Acta Biomed 2016; Vol. 87, N. 3: 314-317

Case report

A case of solitary fibrous pleura tumor associated with severe hypoglycemia: the Doege-Potter's syndrome

Silvia Haddoub[1], L. Gnetti[3], A. Montanari[2], R. Di Ruvo[2], P. Carbognani[4], F. Maccanelli[1], M.G. Magotti[1], M.C. Calderini[1], Federico Cioni[1], S.M. Tardio[1]

[1] S.S.D. Intensive treatment of diabetes and complications, University Hospital of Parma; [2] Clinical and Medical Semiotics, University Hospital of Parma; [3] Anatomy and Histology, University Hospital of Parma; [4] Thoracic Surgery, University Hospital of Parma

Summary. Solitary fibrous pleura tumor is a rare primary intrathoracic tumor of the pleura. It usually has an indolent clinical course, but sometimes it can have an aggressive behaviour. In 1930 Doege and Potter independently described this neoplasm, presenting with symptoms of hypoglycemia, hence the eponim of Doege-Potter's Syndrome. In this report, we illustrate a case of Doege Potter's Syndrome, treated with complete surgical resection. (www.actabiomedica.it)

Key words: solitary fibrous pleura tumor, hypoglycemia, surgical resection

Introduction

Solitary fibrous pleura tumors (TFS) are rare neoplasms, in fact they account for 5% of all pleuric tumors, and they are not correlated with exposure to cigarette smoke or asbestos.

These tumors usually have a slow growth, and are distinguished from malignant mesothelioma for radiological characteristics, for their macroscopic appearance, in addition to the immunohistochemical characteristics. About 80% of these tumors are benign, and usually appear as asymptomatic masses (or incidentaloma) found during a routine chest x-ray.

Symptoms, when present, are represented by a cough, chest pain, dyspnea, hemoptysis, and rarely hypoglycemia. The latter (present in 2-4% of cases) was initially described by Doege and Potter in 1930, hence the name of Doege Potter Syndrome.

Here we report a case of syndrome, found at histology a pleural malignancy.

Clinical case

Our case concerns a patient of 67 years, who went to the Emergency Department for the appearance of insomnia a few days before, associated with mental confusion.

There were also reported, for some months, repeated nocturnal awakenings, with shivering and mental confusion, symptoms that would disappear after food intake.

The patient was not a current neither a former somker. On admission to the Hospital the patient was alert, cooperative, partially oriented in space and time, at times confused.

In his medical history was reported a previous road accident, about 30 years ago, resulting in thoracic lesion (parenchymatous formation to the right lung fields, with documented tac exam).

On physical examination we found normal neurological, thoracic and abdominal objectivity.

The brain tomography performed showed no abnormalities; on chest radiography we discovered the presence of expansive injury in the lower third of the right hemithorax.

Blood tests showed severe hypoglycemia (39 mg/dl), low values of HbA1c (33 mmol/mol), and the remaining exams, as well as the hormonal assays, were normal.

During the hospitalization repeated episodes of symptomatic hypoglycemia have occurred, and were adequately corrected by administering sugar.

The insulin dosages and c-peptide were in the normal range.

Chest and abdomen tomography with contrast confirmed the presence of a massive solid mass of 20x16 cm (Figures 1-2), occupying the middle third of the lower-right hemithorax, with irregular intralesional vascularization, and some holes in the context of degenerative necrosis, associated with pleural effusion and atelectasis of consensual parenchyma. It was described as a pleural neoplasm: a fibrous tumor (in malignant degeneration or a sarcoma). No lymphadenopathy were described, nor signs of bone infiltration, neither direct infiltration of the lung. Other organs were within limits.

Figure 1. Surgical mass of solitary pleuric tumor, intraoperatory specimen: neoformation grayish white, at 26x18x12 cm, with polylobate margins, joined thin lung tissue portions. To cut the tumor had elastic texture and grayish white color, with alternating brownish areas and foci of necrosis plots

Figure 2. Mass of solitary pleuric tumor, surgical specimen

Positron Emission Tomography showed small contrast accumulation, for the presence of areas necrotic areas inside the massive solid mass in lower right hemithorax.

The patient was then evaluated by the team of Thoracic Surgery colleagues to schedule surgery for pleural resection of the tumor.

Histological examination on the surgical specimen showed a mesenchymal spindle cell neoplasm, hypercellular, with moderate atypia, hyperchromasia and nuclear pleomorphism, and architecture in small interwoven beams in a disorganized way. There was a variable deposition of extracellular collagen matrix and the capillary reticulum was woven with some branching ectatic vessels.

The tissue had an expansionary growth. Central areas of involution, with hyaline foci of spontaneous necrosis were also present (figure 3-6).

The mitotic index stood at 9X 10 HPF, in most active areas, with Ki67 proliferative index of 15%.

The immunistochimical showed CD34, CD99, BCL-2, Vimentin, Desmin (focal) reactivity; no ex-

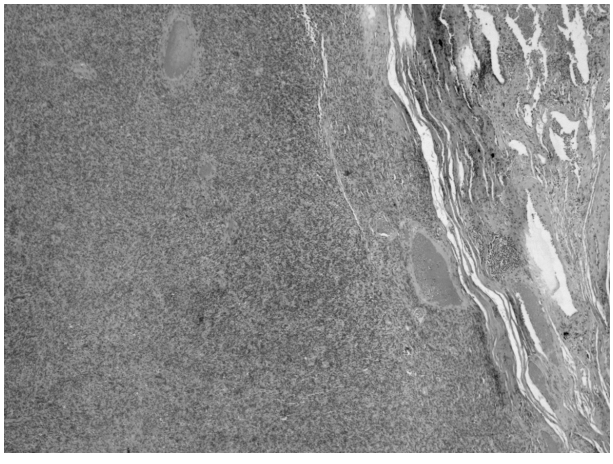

Figure 3. Microscope magnification, 5X: the border area is defined between the part of non-necrotic and necrotic

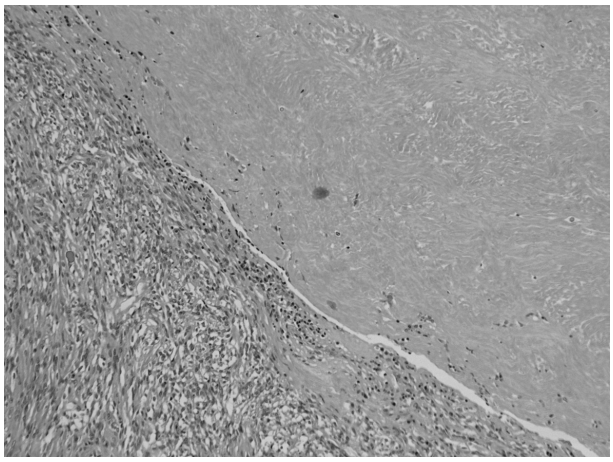

Figure 4. Microscope magnification, 10X: in highlight the necrosis area

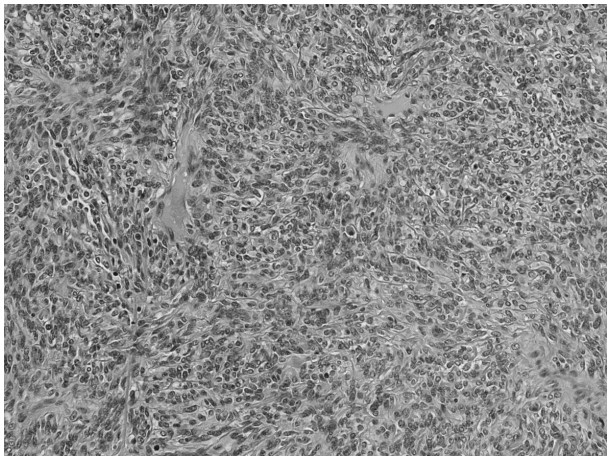

Figure 5. Microscope magnification, 20 X: in highlight the marked cellularity

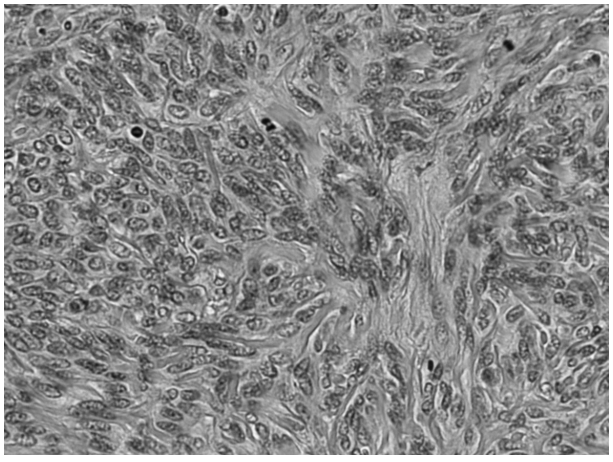

Figure 6. Magnification microscope, 40 X: in highlight mitosis

pression of EMA, SM actin, cytokeratin pool, c-kit, myogenin and s-100. IGF1 R was weakly expressed. All of these findings were subjestive for malignant solitary fibrous pleura tumor.

Discussion

Solitary fibrous pleura tumor (TFS) are rare neoplasms, in fact account for 5% of all pleuric neoplasms (1), and they are not correlated with cigarette smoke or asbestos exposure (2).

These tumors usually have a slow growth, and are distinguished from malignant mesothelioma for their radiological characteristics, for macroscopical appearance (3), as well as immunohistochemical characteristics: TSF tipically presents with reactivity for CD 34, and negativity for cytokeratin markers .

Only about 13% of TFS described in literature have aggressive behavior, with massive local infiltration, local recurrence or distant metastasis. The remaining 87% have benign characteristics, and surgical resection is usually curative. The distribution between sexes shows no difference.

For their slow-growing attitude, they usually present as an accidental mass found on chest radiography.

Only in cases of voluminous masses, with malignacy features we could find symptoms that may be tipically of pulmonary relevance, such as cough, chest pain, dyspnea and hemoptysis (the latter very rare) or systemic symptoms such as fatigue, weakness, night sweats , weight loss, or frequent hypoglycemic crisis.

The presence of the latter symptom outlines the Doege- Potter Syndrome, characterized by frequent hypoglycemia in patients suffering from TFS. The causes of hypoglycemia are not certain, and there are several theories: it may be related to paraneoplastic secretion of insulin-like substances (IGF 2, insulin-like growth factor) directly by tumor tissue, or to some defects in the compensating mechanisms by counter-regulatory hormones secretion. Finally it could also be related to an accelerated consumption of blood glucose by neoplastic cells (4).

The hormone secretion IFG2 or other pro-insulin-like hormones determine an increased glucose uptake by insulin-sensitive tissues (muscle and adipose

tissue), and can also stimulate the glucose uptake by the tumor itself. Laboratory methods capable of dosing these hormones, however, are not yet available on a large scale (5).

Many studies were made, also using continuous glucose monitoring (CGM) applied to patients before and after surgery, and they confirm that hypoglycemic episodes disappeared after the surgical mass resection (6).

The neoplasm size correlates with the prognosis: tumors of major size have a greater degree of malignant histological features and a poor prognosis (7).

The diagnostic process usually does not use CT guided needle aspiration, as often this is not nullifying (8). If clinical conditions are stable, surgery is always the preferable approach, with thoracotomy and complete excision of the lesion.

Usually after surgery patients have the complete regression of symptoms (9), however is recommended a long term instrumental follow-up, given the high risk of recurrence or malignant transformation of even seemingly benign growths.

References

1. Akman C Cetinkaya S, Ulus S, Kaynak K, Oz B. Peduculated localized fibrous tumor of the pleura presenting as a moving chest mass. South Med J 2005; 98(4): 486-8.
2. Amorim E, Solitary fibrous tumor of the pleura: 3 case reports, Rev Assoc Med Bras 2015; 61 (3): 207-8.
3. Perna V, Rivas F, Morera R, et al. Localized solitary fibrous tumors of the pleura: an analysis of 15 patients. International Journal of Surgery 2008; 6: 298-301.
4. Campos R, Gonzalez R, Saldias R, et al. Sindrome de Doege-Potter:hipoglicemia secundaria a tumor fibroso solitario de la pleura, Rev Med Chile 2012; 140: 353-7.
5. Schutt R, Gordon TA, Bhabhra R, et al. Doege-Potter syndrome presenting with hypoinsulinemic hypoglycemia in a patient with a malignant extrapleural solitary firous tumor: a case report. Journal of Medical case reports 2013; 7: 11.
6. Otaje S, Kikkawa T, Takizawa M, Junko O et al, Hypoglycemia observed on continuos glucose monitoring associated with IGF2 producing solitary fibrous tumor. J Clin Endocrinol Metab 2015; 100 (7): 2519-24.
7. England, DM, Hochholzer L, Mc Carthy M, Localized benign and malignant fibrous tumors of the pleura. A clinicopathologic review of 223 cases. Am J Surg Pathol 1989; 13: 640-58.
8. Santos RS, Haddad R, Lima CE, Liu YL, et al. Patterns of recurrence and long term survival after resection of localized fibrous tumors of the pleura. Clin Lung Cancer 2005; 7 (3): 197-201.
9. Rena O, Filosso PL, Papalia E, Molinatti M, Di Marzio P, Maggi G, et al. Solitary fibrous tumor of the pleura: surgical treatment. Eur J Cardiothorac Surg 2001; 19 (2): 185-9

Received: 21 March 2016
Accepted: 29 April 2016
Correspondence:
Silvia Haddoub
Intensive treatment of diabetes and complications
University Hospital of Parma
E-mail: silviahaddub@gmail.com