren's International Collaborative Clinical Alliance) criteria and cutaneous-mucosal involvement (42.3%). Other clinical manifestations included Raynaud's phenomenon (23.1%) and dysphagia (15.4%).

The most prevalent antibody was Jo-1, found in 38.5% of cases, followed by ANA in 26.9%. Other antibodies detected included: AMA (7.7%), Ro (7.7%), Pm-Scl100 (4%), SRP (4%), and RNP (3.8%).

The most common tomographic pattern was NSIP in 57.79%, followed by UIP in 34.61%. For the remaining 7.6%, imaging data were unavailable.

Regarding lung function, at diagnosis patients had a mean FVC of 62.2% of predicted, mean DLCO of 52.5% of predicted, and significant oxygen desaturation during the 6MWT in 50% of cases.

Pharmacologic treatment was analyzed in DILD patients who had clinical, pulmonary function, and/or imaging follow-up from the start of therapy, resulting in a total of 19 patients included in this analysis.

Initial treatment

The most commonly used initial therapeutic regimen was systemic corticosteroids (CS) combined with MMF, administered to 68% of patients. In 2 patients (10.48%), a third drug was added, MTX. Another 2 patients received CS with HCQ. Less frequent combinations included CS with AZA, and CS with MTX + RTX (5.24% in both cases).

Second-line treatment

In refractory cases (9 patients), RTX was the main therapeutic option, accounting for a total of 75%; 50% of those in monotherapy and the other 25% in combination with IVIg (Table 1). Other less common treatment combinations included CS with MMF and CS with AZA.

Changes in medication were primarily due to lack of response to treatment. No cases of drug-related toxicity were reported.

al and second-line treatments.

Mortality

Two deaths were recorded in the analyzed group. One was a patient with antisynthetase syndrome who initially received CS + AZA, but due to refractoriness, treatment was switched to IVIg + RTX + CS, without success. The other case involved a dermatomyositis patient who began treatment with CS and MMF and later escalated to RTX, also without achieving a favorable response.

Subgroup without DILD

Among the 21 patients with DILD, the mean age was 39.8 years, and 57.1% were female. The most prevalent symptom was muscle weakness (90.5%).

TABLE 1. Distribution of the sample according to initial and second-line treatments

Treatments	Therapeutic regimen	Number of patients	Percentage of patients
Initial treatment (n=19)	CS+MMF	13	68.40%
	CS+MMF+RTX	2	10.50%
	CS+HCQ	2	10.50%
	CS+MTX+RTX	1	5.30%
	CS+AZA	1	5.30%
Second-line treatment (n=8)	CS+MMF	4	44.40%
	RTX	2	22.20%
	CS+AZA	2	22.20%
	RTX+IVIg	1	11.10%

Regarding the autoimmune profile, the most frequent antibodies were: ANA (57.1%), Jo-1 (14.3%), Mi-2 (9.5%), and AMA and Ro (4.8% each).

Comparison between subgroups

Among patients with IIM-associated DILD, there was a higher prevalence of antisynthetase syndrome, respiratory symptoms, and anti-Jo-1 positivity.

Patients without DILD most commonly exhibited higher muscle involvement, dysphagia, and ANA positivity (Table 2). *Table 2. Comparison between IIM subgroups with and without DILD.*

DISCUSSION

In our study, we described the main characteristics of patients with DILD associated with IIMs.

The prevalence of DILD among IIM patients was 55.3%, which is consistent with literature findings ranging from 20% to 86%.[10,11] Similarly, we observed the expected predominance of middle-aged women affected by this condition.

Regarding clinical manifestations, it is noteworthy that muscle weakness was present in only half of patients with DILD; these findings align with other publications.[12,13]

TABLE 2. Comparison between IIM subgroups with and without pulmonary involvement

Variables	Categories	Total (n=47)	DILD		p-value
			Yes	No	
Age (years)	Age	44.7 +/- 16	48.3 +/- 13.6	39.8 +/- 17.9	0.081
Sex	Female	74.50%	80.80%	57.10%	0.27
	Male	25.50%	19.20%	33.30%	
Diagnosis	Dermatomyositis	40.40%	23.10%	61.90%	
	Polymyositis	34%	30.80%	38.10%	
	Antisynthetase syndrome	25.50%	46.20%	0%	
Clinical manifestations	Dyspnea	53.20%	84.60%	14.30%	0.0001
	Cough	34%	50%	14.30%	0.013
	Muscle weakness	68.10%	50%	90.50%	0.001
	SICCA	25.50%	34.60%	14.30%	0.096
	Cutaneous-mucosal involvement	42.60%	34.60%	52.40%	0.382
	Joint involvement	34%	42.30%	23.80%	0.153
	Raynoud	68.10%	23.10%	9.50%	0.201
	Dysphagia	25.50%	15.40%	47.60%	0.016
Lung function	FVC %	-	61.10%	-	
	DLCO%	-	52.20%	-	
	SpO_2 drop in 6MWT	-	50%	-	
Tomographic pattern	UIP	-	57.70%	-	
	NSIP	-	34.60%	-	
	No data	-	7.70%	-	
Autoimmune profile	ANA	40.40%	26.90%	57.10%	0.015
	Jo-1	27.70%	38.50%	14.30%	0.042
	AMA	6.40%	7.70%	4.80%	0.612
	Mi2	4.30%	0%	9.50%	0.026
	Pm-Scl 100	2.10%	3.80%	0%	0.336
	Ro	6.40%	7.70%	4.80%	0.612
	PL-12	4.30%	7.70%	0%	0.179
	RNP	2.10%	3.80%	0%	0.285

ANA positivity was observed in 40.4% of the total study population and in 26.9% of patients with DILD. The presence of negative ANA results in patients with antisynthetase antibodies is not uncommon, due to the cytoplasmic localization of the autoantigens. This fact, in the absence of extrapulmonary symptoms, could lead to an erroneous assumption of idiopathic DILD, potentially delaying diagnosis and timely treatment.[14,15]

The anti-Jo-1 antibody was the most frequent specific marker, while anti-Ro was the most common myositis-associated antibody identified. There is still debate regarding its correlation with the course of the disease.[16]

The most common tomographic pattern was NSIP, in line with previous publications.[16] We also observed cases of UIP, but OP –reported in the literature as the second most common pattern– was absent in our cohort.

In our study, we also analyzed the treatment received by patients with DILD associated with IIMs, and found that the most commonly used initial regimen was that of CS together with other immunosuppressants, mainly MMF; and in refractory cases, RTX was the primary treatment. Currently, there are no clinical trials comparing the efficacy of these agents; therefore, drug selection relies mainly on observational studies, expert opinion, local experience, tolerance, and availability.[17,18]

Some limitations of our study include its retrospective and multicenter design, which may have contributed to data loss. Additionally, there was heterogeneity in the autoimmune panels available across centers and over time.

CONCLUSIONS

In our multicenter study, DILD associated with IIMs predominantly affected middle-aged women with an anti-Jo-1-positive autoimmune profile, NSIP tomographic pattern, and restrictive pulmonary functional impairment. A higher prevalence of anti-Jo-1 antibodies was observed among patients with DILD, while ANA positivity and muscle symptoms were more common in those without pulmonary involvement. The treatments used in these patients proved to be effective and safe.

Conflict of interest

The authors of this work have no conflicts of interest to declare in relation to this publication.

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ORIGINAL ARTICLE

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Respiratory Syncytial Virus Pneumonia in The Hospitalized Adult. Study of Direct Costs in Two Public Hospitals of the City of Buenos Aires

Neumonía por virus sincicial respiratorio en el adulto hospitalizado. Estudio de costos directos en dos hospitales públicos de la Ciudad de Buenos Aires

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ABSTRACT

Introduction: There are no studies on costs associated with hospitalization in adults with respiratory syncytial virus (RSV) infection in Argentina.

Objectives: To determine the direct cost structure of adults hospitalized for RSV in public hospitals in the Autonomous City of Buenos Aires (CABA).

Materials and Méthods: Patients >18 years hospitalized for RSV infection from January-June 2024 in two Public Hospitals of CABA. Comparisons were made between patients older than 60 years and those younger than 60 years. Diagnosis: viral panel (PCR) positive only for RSV. Direct costs were calculated from the funder's perspective. Hospitalization cost modules were determined by the CABA Government as of June 2024, official exchange rate parity 9.18 pesos/dollar (sale).

Results: 18 patients were enrolled, mean age 65 years (IQR 48.2-79.2); 56% smokers with high comorbidity burden. Three patients were in the Intensive Care Unit (16.6%); case-fatality rate: 27.7%.

The direct cost was 5,278.88 dollars/patient (IQR 2,932.8-1,1131.1) and the total direct cost was 195,202.33 dollars/all patients. When comparing the group of patients older than 60 years with those younger than 60, it was observed that the group over 60 had 63% higher direct costs and a higher case-fatality rate (34.4% vs. 0%).

Conclusion: The majority of patients hospitalized for RSV infection are aged 65 years, with comorbidities, a history of smoking, and a high case-fatality rate. The direct cost from the funder's perspective was USD 5,278.88 per patient. The direct cost for all patients was USD 195,202.33. Patients >60 years had higher direct hospitalization costs and increased case-fatality rates. This is the first study in Argentina on direct costs associated with RSV infection in hospitalized adults at public hospitals.

Key words: Respiratory syncytial virus; Pneumonia; Hospitalizations; Direct costs; Expenses

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RESUMEN

Introducción: No hay estudios sobre costos asociados a hospitalización en adultos con infección por virus sincicial respiratorio (VSR) en Argentina.
Objetivos: Determinar la estructura de costos directos de adultos hospitalizados por VSR en hospitales públicos de la Ciudad Autónoma de Buenos Aires (CABA).
Materiales y métodos: Pacientes >18 años hospitalizados por infección por VSR desde Enero-Junio 2024 en dos Hospitales Públicos de CABA. Se comparó en < y > 60 años. Diagnóstico: panel viral (PCR) positivo sólo para VSR. Se determinaron costos directos desde la perspectiva del financiador. La modulación de internación fue realizada por Gobierno de CABA a Junio 2024, cotización oficial paridad 9,18 pesos /dólar (venta).
Resultados: Se enrolaron 18 pacientes, edad 65 años (RIQ 48.2-79.2); 56% tabaquistas con alta carga de comorbilidades. Tres pacientes estuvieron en Unidad de Terapia Intensiva (16.6%); Tasa casos fatales: 27.7%.
El costo directo fue 5278,88 dólares/paciente (RIQ 2932.8-11131.1) y el costo directo fue 195202.33 dólares/todos los pacientes. Al comparar > y < de 60 años, se observó en aquéllos 63% mayores costos directos y mayor tasa de casos fatales (34,4% vs 0 %).
Conclusión: La mayoría de los pacientes hospitalizados por infección por VSR tienen 65 años con comorbilidades, tabaquismo y alta letalidad. El costo directo desde la perspectiva del financiador fue 5278.88 dólares/ paciente. El costo directo fue 195202.33 dólares/todos los pacientes. Los pacientes >60 años tuvieron mayores costos directos de hospitalización y letalidad. Es el primer estudio en Argentina sobre costos directos por infección VSR en adultos hospitalizados en hospitales públicos.

Palabras claves: Virus Sincicial Respiratorio; Neumonia; Hospitalizaciones; Costo directo; Gastos

The respiratory syncytial virus (RSV) causes one of the most common acute respiratory diseases in children, leading to hospitalizations and admission to pediatric intensive care units. Currently, it is less recognized in the adult population with comorbidities compared to other respiratory viruses, causing a higher case-fatality rate.[1] It can affect both the upper and lower respiratory tracts, accompanied by fever, headache, myalgia, and asthenia, and can be confused with bacterial pneumonia due to the significant frequency of alveolar patterns in imaging studies.[1] The presentation predominates during autumn/winter but can vary in extent and severity in the at-risk population.[1] It can cause medium- or long-term deterioration, both pulmonary and systemic extrapulmonary.[2-9] Although there is no specific treatment at present, patients should be supported hemodynamically, with oxygen therapy and ventilatory support if required.[1] Less than 30% of acute community-acquired pneumonias in adults are of viral origin.[10] The other most common genera are influenza A, parainfluenza, rhinovirus, metapneumovirus, coronavirus, and adenovirus.[10] Although it has been shown that most adult pneumonias do not have an identified pathogen, the frequency of viral etiology is higher than reported.[11]

In 2019, industrialized countries reported an estimated 5.2 million cases of acute respiratory infection, resulting in 470,000 hospitalizations, and 33,000 deaths among adults over 60 years of age.[1] Immunosenescence starting at age 50 causes a decrease in T lymphocyte response. This situation, along with comorbidities, significantly contributes to increased morbidity and mortality.[12]

It was estimated that in 2019 in Argentina there were 14,604 hospitalizations and 3,518 deaths due to RSV in adults, representing almost 70% in patients over 75 years with multiple comorbidities.[13] In 2024, RSV reached its seasonal peak in week 16 with detection over 14% of samples.[14] In Argentina, there is little information about the impact of severe RSV infection in adults, but a recent multicenter study reported its impact on hospitalized adult patients.[15]

On the other hand, there is no local information about the direct hospitalization costs associated with RSV pneumonia in adults. Therefore, the aim of this study is to describe the direct cost related to hospitalization for RSV pneumonia in adults, stratified by two age groups: patients under 60 years and those over 60 years. This analysis was carried out at two public hospitals in the Autonomous City of Buenos Aires (CABA) during the first half of 2024.

MATERIALS AND METHODS

The medical records of patients hospitalized for community-acquired acute pneumonia (CAP) due to RSV were reviewed from all departments of the Hospital General de Agudos "Dr. J. M. Ramos Mejía and the Hospital "Donación José Santojanni" in CABA between January 1, 2024, and June 30, 2024.

A positive RSV diagnosis was confirmed by PCR viral panel testing of respiratory specimens, with all other respiratory viruses testing negative. The pneumonia diagnosis was based on a combination of clinical symptoms and the presence of pulmonary opacities in chest imaging studies (X-ray and high-resolution computed tomography without contrast).

The study included adults over 18 years of age. Direct costs were determined from the perspective of the funder, based on medication costs and the clinical hospitalization and emergency department cost modules for Public Hospitals provided by the Government of the City of Buenos Aires as of June 1st, 2024.[16-17] The cost module for inpatient care in isolation for infectious disease was 56,750 pesos (USD 269.23) per day; for emergency care with diagnostic studies, the cost was 13,853 pesos (USD 65.72), and the cost for critical emergency care without mechanical respiratory assistance was 78,194 pesos (USD 370.97).[16] Each module included a predetermined number and type of services (biochemical tests, imaging, electrocardiogram, spirometry, mechanical respiratory assistance, oxygen, disposable materials, medications, etc., as well as proportional costs related to salaries, taxes and fees, administrative charges, equipment amortization, food and laundry costs, etc.). When an additional consultation or diagnostic procedure was made, or if some treatment (e.g., medications) outside the module was performed, the cost was determined from the funder's perspective based on the KAIROS Pharmaceutical Manual and the service fee schedule provided by the Government of the City of Buenos Aires.[16-17] All patients were treated within 48 hours of the onset of respiratory symptoms with antibiotics, oseltamivir (75 mg every 12 hours for 5 days), and oxygen therapy.

Due to the fluctuations in the peso/dollar exchange rate, results will be reported in U.S. dollars. The exchange rate used for cost calculation was the official selling rate of Banco Nación as of June 1, 2024 (918 pesos = 1 dollar).

It was planned to analyze the costs in the total adult population, and then compare two groups: those over 60 years old versus those under 60.

Descriptive statistics was used. For quantitative variables with a non-Gaussian distribution, the median was used as the central measure, and the interquartile range (IQR 25%-75%) as the measure of dispersion. For variables with a Gaussian distribution, the mean was used as the central measure, and the standard deviation as the measure of dispersion. Percentages were used for qualitative variables.

RESULTS

General adult population

Eighteen patients were enrolled. The median age was 65 years (IQR 48.2-79.2); 61.1% were female; 56% were former or current smokers (median 50 pack-years, IQR 42-84).

A high prevalence of comorbidities was observed: 61.1% cardiovascular, 33.3% respiratory, and 27.7% oncologic, among the most frequent. Only one patient had no known comorbidities.

The median duration of hospitalization in an emergency room was 1 day (IQR 1-1), and 5 days in the general ward (4-7). Three patients (16.6%) required admission to the Intensive Care Unit (ICU) for 2 to 6 days. The overall case-fatality rate was 27.7% (n = 5).

The median final cost per patient was USD 5,278.88 (IQR 2,932.8–11,131.1), with a total cost of USD 195,202.33 for all 18 patients. 86.54% of those costs were included in the cost-modules, and 13.46% weren't (47.7% from diagnostic studies and 52.6% from medications) (Figure 1).

Population older than 60 years

Of the 18 patients, 14 (77.78%) were older than 60 years. The median age was 77 years (IQR 70.5-90); 72.7% were female; 54.5% were former or current smokers: (median 50 pack-years, IQR 42-108). A high prevalence of comorbidities was found (91% of patients): 63.6% cardiovascular, 27.3% respiratory, and 18.2% oncologic, among others. The median duration of hospitalization in an emergency room was 2 days (IQR 1-2), 14 days in the general ward (5-25) and 27.3% (n=3) in the ICU (range 2-6 days.) Case-fatality rate: 36.4% (n=4).

The final cost per patient was USD 5,575.6, and the total cost for the 14 patients was USD 144,586.9. The direct non-modular cost represented 14.9% of the total (of which 88.8% corresponded to medications and 11.2% to tests).

Population younger than 60 years

Of the 18 patients, 4 (22.22%) were under 60 years old (range 32–57 years), with a median age of 57 years (IQR 50.75–57); 50% were female; 75% were former smokers (median 32 pack-years, IQR 28.5-54). A high prevalence of

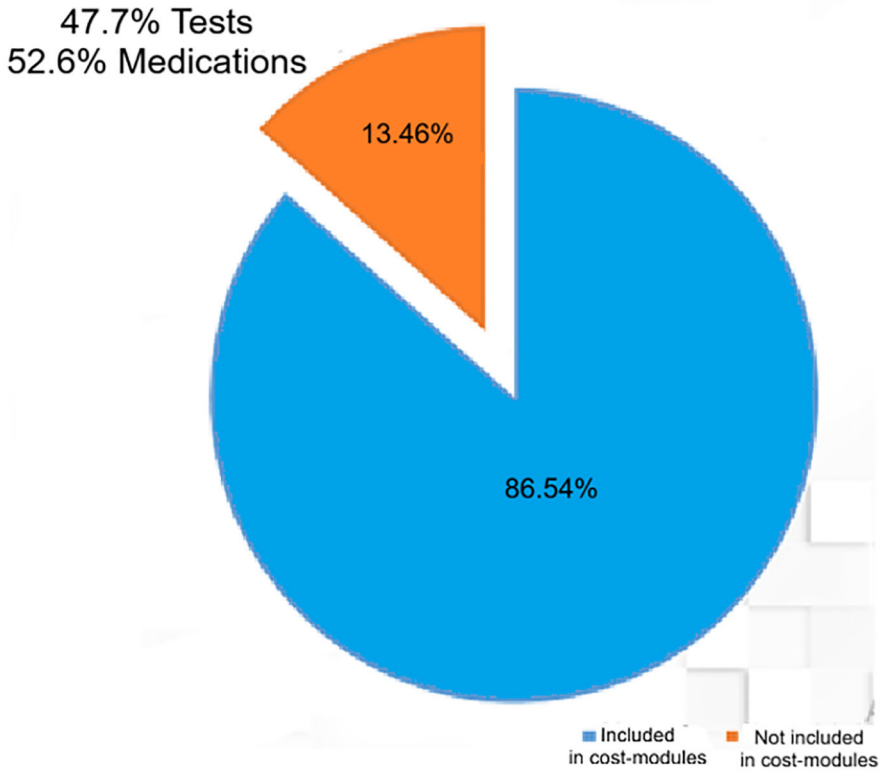

Figure 1. Total direct cost structure

comorbidities was found (100% of patients): 50% cardiovascular, 50% diabetes, 50% COPD (chronic obstructive pulmonary disease), 25% cerebrovascular and 25% obesity. The median stay in the emergency department was 1 day (IQR 1-1), 6.5 days in the general ward (IQR 5-8.5), and 25% required ICU admission (n=1, 12 days). There were no deaths.

The final cost per patient was USD 3,419.37, and the total cost for the 4 patients was USD 16,527.4. The direct non-modular cost represented 10% of the total (of which 90% corresponded to medications and 10% to tests).

Comparison of costs between patients over and under 60 years of age

Table 1 compares both populations (over and under 60 years of age).

The median direct cost for patients over 60 years was USD 5,575.6 (63% higher, p=0.11) compared with USD 3,419.37 for those under 60 years.

The total direct cost for all patients in each group was 5.95 times higher among those over 60 years compared with those under 60 years (USD 98,479.14 vs. USD 16,527.47).

DISCUSSION

The direct hospitalizations costs associated with RSV pneumonia in adults have been determined in two public hospitals in CABA. The sample under evaluation included eighteen patients, most of them female, in their seventies, with a high prevalence of comorbidities and significant smoking history. The total direct hospitalization costs were USD 5,278 per patient, with a high requirement for ICU care and a high case-fatality rate. When comparing patients older than 60 years with those younger than 60, it was observed that the older group used more healthcare resources, had a higher case-fatality rate, and incurred higher direct costs per patient.

The most frequent viruses in community-acquired pneumonia (CAP) are influenza A, parainfluenza, RSV, rhinovirus, metapneumovirus, coronavirus, and adenovirus.[10] The EPIC study

TABLE 1. Demographic data

	Older than 60 years (n = 14)	Younger than 60 years (n = 4)
Age, median (IQR 25- 75%), years	77 (70.5-90)	57 (50.75-57)
Gender, feminine, %	72.7	50
Current smokers, former smokers, %	54.5	75
Packs-year, median(IQR 25-75%)	50 (42-108)	32 (28.5-54)
Comorbidities, %	91	100
Comorbidities, %		
Cardiovascular	63.6	50
Respiratory	27.3	25
Diabetes	0	25
Cerebrovascular	0	25
Neoplasm	18.2	0
Days at emergency room, median (IQR 25-75%)	2 (1-2)	1 (1-1)
Days at general ward, median (IQR 25-75%)	14 (5-25)	6.5 (5-8.5)
ICU, %	27.3 (range 2-6 days)	25% (12 days)
Deceased patients, %	36.4	0
Cost per patient, dollars Median (IQR 25-75%)	5575.6 (3468.7-10369.1)	3419.37 (2140.1-5411)
Total cost, dollars	144586.9	16527.4

Abbreviations: IQR: Interquartile range 25-75%; ICU: Intensive Care Unit

demonstrated that in adults the frequency of viral etiology was higher than previously reported.[11] In a review of 18 studies conducted among older adults in Latin America, it was determined that the detection rate of acute respiratory infection caused by RSV is highly heterogeneous among different countries (0–77.9%).[18] Hospitalizations with co-infections of RSV and influenza were observed (40.9-69.9%), as well as in viral CAP (91.7%).[18] Through the National Laboratory Network (2007-2016), RSV positivity in respiratory samples ranged from 21 to 29%. It was determined that viral circulation began in April, lasted 16 to 18 weeks, and the influenza peak overlapped with the RSV peak during winter.[19] In 2020, due to the SARS-CoV-2 pandemic, an "immunological silence" was observed, with the disappearance of other respiratory viruses.[14] Starting in 2021, a disruption was noted in the timing of peaks of other viral respiratory infections, which, although lower in intensity, persisted until 2023.[14] According to the 2024 National Epidemiological Bulletin from Argentina's Ministry of Health, RSV detections increased from week 16, reaching their peak in week 26.[14]

Acute respiratory disease in adults caused by RSV is more severe, with higher case-fatality rate, and remains underrecognized compared to other respiratory viruses.[1,5-10] As previously mentioned, its clinical presentation can be mistaken for bacterial pneumonia.[1,5-11,15] Immunosenescence beginning around age 50 leads to a reduced T-cell response, which –along with comorbidities (cardiorespiratory, neurological, metabolic, immunocompromised, etc.)– contributes to higher morbidity and mortality.[12] It can cause significant medium- and long-term impairment and systemic extrapulmonary involvement (cognitive, cardiovascular, among others).[2-4] It is important to identify at-risk populations because vaccines are now available for adults in risk groups in Argentina.[20-23]

Underdiagnosis is significant due to the clinical similarity with other respiratory pathogens, lack of medical awareness, delays in ordering diagnostic tests, or unavailability of such tests. There is also a perception that, since there is currently no specific antiviral treatment, diagnosis would not impact clinical outcomes, and this is dangerous due to the risk of in-hospital spread. In a multicenter study conducted across three healthcare centers, the impact of RSV in hospitalized adults in our country has been recently reported.[15] Participants were over 60 years old and had a high burden of

comorbidities, particularly cardiovascular and respiratory.[15] The most common radiological pattern upon admission was alveolar, observed in nearly 70% of the patients.[15] Almost 40% of the patients were admitted to the ICU, and the case-fatality rate was high (19.4%).[15]

The different components of direct and indirect costs of asthma in healthcare have been determined, and they can be extrapolated to other respiratory diseases.[24] A mixed methodology has been used to determine direct costs: cost modules provided by the GCBA (top-down method) and, in addition to the review of each medical record, paying for the patient's expenses outside the cost modules (bottom-up method). In our study, primary data were directly collected from the medical records, which adds a valuable detail.[24] As previously mentioned, we conducted the cost analysis from the perspective of the funder (Government of the City of Buenos Aires, GCBA) in a general acute care public hospital. Therefore, direct comparison with other countries or extrapolation to other institutions is not advisable, since cost structures differ, although this analysis can provide an idea of the magnitude of the problem.[24]

The total direct hospitalization cost was USD 5,278 per patient, and the total cost for the 18 patients in this study conducted across two public hospitals in CABA was USD 195,202. When comparing patients older than 60 years with those younger than 60, it was observed that the older group used more healthcare resources, had a higher case-fatality rate (36.4% vs. 0%), and showed 63% higher direct costs per patient (Table 1).

When compared with hospitalization associated with another virus such as influenza in the same public hospital setting in Buenos Aires, both similarities and differences can be observed. The hospitalized sample of patients with influenza pneumonia was also elderly (in their eighth decade of life) and had a high prevalence of comorbidities and smoking history.[25] However, the total cost per patient hospitalized for influenza was half that of RSV (USD 2,263 per patient), with similar use of emergency and ward hospitalization days. Yet, RSV infection was more severe, requiring ICU care (unlike influenza), and showing double the case-fatality rate (27.7% vs. 14.8%), precisely due to the different clinical profiles of the patients (older and with more comorbidities).[25]

Among the limitations of this study, it should be noted that data collection from medical records was retrospective and the sample size was small, so conclusions should be considered preliminary. Extrapolating the conclusions to other healthcare systems in our country or other regions (external validity) is not advisable. No indirect costs were evaluated (which are presumed to be higher than direct costs based on previously reviewed literature); and costs were not determined from other perspectives (for example, patient or societal perspectives). While costs were initially calculated in pesos, the currency instability and devaluation experienced by our country in recent times led us to report the results in dollars. Finally, the cost modules used by the GCBA did not allow breaking down the internal cost structure to determine which variables have been considered and to what extent. It should also be noted that at the time of conducting the study, the exchange rate gap between the official and parallel dollar rate was significant. If a higher dollar parity value were used, it would likely reduce the cost in dollars.

To conclude, the direct hospitalization costs associated with RSV pneumonia in adults has been determined in two public hospitals in CABA. The sample under evaluation of eighteen patients included mostly females, in their seventies, with a high prevalence of comorbidities and a significant smoking history. The total direct hospitalization cost was USD 5,278 per patient, with a high requirement for ICU care and high case-fatality rate (27%). When comparing patients older than 60 years with those younger than 60, it was observed that the older group used more healthcare resources, had a higher case-fatality rate, and incurred higher direct costs per patient. This is the first study in our country to evaluate the direct costs of hospitalization associated with RSV pneumonia in adults at public hospitals in CABA.

It is imperative to determine the viral etiology of acute respiratory infections in hospitalized adults in order to isolate the patient and prevent in-hospital transmission. There are vaccines available for the at-risk adult population that can help prevent it, due to immunosenescence and a high burden of comorbidities, which lead to high morbidity and mortality. This study would provide additional information to support decision-making in public health. The need to incorporate studies of this kind within the healthcare system is emphasized, as

they enable the collection of data that supports better resource management, allowing for improved planning, organization, and standardization of patient care. This, in turn, enhances efficiency and quality of service while maintaining or even reducing overall healthcare costs.

Conflict of interest

Dr. Martin Sívori has participated in continuous medical education programs for Glaxo SmithKline, Sequirus, and Pfizer.

Dr. Daniel Pascansky has participated in continuous medical education programs for Glaxo SmithKline, Astra Zeneca, Sequirus, ELEA, and SANOFI.

Dr. Saldarini Fernando has participated in medical advisory for GSK.

The other authors have no conflicts of interest to declare

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ORIGINAL ARTICLE

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Evolution of pCO_2 After Hypercapnic Failure in Patients with COPD

Evolución de la pCO_2 post fallo hipercápnico en pacientes con EPOC

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ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) is one of the top three leading causes of morbidity and mortality worldwide. During the disease course, a subgroup of patients develops episodes of acute hypercapnic ventilatory failure, characterized by sustained elevation of arterial partial pressure of carbon dioxide (pCO_2).
Objetive: To analyze the evolution of pCO_2 in COPD patients during the three months following hospitalization for hypercapnic ventilatory failure, exploring the clinical and functional characteristics associated with persistent versus reversible hypercapnia.
Material and Methods: A prospective, multicenter, observational study was conducted, including 27 patients hospitalized in six healthcare centers in Argentina between March 2023 and August 2024. Patients were followed up with clinical, functional, and arterial blood gas tests at 30, 60, and 90 days after hospital discharge.
Results: The mean pCO_2 was 58.4 mmHg at discharge, 48.84 mmHg at 30 days, 45.66 mmHg at 60 days, and 44.67 mmHg at 90 days. Persistent hypercapnia was observed in 43.8% of patients.
Conclusions: The persistence of hypercapnia after hospitalization identifies a clinically more complex subgroup, with a higher risk of poor outcomes. Structured pCO_2 monitoring enables targeted interventions and helps personalize the follow-up of patients with severe COPD.

Key words: COPD, Hypercapnia; Ventilatory failure

RESUMEN

Introducción: La enfermedad pulmonar obstructiva crónica (EPOC) constituye una de las tres principales causas de morbimortalidad a nivel global. En su evolución, un subgrupo de pacientes presenta episodios de fallo ventilatorio hipercápnico agudo, con elevación sostenida de la presión parcial de dióxido de carbono (pCO_2) arterial.
Objetivo: Analizar la evolución de la pCO_2 en pacientes con EPOC durante los tres meses posteriores a una internación por fallo ventilatorio hipercápnico, explorando las características clínicas y funcionales asociadas a la persistencia o reversión de la hipercapnia.

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Materiales y métodos: Se llevó a cabo un estudio observacional, multicéntrico y prospectivo, que incluyó a 27 pacientes internados en seis centros de salud de Argentina entre marzo de 2023 y agosto de 2024. Los pacientes fueron seguidos con evaluaciones clínicas, funcionales y gasométricas a los 30, 60 y 90 días del alta hospitalaria. La pCO_2 media fue de 58,4 mmHg al alta, 48,84 mmHg a 30 dias , 45,66 mmHg a 60 dias y 44,67 mmhg a 90 dias. El 43,8 % presento hipercapnia persistente.

Conclusiones: La persistencia de hipercapnia post internación identifica a un subgrupo clínicamente más complejo, con mayor riesgo de mala evolución. El monitoreo estructurado de la pCO_2 permite orientar intervenciones específicas y personalizar el seguimiento de pacientes con EPOC severa.

Palabras clave: EPOC; Hipercapnia; Fallo ventilatorio

INTRODUCTION

COPD exacerbations account for most of the healthcare system's cost burden, and there is also a direct relationship between disease severity and cost of care.[1] During hospitalization, some patients with COPD may show acute hypercapnic ventilatory failure and require non-invasive ventilation (NIV) as part of their treatment in order to reduce the work of breathing, improve gas exchange, and reverse respiratory acidosis. This intervention has been shown to reduce the need for endotracheal intubation, shorten hospital stay, and improve survival.[2-3] Once clinical stability and normalization of pH are achieved, some patients may continue to have elevated pCO_2 levels, while others return to normal.

The prevalence of hypercapnia in stable COPD is reported to be between 23–38% and is associated with an increase in hospitalizations and mortality.[4-5]

Understanding the behavior of pCO_2 after hospitalization in a COPD patient following an episode of acute hypercapnic failure could provide information to help predict which variables are associated with persistent hypercapnia, and might eventually benefit from the use of home NIV.

OBJECTIVES

To describe the evolution of arterial pCO_2 values during the three months following hospitalization for hypercapnic ventilatory failure in patients with COPD.

To assess differences in demographic, clinical, and functional characteristics between groups with and without persistent hypercapnia three months after discharge.

MATERIALS AND METHODS

A multicenter observational study was conducted, prospectively and consecutively including patients with COPD who were hospitalized for acute hypercapnic respiratory failure and remained hypercapnic (pCO_2 > 45 mmHg) at the time of discharge. The study was carried out in six healthcare centers in our country. All of them have specialized Pulmonology Services and inpatient wards (Hospital Posadas, Hospital Churruca, Hospital Ramos Mejía, Sanatorio Allende in Córdoba, and Hospital Central de San Isidro). *Inclusion criteria*: patients over 18 years of age with a diagnosis of COPD defined according to GOLD guidelines (Global Initiative for Chronic Obstructive Lung Disease), or patients with a smoking history >15 pack-years, CT-confirmed emphysema, and/or use of bronchodilators prior to admission; hospitalization for acute hypercapnic respiratory failure, defined as a clinical presentation with respiratory symptoms (dyspnea and/or cough) leading to admission with arterial pCO_2 > 45 mmHg on arrival; and signing of informed consent. *Exclusion criteria:* a final arterial blood gas (ABG) prior to discharge showing pCO_2 ≤ 45 mmHg; diagnosis of asthma, neuromuscular disease, and/or chest wall disorders causing functional restriction; body mass index > 30 kg/m^2; use of home positive-pressure devices (CPAP [continuous positive airway pressure], or bilevel) prior to hospitalization; psychiatric or cognitive disorders preventing the signing of informed consent; life expectancy < 6 months due to underlying disease.

During follow-up, patients were excluded if, at 30 days after discharge, they presented: non-obstructive spirometry and/or obstructive spirometry with post-bronchodilator reversibility (greater than 12% and 200 mL); exacerbations of their respiratory disease; or, in cases where bilevel positive pressure equipment had been prescribed at discharge, if their objective use was > 4 hours and > 70% of days.

Patients with a diagnosis of COPD who were hospitalized for acute hypercapnic respiratory failure and evaluated for consultation with Pulmonology specialists were consecutively selected. At the first contact during hospitalization, patients were invited to participate in the study and sign informed consent. Three follow-up visits were performed after discharge (V1 at 30 days, V2 at 60 days, and V3 at 90 days).

At V1, demographic, clinical, and recent hospitalization data were collected. Pre- and post-bronchodilator spirometry was performed, and in cases where the patient was using NIV since discharge, objective adherence was verified

through the device software. At V2 and V3, patients were questioned regarding symptoms, new exacerbations, and NIV adherence if applicable. Arterial blood gas samples were taken at V1, V2, and V3. Patients were excluded if they presented a new exacerbation or if home NIV use was adequate (more than 4 hours/day on 70% of days).

Patients were classified according to pCO_2 behavior into four groups: ***1) Early normocapnia***: the patient showed normocapnia (< 45 mmHg) at visit 1. ***2a) Early reversible hypercapnia:*** the patient showed pCO_2 > 45 mmHg only at visit 1 (V1). ***2b) Late reversible hypercapnia***: the patient showed pCO_2 > 45 mmHg only at visits 1 and 2 (V1 + V2). ***3) Persistent hypercapnia:*** the patient showed pCO_2 > 45 mmHg at all three visits (V1 + V2 + V3).

Ethical considerations

The project was approved by the Ethics Committee of each institution, and all participants provided informed consent to take part in the study.

Statistical analysis plan

Results will be presented as mean ± standard deviation or median and range for numerical variables, and as percentages for categorical variables.

The percentage of the categories will be reported with 95% confidence intervals.

To compare demographic and clinical data across the four groups, Chi-Square or Fisher's Exact tests will be used for proportions, and analysis of variance or Kruskal–Wallis tests will be used for numerical variables. A p-value of <0.05 will be considered significant.

RESULTS

A total of 27 patients were enrolled between March 2023 and August 2024 (11 from Hospital Churruca, 6 from Hospital Posadas, 3 from Hospital Central de San Isidro, 2 from Hospital Castex, 2 from Sanatorio Allende, and 3 from Hospital Ramos Mejía). 55.6% were male, with a mean age of 67.69 years (±8.17). A total of 7.4% required invasive ventilation, and 29.6% had to be admitted to the Intensive Care Unit. The mean total length of hospital stay was 11.85 days (±7.63), and 29.6% of patients were discharged with home non-invasive ventilation (NIV) equipment. The pCO_2 at discharge was 58.54 mmHg (±10.5). At the 30-day follow-up (V1), 25 patients (92.6%) were included; 66.7% were included at V2 (n=18), and 59.3% at V3 (n=16). Eleven patients were excluded from the study during follow-up (4 due to adequate adherence to home NIV, 4 lost to follow-up, 1 death, 1 exacerbation, and 1 due to two consecutive samples with pCO_2 < 45). Table 1 shows the characteristics of enrolled patients. The mean pCO_2 values were 58.54 mmHg (±10.5) at discharge, 48.84 mmHg (±8.5) at V1, 45.66 mmHg (±6.1) at V2, and 44.67 mmHg (±6.0) at V3. (Fig. 1).

At 30 days, 64% of patients (n=16) remained hypercapnic; at 60 days, this decreased to 38.9% (n=7); and at 90 days, 43.8% of patients (n=7) were still hypercapnic. (Fig. 2). 36% of patients showed early normocapnia (9/25), and 43.8% had persistent hypercapnia (7/16). 5 patients were classified as having early reversible hypercapnia, and 1 patient as having late reversible hypercapnia.

The persistent hypercapnia group presented mean pCO_2 values of 52.8, 51.7, and 51.7 mmHg during follow-up visits. The Student's T-test was used for numerical variables and the Fisher's Exact test for categorical variables. Characteristics were compared between the early normocapnia group and the persistent hypercapnia group. The reversible hypercapnia groups were not included due to their small sample size. The following variables were analyzed: age, sex, ABG at V0, total days of hospitalization, need for invasive ventilation, non-invasive ventilation, body mass index, spirometry values, smoking status and pack-years, frequent exacerbator phenotype, pharmacological treatment used, and comorbidities. No significant differences were found between the variables analyzed in both groups. (Table 2).

DISCUSSION

To the authors' knowledge, this is the first study in our country aiming to describe the evolution of

	Day 0	Visit 1 (30 days)	Visit 2 (60 days)	Visit 3 (90 days)	Máxima
pCO_2 > 45	YES	NO			Early normocapnia
pCO_2 > 45	YES	YES	NO		Early reversible hypercapnia
pCO_2 > 45	YES	YES	YES	NO	Late reversible hypercapnia
pCO_2 > 45	YES	YES	YES	YES	Persistent hypercapnia

TABLE 1. Baseline characteristics of the studied population

N=25 in V1	N	%	M	SD
Age (years)			67.69	8.17
Masc.	15	55		
Weight (kg)			59.38	23.6
Height (m)			1.61	0.09
BMI (kg/m^2)			24.7	4.6
FVC (L)			1.93	0.7
FVC %			64.38	17.37
FEV1 (L)			0.81	0.26
FEV1%			35.83	15.6
FEV1/FVC			45.5	11.89
Active smoker	16	64		
Former smoker	9	36		
Pack/years			54.8	28.6
Frequent exacerb.	9	36		
ICS+LABA+LAMA	10	40		
LTOT	6	24		
IV during hospitalization	2	7.4		
NIV during hospitalization	14	51.9		
ICU during hospitalization	8	29.6		
ICU (days)			1.67	3.15
Ward (days)			9.83	6.77
Length of hospital stay			11.85	7.63
Discharge with NIV	8	29.6		
Discharge with O_2	11	40.7		

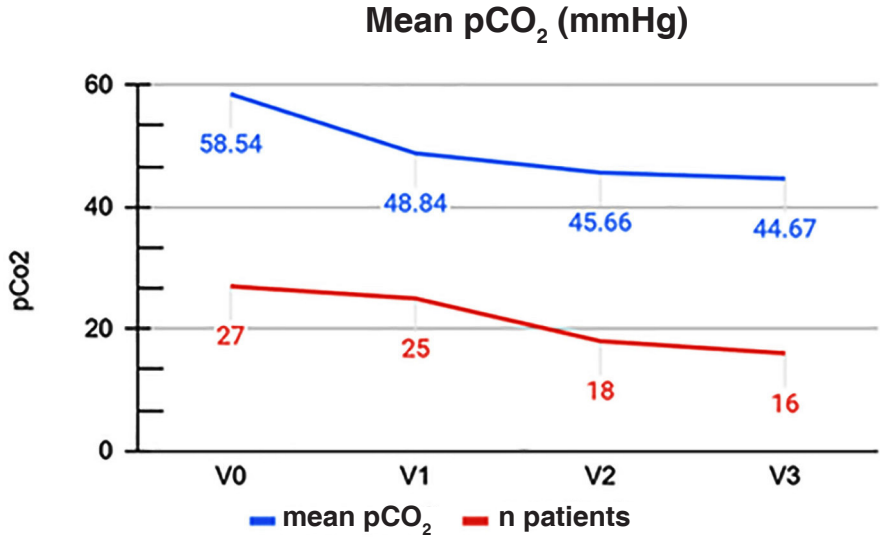

Figure 1. Evolution of mean PCO2 and number of patients according to follow-up visit

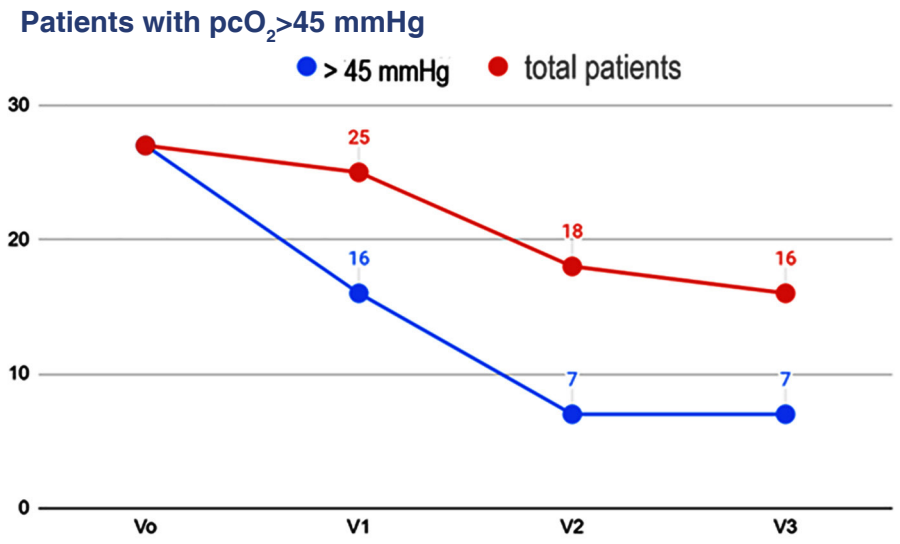

Figure 2. Patients with hypercapnia (pcO_2 >45 mmHg) according to follow-up visit.

TABLE 2. Clinical, gasometric and functional characteristics according to the evolution of

	PH (>45 at V3)	SD	EN (< =45 at V1)	SD	p
Age (years)	69	11.5	66.22	5.14	NS
pH at V0	7.42	0.12	7.41	0.42	NS
PCO_2 at V0	53.97	5.08	54.55	5.12	NS
PO_2 at V0	64.7	5.77	62.88	14.9	NS
Bic at V0	31.07	4.83	33.37	3.84	NS
Total days	13	8.6	12	7.95	NS
Weight (kg)	59.2	16.69	67	19.76	NS
Height (m)	1.59	0.11	1.59	0.82	NS
BMI (kg/m^2)	23	4.12	26.07	5.39	NS
FVC (L)	2.29	0.91	1.7	0.57	NS
FVC %	73.29	26.03	64.44	9.11	NS
FEV1	0.82	0.33	0.77	0.24	NS
FEV1%	36.57	23.1	37.56	10.72	NS
FEV1/FVC	40	12.9	50.4	11.98	NS
Pack/years	58	14.9	56	14.8	NS

pCO_2 levels in COPD patients after a hypercapnic exacerbation.

Although the mechanisms that explain the development of hypercapnia are not fully understood, there is evidence of a worse prognosis in patients who remain hypercapnic during the stable phase (6). A study by Dreher et al found that among stable COPD patients, 16% of those in GOLD stage 3 and 38% of those in GOLD stage 4 developed hypercapnia (7).

In our study, nearly 40% of the patients who completed follow-up at 60 and 90 days continued to have pCO_2 > 45 mmHg.

Costello et al[8], in a cohort followed over 5 years, classified 85 COPD patients after an exacerbation into three types: patients with normocapnic

respiratory failure (type 1), patients who were hypercapnic at hospital admission and subsequently return to normocapnia (type 2.1), and patients who remain hypercapnic after the acute event (type 2.2). Survival was significantly worse in type 2 patients, whereas type 1 and type 2.1 patients had a similar survival. Only 24% of type 2.1 patients progressed over time to type 2.2.

According to current evidence, COPD patients who present hypercapnia during the stable phase (most studies consider 1 month of clinical stability) benefit from the use of home non-invasive positive pressure ventilation, in terms of survival[9-10]. In 2014, Struik et al[11] included 201 COPD patients who had experienced an exacerbation with pCO_2 > 45 mmHg (they were enrolled 48 hours after discontinuation of ventilatory support) to be randomized to receive either home NIV or standard treatment. At 12 months, the NIV arm showed a significant reduction in pCO_2 but no benefit in terms of survival and/or hospital readmissions. In the same year, Köhnlein et al[12] published the first study demonstrating a reduction in mortality after 12 months in COPD patients who received home NIV in addition to standard treatment (12% vs. 33%). Patients included in the NIV + O_2 arm had severe COPD, received outpatient treatment, and had no respiratory symptoms in the previous 4 weeks. Also, their pCO_2 values were greater than 52 mmHg.

Subsequently, Murphy et al[13] showed longer time to readmission or death at 12 months in the group of patients assigned to NIV + O_2 (vs. those with O_2 alone). The study included COPD patients with hypercapnic exacerbations requiring acute NIV at least 2 weeks after resolution of acidosis (pH > 7.30), and who continued to have pCO_2 > 53 mmHg within 4 weeks of clinical stability. It is important to note that in all three studies mentioned above, morbid obesity and sleep apnea were considered as exclusion criteria.

Likewise, in a post hoc analysis of the HOT-HMV trial, the same authors[14] showed that 35% of patients randomized to the O_2 arm experienced an improvement in hypercapnia at 6 weeks (pCO_2 < 53 mmHg) and showed a trend toward better outcomes compared to those who remained hypercapnic. Being able to identify the subgroup of patients who will evolve with hypercapnia is useful for planning follow-up, defining ventilatory treatment more precisely, and modifying medium- and long-term prognosis.

Patients in our study had a mean pCO_2 of nearly 60 mmHg upon discharge, which almost normalized by 60 days (45.66 mmHg at V2). Also, the group of patients with persistent hypercapnia showed no changes between V2 and V3. In other words, 60 days after discharge appeared to be the most appropriate time point to differentiate persistent from reversible hypercapnia. It was also the time when the highest number of dropouts occurred. According to our results, at 30 days, 16 patients still had hypercapnia; at 60 days, only 7 did. This suggests that 56% would have been candidates for home NIV despite spontaneously progressing to normocapnia.

Why does a COPD patient develop hypercapnia? The mechanisms explaining the development of hypercapnia are not fully understood. It has been associated with increased inspiratory loads and reduced strength/endurance of the inspiratory muscles. Inspiratory loads are largely determined by increased airway resistance, air trapping, and increased ventilatory demands (the latter due to greater muscular energy requirements imposed by ventilation with increased dead space). Regarding muscle strength/endurance, reduced performance may be linked to nutritional factors, neuropathic effects, systemic inflammation, diaphragmatic flattening (due to air trapping), and chronic muscle overload.[15-17] As a response to the imbalance between inspiratory load and the respiratory pump capacity, there may be a "down-regulation" of the central respiratory drive and hypoventilation, aimed at reducing energy demand and preventing muscle fatigue (18-20).

De Vito E. describes three physiological characteristics of COPD associated with chronic hypercapnia: 1) inadequate gas exchange (due to ventilation–perfusion mismatch), 2) airflow obstruction with consequent increased resistive work, hyperinflation, and auto-PEEP (intrinsic positive end-expiratory pressure), 3) mechanical disadvantage of the diaphragm, with reduced ability to shorten, reduced tidal volume generation, possibly reduced pressure-generation capacity, and ultimately reduced inspiratory muscle reserve. All of the above indicates that the occurrence of hypercapnia is related to the balance between the magnitude of the inspiratory load and the strength of the inspi-

ratory muscles. Since esophageal pressure (Pes) and P0.1 are elevated, the respiratory centers are already stimulated. That is, these patients "opt" for hypoventilation rather than respiratory muscle fatigue, and its manifestation as chronic hypercapnia may serve a homeostatic purpose: avoiding fatigue and maintaining more comfortable breathing.[21] The variables described in the literature as being associated with persistent hypercapnia after an exacerbation are diverse: low FEV_1, prior acute hypercapnic respiratory failure[22], high pCO_2 at discharge, GOLD D COPD[23], low resting pO_2, low minute ventilation (Ve), high residual volume (RV), low percentage of emphysema on chest CT, chronic oxygen use, and low ventilatory reserve (Ve/MVV [minute ventilation/maximal voluntary ventilation]).[6] In our study, no significant differences were found between the analyzed variables and the persistence of hypercapnia at 90 days.

This is the first study in our country to explore the evolution of these patients, who are at increased risk of readmission and death. Some strict exclusion criteria were selected to reduce potential confounders, such as the absence of obesity, which lowers the likelihood of sleep-related breathing disorders (although these were not ruled out with polysomnography or night polygraphy), or the presence of new respiratory symptoms during follow-up (common in severe COPD), which could alter the natural evolution of pCO_2 levels.

The first and main limitation of the study is the small sample size. Despite designing a multicenter study in facilities with pulmonology services and inpatient bed availability, it was difficult to increase the number of patients included within the planned time frame.

Another limitation of our study was the absence of a systematic record of pre-hospitalization pCO_2 values, which prevented us from reliably determining the presence of baseline hypercapnia in all patients. Nevertheless, the main objective was to evaluate the evolution of pCO_2 following the episode of acute hypercapnic respiratory failure.

CONCLUSION

In our study, a gradual decrease in pCO_2 levels was observed since hospital discharge. 43% of all patients remained with elevated values at 90 days. Assessment at 60 days after discharge proved to be the most appropriate time point to define the management of persistent hypercapnia. The small number of recruited patients, together with those excluded during follow-up, makes it necessary to confirm these findings in larger studies.

Conflict of interest

None of the authors has any conflicts of interest to declare.

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CASE REPORT

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An uncommon triad: Solitary fibrous tumor, Doege-Potter and Bamberger-Pierre-Marie Syndromes

Una tríada infrecuente: Tumor fibroso solitario, Síndrome de Doege-Potter y Bamberger-Pierre-Marie

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ABSTRACT

The solitary fibrous tumor (SFT) is an uncommon mesenchymal neoplasm, typically exhibiting benign behavior. It primarily originates from the serosal membranes, and can be developed across diverse anatomical locations. In rare instances, it can manifest concurrently with paraneoplastic syndromes. We present the case of a male patient with a pleural SFT, diagnosed incidentally via imaging studies, who presented clinically with two simultaneous paraneoplastic syndromes: Doege-Potter syndrome and Pierre-Marie-Bamberger syndrome. The diagnosis was confirmed through histopathological analysis and immunohistochemical techniques. Complete surgical resection was performed without complications, and the patient showed a favorable clinical evolution. This article reviews the clinical, diagnostic, therapeutic, and prognostic characteristics of this entity.

Key words: Solitary fibrous tumor; Pleural; Secondary hypertrophic osteoarthropathy; Hypoglycemia; Thoracic surgery

RESUMEN

El tumor fibroso solitario es una neoplasia mesenquimal infrecuente, habitualmente de comportamiento benigno. Se origina principalmente en las serosas del organismo y puede desarrollarse en múltiples sitios anatómicos. En raras ocasiones puede presentarse acompañada de síndromes paraneoplásicos. Presentamos el caso de un paciente de sexo masculino con un tumor fibroso solitario pleural diagnosticado de forma incidental mediante estudio de imagen, con la presentación clínica de dos síndromes paraneoplásicos en simultáneo (síndrome de Doege-Potter y síndrome de Pierre-Marie-Bamberger). El diagnóstico fue confirmado mediante estudio anatomopatológico y técnicas inmunohistoquímicas. Se realizó resección quirúrgica completa, sin complicaciones y adecuada evolución clínica. Este artículo revisa las características clínicas, diagnósticas, terapéuticas y pronósticas de esta entidad.

Palabras clave: Tumor fibroso solitario; Pleural; Osteoartropatía hipertrófica secundaria; Hipoglucemia; Cirugía torácica

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INTRODUCTION

Pleural neoplastic pathology encompasses a wide spectrum of entities, with a clear predominance of secondary malignant processes, mainly due to metastatic dissemination of lung, breast, ovarian, and gastric carcinoma, and melanoma. Primary neoplasms of the pleura are rare, representing between 10-15 % according to different clinical series. Within this group, the World Health Organization (WHO 2015) classification of pleural tumors recognizes three main categories: mesothelial tumors, hematolymphoid neoplasms, and mesenchymal tumors.[1-3]

Among the primary mesenchymal tumors of the pleura, the solitary fibrous tumor (SFT) stands out. This entity may present with a wide range of biological behavior, from benign forms to lesions with histological features associated with a higher risk of aggressiveness or recurrence. Although these tumors may originate in multiple anatomical locations, including deep soft tissues and visceral organs, a significant percentage (around 30%) are located in the thoracic cavity, particularly in association with the visceral or parietal pleura. Presentations have also been reported on other serosal surfaces, such as the abdominal cavity and retroperitoneum, which are common extrapleural sites.[1-3]

SFTs are typically slow-growing lesions that may reach a considerable size before producing clinical symptoms, and their definitive diagnosis requires a comprehensive histological and immunohistochemical evaluation.[1,2]

The presentation of paraneoplastic syndromes associated with SFTs is rare. Doege-Potter syndrome (less than 5 % of cases), caused by tumor secretion of insulin-like growth factor 2 (IGF-2), and Pierre-Marie-Bamberger syndrome (less than 10% of cases), characterized by hypertrophic pulmonary osteoarthropathy (HPO) of unclear etiology, have been described.[2]

CASE REPORT

Medical record

63-year-old male patient, with no known relevant medical history, consulted due to progressive asthenia, a three-month history of dry cough, and recurrent neurovegetative symptoms characterized by diaphoresis and predominantly morning dizziness. Due to the recurring episodes of hypoglycemia observed during outpatient follow-up, the patient was referred to a higher-level care hospital for further evaluation and to establish the most appropriate treatment plan.

Upon admission, the physical examination revealed decreased breath sounds in the left hemithorax, associated with dullness to percussion. In addition, digital clubbing was observed in upper and lower limbs. During hospitalization, the patient experienced multiple episodes of symptomatic hypoglycemia that required treatment with intravenous dextrose.

Diagnosis

A chest X-ray was performed. In the posteroanterior view, a large, well-defined radiopaque image is observed, located at the left pulmonary base, occupying a significant portion of the ipsilateral lower hemithorax. No cavitary images or obvious calcifications are identified within it.

Subsequently, contrast-enhanced chest CT reveals a solid, expansive, homogeneous lesion in the lower lobe of the left lung, with soft-tissue density, approximately 205 mm × 142 mm (longitudinal by anteroposterior diameter), in close contact with the pleura but without invasion of the thoracic wall. After intravenous contrast administration, signs of marked vascularization are observed (Figure 1). No mediastinal or axillary lymphadenopathy is noted. These findings are suggestive of a solitary fibrous tumor of the pleura.

Due to repeated episodes of severe hypoglycemia, posing a life-threatening risk for the patient, and considering the strong clinical and imaging suspicion of a solitary fibrous tumor, an interdisciplinary decision was made to proceed with surgical intervention for diagnostic and therapeutic purposes, once other causes of refractory hypoglycemia had been ruled out. Chest magnetic resonance imaging and PET-CT were not performed as complementary studies because of the patient's critical clinical condition and the lack of immediate availability of these resources.

The histopathological examination of the specimen revealed the presence of hypocellular and hypercellular areas, composed of ovoid or spindle-shaped cells with vesicular nuclei, irregular chromatin distribution, and scant, poorly defined cytoplasm, separated by bands of hyalinized collagen tissue, with prominent branching vessels. Mitotic activity was low (1 mitosis per 10 high-power fields), with areas of myxoid change, fibrosis,

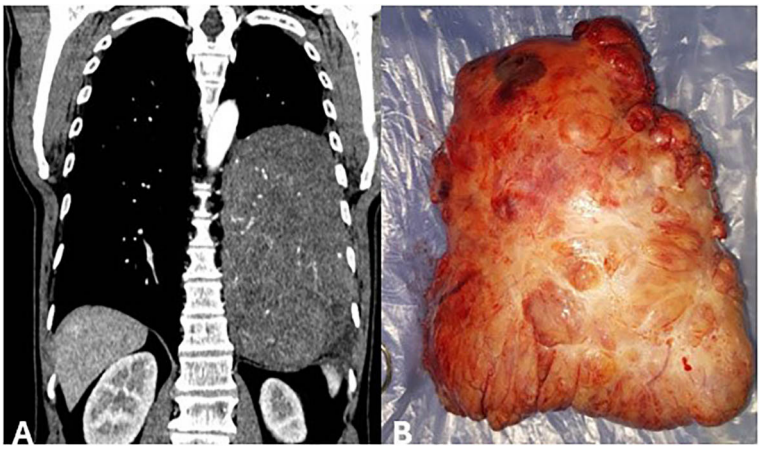

Fig. 1 A. Contrast-enhanced chest computed tomography shows an expansive lesion in the lower lobe of the left lung, in close contact with the pleura, with marked vascularization following contrast administration. B. Firm pleural tumor with a fibrous appearance, weighing approximately 1800 mg.

and no foci of necrosis. In this material, the pleura is identified, with partially denuded mesothelial lining, showing hemorrhage, congested blood vessels, and foci of inflammatory infiltrates composed of lymphocytes, plasma cells, and eosinophils; no atypical cells are observed in these sections. Immunohistochemistry: cytokeratins AE1-AE3: negative; cytokeratin 7: negative; CD34: diffusely and strongly positive; Bcl-2: positive; Ki-67: positive in 10%, findings consistent with a solitary fibrous tumor.

Given the suspicion of paraneoplastic syndromes associated with the tumor, plasma insulin (0.4 μU/mL) and C-peptide (<0.1 ng/mL) levels were requested, both of which were below normal limits, supporting the diagnosis of Doege–Potter syndrome. It was not possible to measure insulin-like growth factor 2 (IGF-2) due to lack of laboratory supplies. X-rays of long bones were performed, showing periosteal reaction on the medial surface of the diaphysis of both ulnae, compatible with Pierre–Marie–Bamberger syndrome (Figure 2).

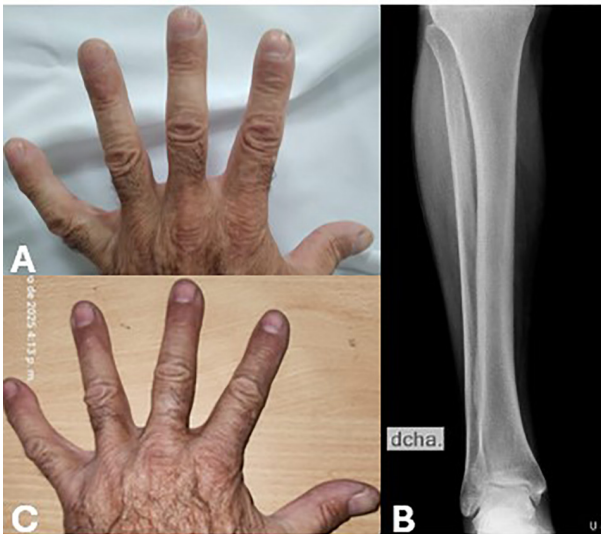

Fig. 2. A. Digital clubbing prior to surgical treatment. B. Regular periosteal reaction on the medial surface of the ulna diaphysis. C. Image taken two years after surgical treatment showing resolution of digital clubbing.

Treatment plan:

By surgical resection through a left posterolateral thoracotomy, a pedunculated mass connected to the parietal pleura by 3 vascularized pedicles, weighing 1800 mg, is removed, without involving the pulmonary parenchyma or mediastinal structures (Figure 1), with tumor-free margins.

The postoperative course was uneventful, and the patient showed symptom improvement, with no further episodes of hypoglycemia. The patient remained under follow-up for two years, during which resolution of digital clubbing of hands and feet was observed, with no tumor recurrence on subsequent CT scans (Figure 2).

Case discussion

SFTs account for 5–10% of all pleural tumors. Their incidence is 2.8 per 100,000 individuals,

typically occurring between the fifth and seventh decades of life. They encompass a histologic spectrum of mesenchymal neoplasms of fibroblastic origin. [4]

Although they are commonly considered tumors of thoracic origin, the most frequent location is actually the abdominal cavity and retroperitoneum (in 50–70% of cases). 30% of those tumors are developed within the thoracic cavity, with the visceral pleura being the most common site (80%), and less frequently the parietal or diaphragmatic pleura. [4]

Solitary fibrous tumors are typically oligosymptomatic, presenting with nonspecific symptoms such as cough, dyspnea, and chest pain. They generally exhibit slow growth and can attain large sizes due to their development within serosal surfaces of the body. In most cases, they show benign behavior; however, 13% to 23% of cases may demonstrate aggressive progression, often associated with increased mitotic activity and locally invasive growth, favored by the large size these tumors may attain in certain circumstances. [4]

The presentation of paraneoplastic syndromes associated with SFT is rare. Two syndromes have been described: Doege-Potter syndrome and Pierre-Marie-Bamberger syndrome. [4]

Doege–Potter syndrome (less than 5% of cases) was first described by Doege and Potter in 1930. Reviews conducted between 1981 and 2020 suggest that only 48 cases have been identified. The mechanism through which hypoglycemia occurs is the release of a high molecular weight form of IGF-2, which is unprocessed or incomplete, and has the ability to activate insulin receptors. As a result, hepatic gluconeogenesis is inhibited and peripheral glucose uptake increases, promoting hypoglycemia. Additionally, IGF-2 can bind to IGF-1 receptors and suppress the release of both IGF-1 and insulin. However, not all SFTs exhibit elevated IGF-2 levels; it has been shown that only 80% of SFTs express this factor. [2,4,5]

On the other hand, Pierre–Marie–Bamberger syndrome is characterized by hypertrophic osteoarthropathy, clinically observed with digital clubbing, periostitis, and synovial effusions. It is associated with approximately 10% of pulmonary SFTs. The mechanism underlying this syndrome is not well understood, but there is a widely accepted hypothesis that proposes the presence of megakaryocytes reaching the systemic circulation through disrupted pulmonary circulation due to the abnormal vascularization developed by these tumors. A small fraction of these megakaryocytes may reach distal capillaries, producing platelet-derived growth factors (PDGF) and vascular endothelial growth factors (VEGF), which can induce the changes observed. [2,5,6]

Radiologic imaging (chest X-ray and chest CT) is usually the first step in diagnosing these tumors. Contrast-enhanced computed tomography is the diagnostic method of choice for solitary fibrous tumors, typically showing well-defined, hypervascular masses with heterogeneous enhancement, particularly in aggressive SFTs. They often present areas of necrosis, hemorrhage, or cystic degeneration, which appear as regions of low attenuation. Pleural effusion or calcifications may also be present, and these features are considered suggestive of malignancy. The **MRI** (magnetic resonance imaging) demonstrates a mixture of solid components (isointense or hypointense relative to muscle) along with cystic areas (hyperintense on T2), with strong enhancement after contrast administration, making it useful for differentiating SFTs from other masses. **18F-FDG PET/CT** (fluorodeoxyglucose positron emission tomography and computed tomography imaging) can help detect metastases, evaluate recurrence, and monitor treatment response, although it does not clearly distinguish between benign and malignant SFTs. [2.4]

The diagnosis is guided by histological examination of the surgical specimen and is confirmed through immunohistochemical techniques. Based on histopathological characteristics, mitotic index (number of mitoses per field), the presence of tumor necrosis, tumor size, and other factors, SFTs are classified as follows: [1, 4,7]

- **Low-grade (low-risk) SFT:** Low-grade forms typically show paucicellular or moderately cellular areas with spindle cells that are mildly atypical, arranged in a disorganized pattern with a prominent collagenous stroma, often with thick collagen bands and focal myxoid changes. Variants with mature adipose tissue (fat-forming subtype) may occur, along with the characteristic "staghorn" pattern of thin-walled, branching vasculature. Mitotic activity is low, and the absence of necrosis supports a low-risk behavior. These features are generally associated with a lower risk of recurrence or metastasis, although they do not completely rule out the possibility. [8]
- **High-grade SFT:** These tumors are charac-

terized by pronounced hypercellularity, marked nuclear pleomorphism, high mitotic index, and frequent areas of necrosis. Many studies use an increased mitotic count as a practical indicator of higher risk, and the combination of large tumor size, older patient age, and necrosis increases the likelihood of metastasis. Histologically, the collagenous stroma may be reduced or replaced by a more cellular tissue; nests of ovoid or round cells arranged in a more compact architecture may be seen. These features correlate with a higher rate of local recurrence and metastasis. [9]

• **Dedifferentiated SFT (DD-SFT):** This subtype shows abrupt transitions to a high-grade sarcoma (rhabdomyosarcomatous or osteosarcomatous) and an undifferentiated, cell population with high-grade morphology (very high mitotic activity, marked pleomorphism, necrosis). These tumors present a much more aggressive clinical behavior and poorer prognosis. [10]

The immunohistochemical study is characterized by the expression of CD34 in 81–95% of cases, Bcl-2 in over 90%, CD99 in 75%, and vimentin in the absence of actin, desmin, S-100 protein, and epithelial markers such as low-molecular-weight cytokeratins. These markers have good diagnostic sensitivity but low specificity. These markers are essential to perform the differential diagnosis with other types of neoplasms. Currently, staining for the transcription factor STAT6 has become an excellent marker with high sensitivity and specificity; however, it may also be expressed in soft tissue neoplasms and tumors of the central nervous system, so its detection must be interpreted with caution. [1,4] In DD-SFTs, markers such as CD34, CD99, Bcl-2, and STAT6 are frequently absent, unlike in low-risk SFTs.

Due to the low incidence of this disease, there is no established consensus regarding its management. The treatment of choice is surgical resection. In this case, a complete resection (R0) was performed according to surgical protocol and confirmed by pathology.

The role of other therapeutic approaches-such as radiotherapy (useful as an adjuvant in cases with close margins or in unresectable tumors), chemotherapy for DD-SFT, and emerging targeted therapies such as antiangiogenic agents for DD-SFT with progressive disease-may be beneficial, but their indications are not yet fully defined. For this reason, multidisciplinary collaboration is essential to ensure early diagnosis and optimal management of these patients. [2,5]

Follow-up

There are no formally established guidelines for the follow-up of these tumors. Relapses have been observed even after 10 years, in up to 10% of cases. In low-risk tumors, less frequent follow-up may be reasonable; however, at least 10 years of imaging surveillance is recommended due to the possibility of late recurrence. In high-risk or dedifferentiated (DD-SFT) tumors, closer and more intensive follow-up is advisable. [2]

CONCLUSION

Pleural SFT is an uncommon neoplasm that should be considered in the differential diagnosis of thoracic tumors. This case is noteworthy due to the simultaneous presence of two paraneoplastic syndromes, making it an extremely rare clinical event. Its diagnosis requires high clinical suspicion, imaging studies, and histopathological and immunohistochemical confirmation. Complete surgical resection is the treatment of choice, resulting in the resolution of hypoglycemic episodes initially and, subsequently, improvement of digital clubbing. Although the recurrence risk is low, the overall prognosis is favorable.

Conflict of interest

Authors have no conflicts of interest to declare.

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CASE REPORT

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Congenital Pulmonary Airway Malformation in a Newborn: Case Report

Malformación congénita de la vía aérea pulmonar en un recién nacido: Reporte de caso

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ABSTRACT

Congenital lung malformations represent a disruption both in the formation of functional pulmonary parenchyma and in the distribution of pulmonary vasculature. Prenatal imaging studies have become widely accessible tools for detection of congenital disorders, contributing to increase the incidence of this condition. However, the classification, diagnosis, and treatment of this disorder are still a challenge in clinical practice. We present the case of a female newborn with a prenatal history of congenital pulmonary airway malformation, initially detected through routine obstetric ultrasound and confirmed postnatally by computed tomography and histopathological analysis. This case report aims to describe a disease with a complex classification and variable clinical course.

Key words: Lung; Congenital lung malformation; Lung volume reduction surgery

RESUMEN

Las malformaciones pulmonares congénitas constituyen un factor disruptivo tanto en la formación de parénquima pulmonar funcional, como en la distribución de los vasos sanguíneos. Los estudios de imagen en la etapa gestacional se han convertido en una herramienta ampliamente disponible para la detección de patologías congénitas, que a su vez han contribuido a un aumento en la incidencia de esta entidad. Sin embargo en la práctica clínica, sigue siendo un reto la nomenclatura, el diagnóstico y el tratamiento de este trastorno. Presentamos el caso de un recién nacido de sexo femenino con antecedente prenatal de malformación congénita de la vía aérea pulmonar evidenciado en ultrasonido de rutina y confirmado en el periodo posnatal por tomografía y estudio histopatológico. Este reporte de caso tiene como objetivo describir una entidad de clasificación compleja con un curso clínico variable.

Palabras clave: Pulmón; Malformación congénita pulmonar; Cirugía de reducción de volumen pulmonar.

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INTRODUCTION

Congenital lung malformations are a group of diseases with a prevalence of 30 to 42 cases per 100,000 people, and in some studies they represent between 5% and 18% of all congenital anomalies. In recent years, the incidence of this condition has increased thanks to advances in ultrasound technology for screening fetal malformations, so in the long term it is expected to be excluded from the list of rare disorders.[1]

The current nomenclature remains complex, as it takes into account criteria such as genetic variants, morphological lesions, histological patterns, and clinical manifestations –among other factors– that are useful for practical differentiation but are not mutually exclusive. Langston's classification describes several pathological findings: large-cyst cystic adenomatoid malformation (Stocker 1), small-cyst cystic adenomatoid malformation (Stocker 2), solid/adenomatoid cystic adenomatoid malformation (Stocker 3); extralobar sequestration; bronchogenic cyst; congenital lobar hyperinflation; pulmonary hyperplasia; bronchial atresia. In 2002, five subtypes of congenital pulmonary airway malformation were included, corresponding to a new classification proposed by Stocker, based on anomalies that occur at different levels of the tracheobronchial tree and at different stages of lung development.[2,3]

The diagnostic method of choice in the prenatal period is ultrasound, as it offers a good safety profile and is considered a reproducible and cost-effective study. In the postnatal evaluation, chest computed tomography is the preferred study, offering superior diagnostic performance compared with other modalities. Low concordance has been demonstrated between prenatal ultrasound and postnatal histological examination, making ultrasound insufficient as the sole diagnostic method, whereas postnatal chest CT shows greater concordance with histological findings, especially in the detection of abnormal systemic vessels.[4]

Expectant management is an option for asymptomatic patients with lesions of favorable prognosis. However, in cases with hemodynamic instability or high risk for the later development of infections or neoplasms, anatomical resection is the recommended treatment.[5]

CASE DESCRIPTION

A female newborn, the product of a second pregnancy that was adequately monitored, born to a 21-year-old mother with no comorbidities. An obstetrical ultrasound performed at 24 weeks of gestation described increased bilateral pulmonary echogenicity accompanied by displacement of the cardiac axis to the right, with no other identifiable fetal morphological abnormalities. This ultrasound study was concluded as consistent with cystic adenomatoid malformation of the lung. Delivery occurred by cesarean section at 36 weeks of gestation due to the onset of preterm labor and the previously described fetal comorbidity. She was born weighing 2,900 grams, measuring 49 centimeters in length, with a head circumference of 33 centimeters, and had a low Apgar score of 4/10, for which she required high-frequency invasive mechanical ventilation as well as inotropic and inodilator support. On head-to-toe examination, a significant finding was a markedly decreased vesicular breath sound over the left hemithorax. Postnatal chest radiography and computed tomography showed extensive involvement of the left lung parenchyma by cystic lesions producing a mass effect, displacing mediastinal structures, with significant atelectasis of the ipsilateral lower lobe, in addition to small cystic foci in the upper and lower lobes of the right lung (Figure 1). Echocardiography revealed dextrocardia with situs solitus, tricuspid regurgitation, mitral insufficiency, and pulmonary hypertension. At 8 days of life, she underwent a surgical procedure through video-assisted thoracoscopy, which revealed a large cystic mass involving both lobes of the left lung, especially the upper lobe. A left upper lobectomy via thoracotomy was required due to the challenging approach posed by the lesion's large size. The specimen was studied by the Pathology Department, which described a rectangular, blackish-colored mass measuring 7 × 5 × 3 cm, with a firm consistency but with softened areas. Microscopically, adenomatous and cystic regions delimited by simple cuboidal to low columnar epithelium were observed, accompanied by recent intra-alveolar hemorrhages and no evidence of neoplastic infiltration (Figure 2). Based on the clinical, histological, and imaging findings, a diagnosis of congenital pulmonary airway malformation type III was made. After surgery, her postoperative

course was poor, with no possibility of ventilator weaning and an increased need for vasoactive support; she therefore died at 29 days of life.

DISCUSSION

Congenital pulmonary airway malformation (CPAM) is defined as a disorder of the airways secondary to an alteration of the epithelial component of the bronchial bud, which manifests as exaggerated growth of bronchial structures and a reduction in the number of alveoli. This predisposes to the development of a multicystic mass of nonfunctioning lung tissue and/or adenomatous pulmonary areas. The inheritance pattern is usually sporadic, and to date no aggravating maternal factors have been described.[6,7]

The nomenclature has changed since 1949, when it was first described by Ch'in and Tang as congenital cystic adenomatoid malformation (CCAM). However, it was later shown that cystic lesions were present in only three of the five subtypes described by Stocker, and adenomatous lesions in only one subtype, which could lead to confusion when categorizing them. In 1977, Stocker replaced the term CCAM with CPAM, as it is currently known, and grouped the lesions into three types. In 2002, the same author expanded this classification to five subtypes.[3,5]

Type 0 lesions, also known as tracheobronchial lesions or acinar dysplasia, are the least frequent, accounting for 1–3% of all subtypes. Involvement is bilateral, with small, hypoplastic lungs, and this condition is considered incompatible with life. Type 1 lesions, or bronchial/bronchiolar lesions, are the most frequent, accounting for 60–65% of cases. They are usually unilobar and may be morphologically multicystic or present with a dominant cyst. Patients with this abnormality may have respiratory symptoms, but prognosis improves with surgical resection of the affected anatomical segment. Type 2 lesions, or bronchiolar

Figure 1. Panel A: Chest X-ray showing displacement of mediastinal structures due to cystic lesions. Panel B: Chest CT scan (lung window) showing, on axial view, multiple cysts in the left hemithorax.

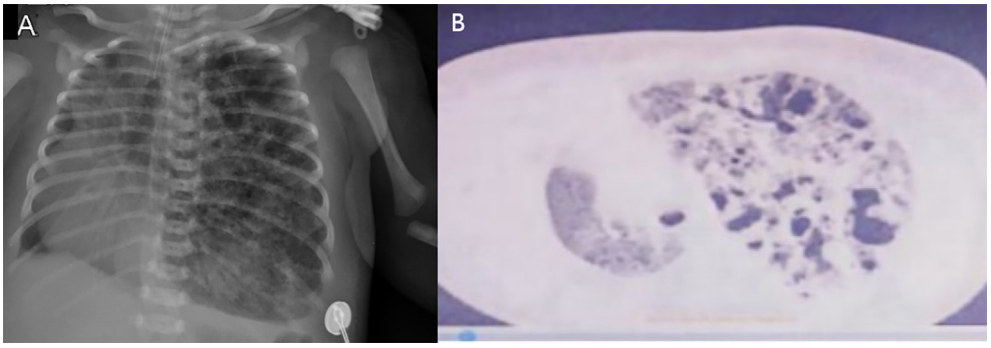
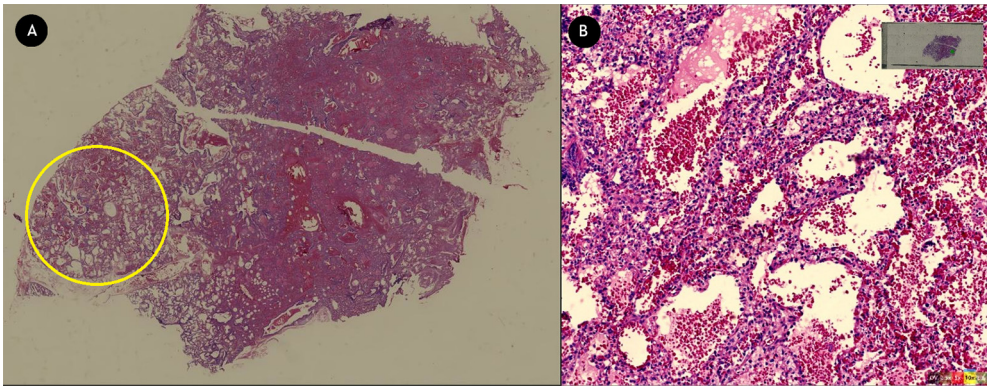


Figure 2. Panel A: Histological section of lung tissue stained with H&E. (Panoramic view). An area of tissue replacing normal alveolar tissue is outlined, forming a multicystic pattern. Panel B: Microscopic detail of the structures showing loss of the normal alveolar pattern associated with intraalveolar hemorrhages.



lesions, are usually diagnosed in the first year of life. They may partially involve a lobe or, in some cases, an entire lung. This subtype has been associated with other congenital malformations in up to 50% of cases. Type 3 lesions, or bronchiolar/alveolar lesions, are usually diagnosed in utero due to the presence of a large adenomatous-like mass that generally involves an entire lung. These patients are born with severe respiratory distress due to mediastinal displacement. Type 4 lesions, or alveolar lesions, are hamartomatous malformations of the acinus. They tend to involve a single lobe, are often diagnosed incidentally due to pneumothorax or infectious processes, and are usually associated with neoplasms. [5, 8]

Considering recent advances in terms of availability of prenatal diagnostic methods, Andrew Bush, one of the most widely recognized pediatric pulmonologists today, points out the inconsistency that may arise when using the term congenital cystic adenomatoid malformation in both the prenatal and postnatal periods. In the prenatal stage, this term may be applied to a lesion that could even disappear before birth; however, in the postnatal period, it is also used to describe an anomaly severe enough to require a lobectomy. Therefore, to achieve greater diagnostic accuracy, it is suggested to use clear, descriptive language for findings, avoiding speculation on embryological origins and keeping clinical and pathological descriptions separate. [9]

At present, the exact cellular mechanisms involved in the pathogenesis of this disorder remain under investigation. Studies in transgenic mice have identified the overexpression of fibroblast growth factors (FGF) types 7 and 10 in the pulmonary mesenchyme, which interfere with lung morphogenesis in CPAM. Acinar dysplasia has been associated with genes encoding the transcription factor TBX4, in which there is a disruption of the TBX4–FGF epithelial–mesenchymal signaling pathway. In type 1 lesions, atypical hyperplasia of goblet cells has been described, which may predispose to mucinous adenocarcinoma. The distinction between type 1 and type 2 lesions is complex, since mutations have been reported in both, in the KRAS, GNAS, and EGFR genes. Similarly, it has been suggested that type 3 lesions may result from mosaic KRAS mutations arising in the pulmonary epithelium during early stages of development, placing them within the growing group of RASopathies; however, no association between bronchiolar/alveolar lesions and mucinous adenocarcinoma has been reported. Type 4 lesions have been studied in several families, and in some cases high-grade rhabdomyosarcomatous features have been identified. In this subtype, mutations in the DICER1 gene have been detected in more than 70% of children with alveolar lesions, in addition to others identified in the TP53 gene. Recent studies have suggested a change in the designation of this subtype, considering it to be a pleuropulmonary blastoma.[10,11]

The treatment of choice for congenital pulmonary malformations with poor prognosis and significant clinical impact at an early age remains surgical; however, in asymptomatic patients with a high life expectancy, this option is debatable. Although pulmonary resection is considered an alternative to preserve alveolar capacity, minimize the risk of malignancy, and prevent infectious complications, the risk of subsequent respiratory morbidity must be taken into account. Expectant management is a reasonable option for small lesions accompanied by mild symptoms, and a chest CT scan is suggested around 6 months of age, according to each patient's particular circumstances, since lesions detected prenatally have been described to regress spontaneously during postnatal evolution.[12]

Long-term follow-up of post-surgical patients with congenital pulmonary malformation is very limited. In a study conducted in Spain, acute postoperative complications were reported in 28% of the studied population; however, follow-up was performed only during the first month after pulmonary lobectomy. In Italy, patients undergoing pulmonary resection were assessed, with long-term effects after one year of follow-up ranked by frequency as follows: chronic cough, recurrent infections, wheezing, poor exercise tolerance, and the development of chest and spinal deformities. These findings were not statistically significant for most of the variables studied, except for spirometry results, in which a significant correlation was demonstrated between pneumonectomy and long-term deterioration of pulmonary function. Further follow-up studies are needed to explain the risk–benefit ratio of surgical procedures in patients with CPAM, considering that in the previously described single-center studies, this was the most frequent diagnosis among congenital pulmonary

malformations and that most patients remained free of respiratory symptoms prior to surgical intervention.[13,14]

In Latin America, some descriptive studies of patients with congenital pulmonary malformations have been conducted, with CPAM being the most common type of lesion, followed by pulmonary sequestration and hybrid lesions. Regarding the clinical spectrum, and in contrast to European countries, a higher proportion of patients have been found to be symptomatic prior to the procedure, ranging from potentially fatal perinatal respiratory failure to recurrent bronchopulmonary infections in older children.[15,16]

In this case report, the patient was born with a large pulmonary lesion with respiratory and hemodynamic compromise; therefore, the final outcome was death, despite timely surgical treatment. The changes reported on echocardiography may be secondary to displacement of mediastinal structures; however, the possibility that these findings indicate associated congenital malformations cannot be ruled out.

CONCLUSION

Congenital pulmonary malformations represent a heterogeneous group of disorders that require the participation of multiple specialties in order to harmonize therapeutic approaches. The dilemma between conservative management and surgical treatment remains controversial in patients with mild symptoms; therefore, more prospective studies are needed.

ETHICAL CONSIDERATIONS

This clinical case was previously presented at the XII Symposium on Rare Diseases, held in March 2025 in the city of Barranquilla, where it was presented in poster format. This article is not currently under consideration by another journal. Permission was obtained from the individuals responsible for the child's care to collect the information, and confidentiality was guaranteed; all of this was clearly explained verbally and supported through informed consent. This manuscript has been read and approved by all authors listed in the publication, who also declare that they have no potential conflicts of interest. This research did not receive funding, and no experiments involving humans or animals apply in this case.

Conflict of interest

The authors have no conflict of interest to declare.

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CASE REPORT

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Aerobic Treadmill Training in a Children with Postinfectious Bronchiolitis Obliterans. Case Report

Entrenamiento aeróbico sobre cinta en un niño con bronquiolitis obliterante post infecciosa. Reporte de caso.

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ABSTRACT

Postinfectious bronchiolitis obliterans (PIBO) is a lung disease characterized by chronic airflow obstruction associated with inflammatory changes that lead to fibrosis and small airway obliteration. This results in chronic airflow obstruction and reduced tolerance to daily activities and exercise. The objective of this study was to describe the aerobic treadmill training plan in an 11-year-old patient with PIBO, which resulted in increased distance covered in the 6-Minute Walk Test and Maximal Exercise Capacity. This is the first case report of lung function rehabilitation in a pediatric patient with PIBO, to our knowledge.

Key words: bronchiolitis obliterans; Pediatrics; Aerobic exercise; Walk test

RESUMEN

La Bronquiolitis Obliterante Post Infecciosa (BOPI) es una enfermedad pulmonar caracterizada por obstrucción crónica al flujo de aire asociado a cambios inflamatorios, que conducen a fibrosis y obliteración de vía aérea pequeña. Esto genera una obstrucción crónica al flujo aéreo y reducción de la tolerancia a actividades de la vida diaria y al ejercicio. El objetivo de este trabajo es describir el plan de entrenamiento aeróbico sobre cinta en un paciente de 11 años de edad con BOPI, donde se obtuvo un aumento de la distancia recorrida en el Test de 6 Minutos y la Capacidad Máxima de Trabajo. Éste es el primer reporte de un caso de una rehabilitación de la función pulmonar en un paciente pediátrico con BOPI que tengamos conocimiento.

Palabras claves: Bronquiolitis obliterante; Pediatría; Ejercicio aeróbico; Test de marcha

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INTRODUCTION

Postinfectious bronchiolitis obliterans (PIBO) is a severe chronic obstructive pulmonary disease that develops after injury to the lower airways, followed by persistent inflammation, and leads to chronic airflow obstruction and fibrosis of the terminal bronchioles.[1,2] As a consequence, there is a progressive loss of ventilatory muscle strength, a reduction in the ability to perform physical activity, and decreased exercise tolerance.[3]

In our country, PIBO most commonly occurs secondary to severe viral infections, especially those caused by adenovirus.[4,5] In other countries, it is more commonly a consequence of bone marrow or lung transplantation.[6]

Postinfectious bronchiolitis obliterans usually occurs in children under 12 months of age. Initially, during hospital admission, patients present with symptoms that do not differ from those of severe bronchiolitis; most have severe airway obstruction with hypoxemia, and in many cases require mechanical ventilation. Once established, PIBO is clinically characterized by tachypnea, increased anteroposterior chest diameter, crackles, wheezing, and hypoxemia lasting for at least 30 days after the initial injury. High-resolution chest computed tomography (CT) shows characteristic mosaic patterns and bronchiectasis.[23]

Reduced exercise tolerance in patients with chronic respiratory diseases impairs quality of life, increasing hospitalization rates and medication use. Functional tests, such as the six-minute walk test (6MWT) and cardiopulmonary exercise testing (CPET), are tools used to measure overall physical capacity. The 6MWT is particularly valuable because of its simplicity and reliability, with good correlations in children with chronic respiratory diseases.[7,8] Additionally, the 6MWT has gained increased use in recent years as a prognostic indicator of disease severity in cystic fibrosis.

Research on bronchiolitis obliterans (BO) predominantly addresses post-transplant cases, with limited data available on postinfectious BO.[9] Studies on aerobic training have mainly focused on adults with chronic obstructive pulmonary disease (COPD). Cases have also been reported in children with asthma and cystic fibrosis,[10,11] but not in children with PIBO. Therefore, the aim of this study was to describe an aerobic training program carried out in a patient with PIBO and its impact on clinical variables.

CASE DESCRIPTION

The 11-year-old boy, diagnosed with PIBO and chronic airflow obstruction, was referred by his pediatrician to begin pulmonary rehabilitation. He was born in 2013 via C-section at 38 weeks' gestation. At one year of age, he was hospitalized for massive atelectasis caused by pneumococcus, when left pulmonary necrosis with involvement of the right lung base was identified. After prolonged use of mechanical ventilatory assistance and two failed extubation attempts, a tracheostomy was performed, and he remained in the Pediatric Intensive Care Unit for two months. He was discharged requiring continuous oxygen, and underwent decannulation at age four; however, he has required ongoing home oxygen due to chronic hypoxemic respiratory failure ever since. The care team consisted of the primary pediatrician, a pulmonologist, motor and respiratory physical therapists, a nutritionist, a nurse, and therapeutic support at school.

Therapeutic intervention

At 11 years of age, the patient underwent aerobic training between April and May 2024 in a private practice in the city of San Nicolás, Province of Buenos Aires. He was evaluated at the beginning and at the end of the treatment using the 6MWT and CPET. The 6MWT was performed in accordance with the recommendations of the ATS (American Thoracic Society),[11,12] which recorded the total distance walked, respiratory rate (RR), heart rate (HR), and oxygen saturation (SpO_2) using a portable Nonin pulse oximeter (Nonin Advantage 9590), at baseline and immediately after the test (Table 1).

The treadmill-based CPET (Life Fitness T9i Treadmill, Illinois) was used to establish maximal exercise capacity. The test began with a 3-minute warm-up, and the speed increased by 0.5 km/h every minute until the appearance of any of the stopping criteria described by Torres-Castro et al (2016).[13] During the test, maximum speed achieved, HR, SpO_2, and Borg dyspnea scores were recorded (Table 2).

Treadmill training plan

The plan consisted of 24 sessions (three per week) with intervals of moderate and high intensity and continuous monitoring of vital signs. During the first three sessions, workloads of 50% and 80% of

TABLE 1. Values obtained in the physiological variables of the 6MWT before and after treatment

Physiological variables	Before	After	% of change
HR at rest (bpm)	103	89	-13.59
Final HR (bpm)	151	154	1.98
RR at rest (bpm)	30	27	11.11
Final RR (bpm)	38	34	–1052
Baseline O_2 sat	95	96	1
Final O_2 sal	90	93	–3.33
Baseline SAP/ DAP (mmhg)	138/80	135/80	–2.17/0
Final SAP/ DAP (mmhg)	150/88	140/88	–15.66/0
6MWT (meters)	180	255	–41.66

HR: heart rate; **RR:** respiratory rate; **O_2 sat:** oxygen saturation; **SAP:** systolic arterial pressure; **DAP:** diastolic arterial pressure; **6MWT:** 6-minute walk test.

TABLE 2. Incremental load test before and after aerobic treadmill training

Before training					After training					% of change
Time	Speed km/h	O_2 sat	HR	Dyspnea	Time	Speed km/h	O_2 sat	HR	Dyspnea	
1’	3	96	117	1	1´	3	96	110	0,5	
1’	3.5	94	130	2	1´	3.5	95	119	1	
1’	4	91	150	7	1´	4	94	130	2	
						4.5	92	146	4	
						5	91	151	5	
						5.5	90	160	7	
MAS 4 km/h					MAS 5.5 Km/h					–37.5

O_2 sat: oxygen saturation; **HR:** heart rate; **MAS:** maximal aerobic speed.

the speed obtained in the CPET were used; in the following six sessions, intensities of 50% and 85% were applied; and in the remaining 15 sessions, interval intensities ranged between 50% and 90%. The type of training was high-intensity interval training (HIIT).

Each session included 3 minutes of warm-up with mobilization of the shoulder, hip, and ankle joints, trunk rotations, and stretching of the posterior muscle chain; followed by 30 minutes of training with intervals of 1 minute of exercise and 2 minutes of passive recovery; and finally, a 2-minute cool-down with monitoring of heart rate, oxygen saturation, and dyspnea. At each session, the date, duration, training intensities, and vital signs (at baseline and post-session) were recorded.

RESULTS

The results of the 6MWT showed that post-training baseline heart rate was lower at the end of treatment (Table 1), indicating reduced cardiovascular effort to perform the test. Although the final heart rate was 154 bpm with a change of 1.98%, the distance covered increased by 41.66%. In the CPET, the maximum aerobic speed was 5.5 km/h, with an improvement of 1.5 km/h (Table 2). Dyspnea also showed improvement, reflecting vascular adaptation.

DISCUSSION

This case report describes the aerobic training plan in a child with PIBO and shows changes in

physiological variables related to physical capacity, as reflected in the 6MWT and CPET both before and after treatment.

The main causes of exercise intolerance in patients with pulmonary disease include factors such as lower limb fatigue, dyspnea, dynamic hyperinflation, peripheral muscle dysfunction, abnormalities in oxygen transport, and physical deconditioning due to inactivity. The lack of ventilatory reserve –evidenced by high ventilation during cardiopulmonary exercise testing– is associated with poor physical performance and can be attributed to an obstructive pattern that limits airflow.[14]

The distance walked in the 6MWT improved by 41.66% after aerobic treadmill training; and post-treatment resting heart rate was lower than baseline values, indicating reduced cardiovascular effort to perform the test (Table 1). Although training does not produce morphological changes, cardiovascular and functional improvements can be observed. This increase was reported by Grumber et al and Latorre-Román et al, who observed significant improvements of 4% and 23%, respectively, in the 6MWT after an aerobic training protocol in children with cystic fibrosis and asthma.[15,16] Regarding the physiological variables evaluated in the 6MWT, Moalla et al observed a similar HR response in children with congestive heart disease, attributing this response to changes in autonomic tone as a result of endurance training.[17]

With respect to CPET, although maximal aerobic speed (MAS) increased by only 1.5 km/h, the patient tolerated a longer workload duration, demonstrating adequate resistance to the stimulus. (Table 2). Concerning dyspnea during the pretreatment CPET, the test ended with a dyspnea score of 7 at 3 minutes, whereas post-treatment the patient reached a dyspnea score of 7 after 6 minutes, indicating a significant vascular adaptation. Longitudinal studies have shown that forced expiratory volumes undergo significant increases between 5 and 20 years of age; however, forced vital capacity (FVC) increases disproportionately (+11% per year) compared with FEV□ (+9%), leading to a progressive reduction in the FEV□/FVC ratio (−1.9%).[7,18] This phenomenon is likely related to neoalveolarization during childhood and adolescence (Narayanan et al, 2013).[22,23]

In pediatric patients with chronic respiratory disease (CRD), the assessment of physical fitness is considered part of a multidimensional evaluation, as it assesses interaction among the cardiac, ventilatory, muscular, and metabolic systems.[3] These findings highlight the importance of the team that thoroughly evaluates these patients, taking into account that other factors –such as habitual physical activity level, physical conditioning, and muscular capacity (both peripheral and respiratory)– may also play an important role in their aerobic fitness.[3] The guidelines published by Torres-Castro et al (2016), currently in force in our country, recommend regular general physical training at threshold intensity in order to trigger physiological response and adaptation mechanisms.[7,13]

At present, there are no studies specifically designed to evaluate the effects of physical training in patients with PIBO. Existing studies have been conducted in patients with post-transplant bronchiolitis obliterans and in individuals with other chronic respiratory diseases, such as cystic fibrosis.[18] The available evidence indicates that physical training protocols are effective in improving physical capacity, exercise tolerance, and cardiovascular fitness in patients with chronic respiratory diseases.[7,19,20,21]

One limitation of this study is that, as it is a single case report, the results are not generalizable to other patients. Nevertheless, it may serve as a starting point for future studies with larger sample sizes and multicenter designs, given that this is a rare condition.

CONCLUSION

An improvement in exercise capacity was observed in a child with PIBO following an aerobic treadmill training program, with increases in the distance covered in the 6MWT and greater tolerance to workload duration in the CPET. Despite challenges related to pulmonary health, the patient experienced improvements in overall physical capacity.

Conflict of interest

The authors have no conflicts of interest to declare.

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HIGHLIGHTS

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Highlights of International Congresses. Report from our Representatives at the Following International Events

Highlights de los Congresos Internacionales. Informe de nuestros representantes en los siguientes eventos internacionales

18TH ALAT CONGRESS – CANCÚN, MEXICO, JULY 9 TO 12, 2025

Overview and Argentine Participation

By Dr. Walter Mattarucco, former President of the AAMR

At the 18th ALAT Congress in Cancún (July 9-12, 2025), Argentina's strong participation stood out in both scientific presentations and clinical update and discussion forums. Below are some of the most relevant highlights:

- **Presentation of the Work of the Obstructive Diseases Section.** Poster No. 242, entitled "Brechas de conocimiento en el manejo del asma durante el embarazo: un estudio transversal" (Knowledge gaps in the management of asthma during pregnancy: a cross-sectional study) was presented by the AAMR Obstructive Diseases Section.
- **New Paradigms in COPD.** In a master class open lecture, Drs. Antonio Anzueto, Bartolomé Celli, and Francisco de Borja García Cosio Piqueras explored the "upstream" treatment of COPD, that is, intervening from the very early stages of the disease. The GeTOmics hypothesis by Agustí and Celli was discussed, framing COPD development as the result of lifelong gene-environment interactions (e.g., maternal smoking, low birth weight, lack of breastfeeding, vaping, biomass exposure). Also, experts proposed incorporating the "pre-disease" concept-evaluating symptomatic patients with normal spirometry via imaging studies and other methods.
- **Phenotypes and Multimorbidity.** The importance of recognizing different clinical phenotypes was emphasized (inflammatory phenotype with high BMI and multiple comorbidities vs. emphysematous phenotype with low BMI and sarcopenia). Experts also stressed the need for personalized medicine guided by functional tests (walking tests, BMI, mMRC [modified Medical Research Council dyspnea scale]), as well as redefining key concepts of the disease.
- **Triple Therapy and Biologics in COPD.** The speakers presented the benefits of initiating triple therapy at earlier stages. Regarding biologics, they emphasized the use of dupilumab in patients with more than 300 eosinophils/mm^3, showing significant benefits in lung function and reduced exacerbations (BOREAS and NOTUS studies).
- **Exacerbations: New GOLD Definitions** .The session on exacerbations (with Drs. Montes de Oca, Marc Miravitlles, and B. Celli) presented a redefinition based on objective clinical criteria, following the ROMA proposal, which could transform the diagnostic and therapeutic approach in these situations. References: Celli B, AJRCCM 2021; 204: 1251–1258.
- **Treatment of Comorbidities.** The use of new drugs such as SGLT2 inhibitors was explored. This drug may benefit COPD patients with comorbidities such as heart failure or cardiorenal–metabolic syndrome.
- **Severe Asthma and New ALAT Guidelines.** The new ALAT 2024 Clinical Practice Guideline of Severe Asthma, already published in Respirar, which includes phenotypic assessment and selection of the appropriate biologic therapy was presented. A new definition of asthma exacerbations was also introduced (mild, severe, very severe), differentiating the management of the disease according to the clinical setting.
- **A new paradigm?** Several presentations concluded that a comprehensive approach to inflammatory airway diseases may be emerging, blurring the traditional boundaries between asthma, COPD, and bronchiectasis.

Lung Transplantation Department

By Dr. Pablo Curbelo, Director of the ALAT Transplantation Department

During the recent ALAT Congress held in Cancún, the Lung Transplantation Department had a prominent participation, with numerous academic activities, international cooperation projects, and progress on key documents for the region. Below, we share the main focus areas:

- **Pre-Congress Course on Lung Transplantation.** It featured the participation of leading experts from lung transplant centers across Latin America, as well as prestigious international institutions such as the University of Miami, San Francisco, Chicago, and Toronto General Hospital. The course promoted academic exchange, sharing of clinical experiences, and the strengthening of collaboration among professionals dedicated to the treatment of advanced lung diseases.
- **ALAT Lung Transplantation Recommendations.** The region's first document on lung transplantation in Spanish is in its final phase. With chapters developed by specialists from reference centers, it addresses topics ranging from indications, contraindications, and referral criteria to the role of nursing, ECMO (extracorporeal membrane oxygenation), rehabilitation, and self-care for transplant patients.
- **ALAT–ISHLT Cooperation Agreement.** Initial steps have been taken to establish an agreement between ALAT (Latin American Thoracic Association) and the International Society for Heart and Lung Transplantation (ISHLT). The goal is to promote human resource training through clinical rotations, academic cooperation, and joint activities such as webinars in Spanish.
- **Framework Document to Promote Organ Donation and Allocation.** Work is underway on a regional proposal aimed at strengthening organ donation in Latin America, improving organ preservation, and reducing mortality on the waiting list. The document will be presented to regulatory agencies to promote the creation of a regional organ allocation network, similar to Eurotransplant.
- **Best Oral Presentation – Innovation in Lung Preservation.** 'Optimization of Lung Preservation from uDCD Donors'. Juan Montagne and colleagues (Toronto General Hospital) presented a study on lung preservation in uncontrolled donation after cardiac death (uDCD). The combination of storage at 10°C and ex vivo lung perfusion (EVLP) demonstrated significant improvements in lung function, even in settings of warm ischemia.

Respiratory Pathophysiology and Pulmonary Function Laboratory Department

By Dr. Santiago Arce, member of the Respiratory Pathophysiology and Pulmonary Function Laboratory Section of the AAMR

The ALAT Pathophysiology Program had an active and outstanding Argentine participation during the ALAT 2025 Congress in Cancún. Below, we share the most relevant highlights:

- **Pre-Congress Spirometry Course.** With an excellent level of organization and a room filled with participants, the pre-congress spirometry course demonstrated the high level of interest and commitment within the respiratory community. Argentine professionals were part of the faculty, providing their clinical and academic experience.
- **Cardiopulmonary Exercise Testing Workshop.** This session featured renowned European and Latin American experts. Key technical and clinical aspects for interpreting this essential diagnostic tool were covered, creating a high-level training environment.
- **High-Altitude Medicine Symposium.** The symposium featured regional experts who shared their clinical and research expertise on high altitude medicine. Initiatives to promote collaborative studies in this field were discussed, reflecting its growing interest and impact on the Andean region.

Respiratory Rehabilitation Department

By Mr. Santiago Larrateguy, member of the Respiratory Rehabilitation Section

I had the privilege of participating in the 18th Congress of the Latin American Thoracic Association (ALAT), a forum that reaffirms the region's commitment to scientific updating and exchange among colleagues from across Latin America.

Symposium: **Therapeutic Exercise in Chronic Respiratory Diseases**

I co-chaired this symposium with Rodrigo Torres (Chile), where training strategies applied to patients with chronic respiratory diseases were discussed.

Jhonatan Betancourt (Colombia) opened the session with a presentation on **interval training**, assessing its applicability and tolerance compared to continuous methods, especially in patients with ventilatory limitation. **Rodrigo Torres** then delved into the **estimation of oxygen consumption** using field tests, highlighting the importance of an accessible yet accurate assessment for guiding exercise prescription. **Alejandro Casas Herrera (Colombia)** concluded with an innovative perspective by presenting **non-conventional rehabilitation models** such as tai chi, yoga, and rumba, underscoring their value in improving adherence, motivation, and overall patient well-being. An approach that invites us to broaden the therapeutic options beyond traditional training.

Lecture: **Keys to Success in Oxygen Therapy for People with Chronic Respiratory Diseases**

I attended this lecture, which addressed fundamental aspects of the use of home oxygen therapy. One of the most notable points was the need to use **FDA-validated oximeters**, given the inconsistent accuracy of devices available on the market. The personalization of treatment according to activity level, patient adherence, and functional assessment was also covered.

Practical Workshop: Airway Clearance in the Chronic Respiratory Patient

I also participated in the workshop focused on **airway clearance strategies**, co-chaired by Matías Otto (Chile) and Diego Sossa (Costa Rica).

Topics ranged from the **role of secretions** in the clinical course of chronic respiratory diseases to the use of practical tools such as: **Manual Airway Drainage Techniques, OPEP Devices, Mechanical Cough Assistance.**

I concluded with a presentation on **physical exercise as an active airway clearance technique**, underscoring its impact on secretion mobilization, improved functional capacity, and patient autonomy.

This congress was a great opportunity to continue learning, share experiences with colleagues, and reaffirm the value of interdisciplinary work in respiratory health.

Tuberculosis Department

By Dr. Sandra J. Inwentarz, member of the AAMR Tuberculosis Section and the ALAT TB Department

The ALAT Tuberculosis Department had a very diverse program with numerous educational and update activities.

- During the Pre-Congress Course, strong emphasis was placed on subclinical TB, its pathophysiological mechanisms, and the importance of imaging for its diagnosis.
- The treatments were updated, highlighting the new treatments proposed by the WHO for multidrug-resistant tuberculosis (MDR-TB), pre–extensively drug-resistant tuberculosis (pre-XDR), and extensively drug-resistant tuberculosis (XDR). Experiences with the BPaL and BPaLM regimens were addressed, with an initial duration of 6 months that can be extended to 9 months depending on clinical, bacteriological, and radiological progression. New proposals from the BEAT TB Trial, with a 6-month regimen, and the END TB Trial, with a 9-month regimen, were introduced, featuring bedaquiline with or without delamanid.
- The "National TB Guidelines Forum in Latin America" analyzed TB guidelines from various countries, evaluating their similarities and differences, and proposed a unified guideline for the entire region.
- Updates were also provided on extrapulmonary forms of TB, TB and comorbidities, and TB in vulnerable groups and in people deprived of liberty.
- The need to monitor pregnant women was emphasized, given that the number of TB patients in this group has progressively increased throughout Latin America.
- Twenty-eight scientific papers were evaluated in poster format, demonstrating high academic quality and broad representation from Latin America.
- The Recommendations on Post-Tuberculosis Lung Disease were presented, as well as the **Latin American Registry of Patients with Post-Tuberculosis Lung Disease: Analysis of clinical conditions, lung function, quality of life, and rehabilitation**. It is a **multicenter study** that will soon be launched through ALAT's REDCap platform.
- The "Molecular Diagnostics Summit: Barriers to Molecular Diagnosis of Pulmonary TB"

was also held. In the months leading up to this event, joint meetings were conducted among experts from different Latin American countries. Through the development of PICO questions (population/problem, intervention, comparison, outcome), various challenges and potential solutions related to the molecular diagnosis of TB were addressed and developed, some of which were presented during the summit at the congress. The conclusions of this initiative and the final report will be published shortly.

Clinical and Critical Care Department

By Dr. Sebastián Wustten, Coordinator of the Clinical and Critical Pulmonology Section, and Dr. Miguel Penizzotto

The Best of Interstitial Lung Diseases

Two award-winning scientific studies were presented, providing innovative evidence in diffuse interstitial lung diseases (DILDs). The awarded study addressed the importance and usefulness of the biomarker KL-6 in patients with interstitial lung disease, based on a cohort of more than 900 patients in Spain. Progress on the REGINHA project the Ibero-American Registry of Hypersensitivity Pneumonitis, which includes more than 1,200 registered patients, was also discussed. This important registry is currently in the analysis phase, and the first results are expected to be available soon. The poster session reflected active scientific production in Latin America.

Progressive Pulmonary Fibrosis in Connective Tissue Diseases

This session addressed the relationship between autoimmune diseases and progressive pulmonary fibrosis. Cases of interstitial lung disease associated with systemic sclerosis, Sjögren's syndrome, inflammatory myopathies, and rheumatoid arthritis were discussed. The use of imaging, functional tests, and biomarkers for early detection was highlighted. Finally, the current and future role of antifibrotic therapies in this group of patients was evaluated.

New Therapies for IPF and PPF

Updates were presented on the recently published FIBRONEER-IPF and FIBRONEER-ILD studies regarding the efficacy and safety of nerandomilast as a new antifibrotic treatment that will soon be available for our patients. This new molecule shows promising results, although it is not yet commercially available in Latin America. Its potential impact on patients with progressive pulmonary fibrosis (PPF) and idiopathic pulmonary fibrosis (IPF) was analyzed. The discussion focused on improving accessibility and patient selection criteria.

Interstitial Lung Disease Registries

Experts highlighted the importance of having national and regional registries for interstitial lung diseases to better understand their epidemiology and improve clinical decision-making. REFIPI was presented as the first Latin American IPF registry, which demonstrates significant progress. They also introduced advancements in the Spanish registry and the emerging EPI-MIO registry for inflammatory myopathies. These registries allow for better patient characterization and foster international collaboration.

Environmental Exposures and DILD

Dr. Laura Alberti reviewed the latest data on hypersensitivity pneumonitis in Latin America, highlighting current diagnostic and treatment challenges. Dr. Annie Pardo addressed epigenetic mechanisms induced by environmental exposures and their role in the progression of DILD. There is increasing scientific evidence supporting the fact that environmental exposures can induce epigenetic modifications, which alter gene expression without changing the DNA sequence, and this may contribute to the development and progression of fibrosing interstitial lung diseases. The need to improve the identification of causal agents was emphasized. Preventive strategies and early diagnosis were central topics of the discussion.

ALAT ILD–RA Guideline

Dr. Laura Alberti presented the diagnostic and therapeutic guidelines for ILD associated with rheumatoid arthritis. This guideline emphasizes the protective role of methotrexate in patients with diffuse interstitial lung disease (DILD). It also provides answers to frequently asked questions regarding the management of DILD associated with rheumatoid arthritis. The need for rheumatology-pulmonology collaboration was emphasized. This document represents a regional step forward toward evidence-based medicine. It is expected to

be published soon by the Latin American Thoracic Association (ALAT).

Decoding Fibrosis

Dr. Moisés Selman presented recent findings on fibrosis-associated comorbidities and molecular advances in pathophysiology. Dr. Lorena Noriega discussed emerging treatments for pulmonary fibrosis, evaluating future perspectives. The session concluded with questions addressing personalized approaches for patients with fibrosis.

Comprehensive Treatment of Patients with Interstitial Lung Disease

Unmet needs, barriers to antifibrotic treatment, and opportunities for improvement in clinical practice were discussed. Dr. Ivette Buendía and Dr. Martín Fernández highlighted the importance of medical education, pulmonary rehabilitation, and a comprehensive approach to patients with interstitial lung disease. Insights derived from real-world patient cohorts were shared. Opportunities to expand indications and improve clinical efficacy were identified.

Sarcoidosis

Dr. Jacobo Sellares presented an update on the diagnosis and clinical management of sarcoidosis. He highlighted new evidence supporting early use of methotrexate, supported by recent findings published in the New England Journal of Medicine. Dr. Randall Rojas highlighted the role of imaging in assessing pulmonary involvement. Long-term follow-up and criteria for initiating immunosuppressive therapy were addressed. The workshop promoted a structured approach to differential diagnosis.

Challenges of Pulmonary Fibrosis

Dr. Selman explained current pathophysiological mechanisms and risk factors associated with fibrosis. Dr. Jacobo Sellares complemented this with high-precision diagnostic methods and therapeutic strategies. The importance of a comprehensive and personalized approach was reinforced. The panel discussion allowed for comparison of clinical experiences from different countries.

As Secretary of the Interstitial Lung Disease Department, it was an honor to be part of the organization of this prestigious congress.

Events like this not only strengthen ties among colleagues throughout the region, but also drive advances in our knowledge and the quality of care we provide to our patients.

I would like to express my deep gratitude to all the speakers, moderators, and attendees for their commitment and enthusiasm.

We will continue working together to ensure that scientific excellence and collaboration remain the pillars of the development of our specialty.

Department of Interstitial Lung Diseases (ILDs)

By Dr. Santiago Auteri, a member of the section and Secretary of the Department of Interstitial Lung Diseases of the Latin American Thoracic Association (ALAT)

Coordinator of the educational-scientific project Academia EPI –ILD

Presentation of the First 600 Patients from the Argentine Registry of Non–Cystic Fibrosis Bronchiectasis (ReBroAr)

Sebastián Wustten presented a poster on the ReBroAr registry together with other co-authors, all of them members of the AAMR. The work was highly appreciated, as it represents the first registry in Latin America focused on this condition. Below are the most important results of the study:

- The first 600 patients in the registry were presented: 67% men and 33% women, with a mean age of 61 years.
  - The most frequent etiologies were post-infectious (25.1%), post-TB (20.7%), idiopathic (19.4%), COPD (10.3%), and asthma (7.8%).
  - At diagnosis, 44% of patients presented three symptoms (dyspnea, cough, and sputum production).
  - In CT scan, 15% had involvement of one lobe, 35% of the two lobes, and 50% three or more lobes.
  - Lung function testing showed an obstructive pattern in 52%, possible restriction in 32.8%, and normal findings in only 14.9%.
  - The most frequently isolated pathogen was Pseudomonas aeruginosa (24.9%), while 51.1% of patients had no microbiological isolation.
  - 73% of patients experienced outpatient exacerbations, and 20% had at least one hospitalization.

  - According to the E-FACED score, 52% were mild, 37% moderate, and 11% severe.
  - A total of 87.2% patients were treated with inhalers, most commonly ICS + LABA (39.9%) and triple therapy (ICS + LABA + LAMA) in 17.5%.
  - Azithromycin was part of the therapeutic regimen in 35% of cases.
- Miguel Penizzotto delivered a lecture on non–cystic fibrosis bronchiectasis, highlighting the evolution of knowledge on this condition and advances in novel therapeutic approaches.
- The directors of the ALAT Infections Department conveyed to AAMR members leading the ReBroAr initiative their intent to expand the registry by incorporating additional Latin American countries, aiming to establish a large regional registry on bronchiectasis. Both parties agreed to begin working together on this important project.