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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

Barro, Rodrigo[1]; Bonavia, Luis Manuel[1]; Gatica, Hernandez David Patricio[1]; Alvarez Bertea[1] Juan Pablo[1]; Perone, Gustavo[1]; Gatica Roberto[1]; Sosa Marcelo[1]; Grosso Mariana[1]

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Correspondence
Rodrigo Barro
Email:
barro.rodrigo96@gmail.com

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

[1] Hospital Del Carmen, Province of Mendoza, Argentina.

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,

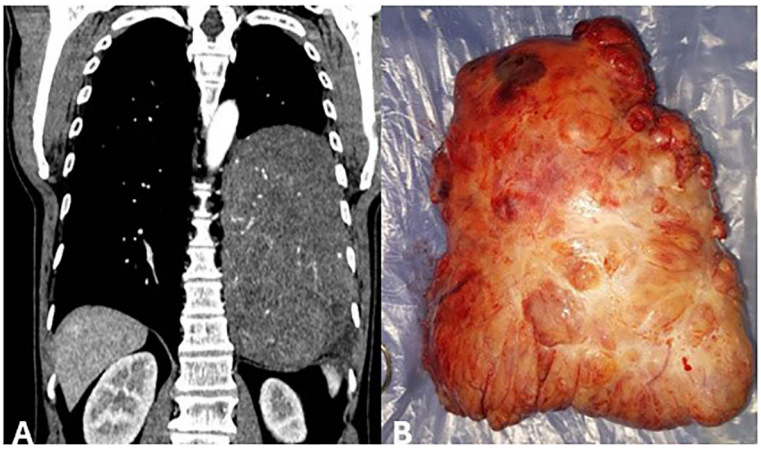

Fig. 1 A. Contrast-enhanced chest computed tomography shows an expansive lesion in the lower lobe of the left lung, in close contact with the pleura, with marked vascularization following contrast administration. B. Firm pleural tumor with a fibrous appearance, weighing approximately 1800 mg.

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).

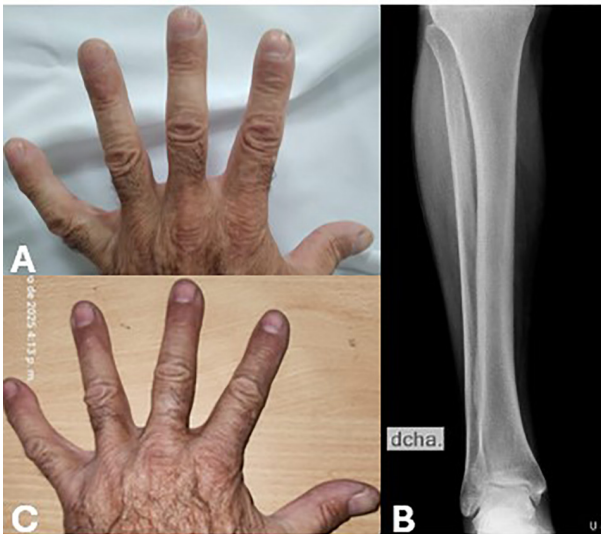

Fig. 2. A. Digital clubbing prior to surgical treatment. B. Regular periosteal reaction on the medial surface of the ulna diaphysis. C. Image taken two years after surgical treatment showing resolution of digital clubbing.

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.

REFERENCES

1. Martin-Broto J, Mondaza-Hernandez JL, Moura DS, Hindi N. A Comprehensive Review on Solitary Fibrous Tumor: New Insights for New Horizons. Cancers (Basel). 2021;13:2913. https://doi.org/10.3390/cancers13122913
2. Ruiz López E, Gónzalez García FJ, Moreno Casado PM, et al. Doege-Potter Syndrome as a Manifestation of Solitary Fibrous Tumor of the Pleura. Should we Consider Chest Tumor in the Presence of Refractory Hypoglycemia?. Open Respir Arch 2021;3: 100102. https://doi.org/10.1016/j.opresp.2021.100102
3. Abodunrin FO, Collier SA, Killeen RB. Tumores fibrosos solitarios. [Actualizado el 1 de mayo de 2024]. En: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; enero de 2025. https://www.ncbi.nlm.nih.gov/books/NBK585038/
4. Solsi A, Pho K., Shojaie S, Findakly D, Noori T. Doege-Potter Syndrome and Pierre-Marie-Bamberger Syndrome in a Patient With Pleural Solitary Fibrous Tumor: A Rare Case With Literature Review. Cureus, 2020;12: e7919. https://doi.org/10.7759/cureus.7919
5. Kalebi AY, Hale MJ, Wong ML, Hoffman T, Murray J. Surgically cured hypoglycemia secondary to pleural solitary

fibrous tumour: case report and update review on the Doege-Potter syndrome. J of Cardiothorac Surg 2009;4:45. https://doi.org/10.1186/1749-8090-4-45

6. Demicco EG, Park MS, Araujo DM, et al. Solitary fibrous tumor: a clinicopathological study of 110 cases and proposed risk assessment model. Mod Pathol 2012;25: 1298-06. https://doi.org/10.1038/modpathol.2012.83
7. Galateau-Salle F, Churg A, Roggli V, Travis WD; World Health Organization Committee for Tumors of the Pleura. The 2015 World Health Organization Classification of Tumors of the Pleura: Advances since the 2004 Classification. J Thorac Oncol 2016;11:142-54. https://doi.org/10.1016/j.jtho.2015.11.005.
8. Martin-Broto J, Mondaza-Hernandez JL, Moura DS, Hindi N. A Comprehensive Review on Solitary Fibrous Tumor: New Insights for New Horizons. Cancers (Basel). 2021;13:2913. https://doi.org/10.3390/cancers13122913.
9. Demicco E, Wagner M, Maki R, et al. Evaluación del riesgo en tumores fibrosos solitarios: validación y refinamiento de un modelo de estratificación del riesgo. Mod Pathol 2017;30:1433-42. https://doi.org/10.1038/modpathol.2017.54
10. Olson NJ, Linos K. Dedifferentiated Solitary Fibrous Tumor: A Concise Review. Arch Pathol Lab Med. 2018;142:761-6. https://doi.org/10.5858/arpa.2016-0570-RS. https://pubmed.ncbi.nlm.nih.gov/29848035/