Case Report **Open Access**

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Integrated therapeutic approach to Giant Solitary Fibrous Tumor of the Pleura: report of a case and review of the literature

DOI 10.1515/med-2016-0042
received January 5, 2016; accepted March 7, 2015

Abstract: The fibrous tumors of the pleura are rare primary tumors, accounting for 5% of malignant pleural neoplasms, which generally originate from sub-mesothelial mesenchymal tissue of the visceral pleura. These tumours generally exhibit clinical benign behavior although 12% of solitary fibrous tumors can be malignant and have worse outcomes. These tumors are considered "giant" when the lesion > 15 cm. Surgical treatment is the best choice for both benign and malignant neoplasms. We retrospectively analyzed the main case series of giant fibrous tumors of the pleura. In addition we report our experience of a 76-year-old woman treated by pre-surgical embolization involving implantation of vascular plugs. Surgery was successfully carried out without complications; imaging and functional assessment 6 months post intervention demonstrated both the absence of recurrence and improvement of lung function parameters.

Keywords: Solitary fibrous tumor of the pleura (SFTP), Surgical treatment, Embolization, Giant tumors.

1 Introduction

The solitary fibrous tumor of the pleura (SFTP) is a rare neoplasm that originates from sub-mesothelial mesenchymal tissue of pleura [1], and accounts for only 5% of pleural neoplasms. Due to the slow growth of these types of tumor diagnoses are often incidental. The most frequent symptoms are cough, chest pain and dyspnea that are common to several respiratory diseases [2-10]. Less frequent presentations are hemoptysis, obstructive pneumonia, atelectasis and clubbing; some reports have documented cardiac tamponage [11] and respiratory failure [11]. SFPT may rarely present as Doege-Potter syndrome characterized by hypoglycemia due to inappropriate secretion of insulin-like factor II.

Benign fibrous tumors can be defined as giants when diameter is greater than 15 cm or when tumors occupy more than 40% of the hemithorax [12]. These tumors may originate from sub-mesothelial stromal cells exhibiting fibroblastic or myofibroblastic phenotype whose growth are promoted by an aberrant inflammatory reaction as well as hormonal stimuli [12]. Solitary fibrous tumors have a greyish white surface with areas of soft tissue, necrosis and hemorrhage. Sections are macroscopically composed of dense fibrous tissue nodules, which frequently contain cystic structures; a small vascularized peduncle has been described in about 38-50% of cases.

Histological appearance shows spindle cells with round nuclei immersed in a rich stroma of collagen fibers. Peculiar immune histochemical features are cytokeratin-negativity and positivity to vimentin, a marker of mesenchymal cells. CD34 positivity determines exclusion of other lung cancers. Some malignant forms may be

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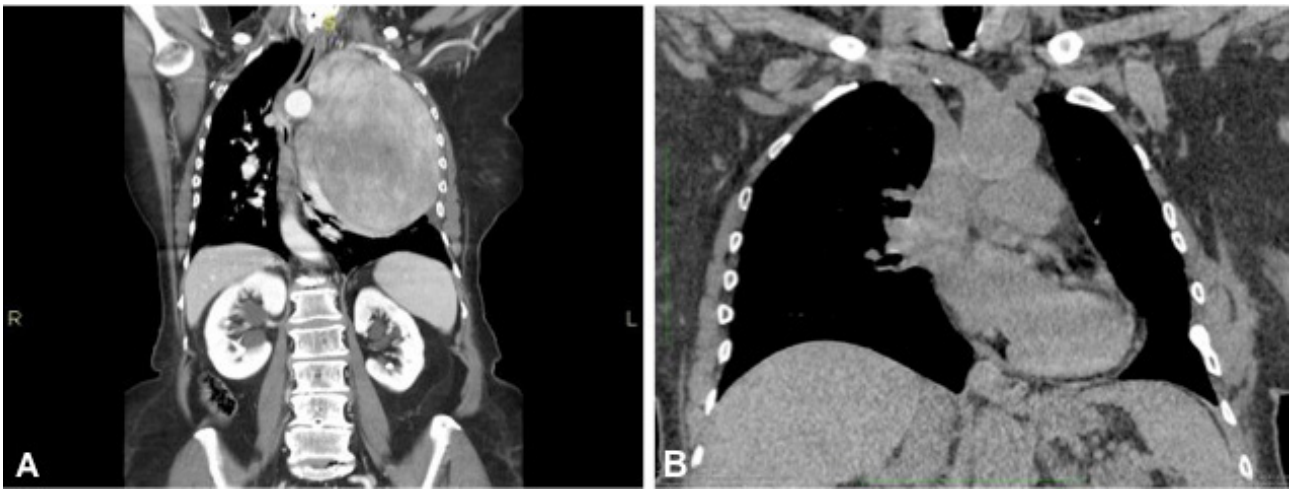

Figure 1: Giant solitary fibrous tumor of the pleura CT-scan (coronal view): pre-surgical assessment (A); post-surgical view (B).

also CD34 negative and exhibit overexpression of Bcl-2, an antiapoptotic proto oncogene [13]. Appearance at CT scans, which is central to diagnosis [14-16] shows these tumors as hypodense or hyperdense compared to muscle density. The attenuation depends on the content of collagen fibers and the possible concomitant presence of hemorrhage, cysts, necrosis or calcification and over half of all benign cases are known to exhibit a heterogeneous enhancement.

At MRI, SFTP are isointense in T1-weighted sequences and exhibit variable intensity on T2. Their rich vascularization and intense enhancement produces a "chocolate chip cookies" appearance. The role of the 18 FDG PET-CT has not been clearly established [15]. Pre-surgical diagnosis requires tissue sampling which is often difficult to achieve using FNAB [17]; tru-cut or core biopsy [18] are therefore also performed.

Surgical excision is gold standard treatment, although intra-operative bleeding is one of the major complications. Preoperative evaluation of vascularity of the tumor is essential in order to optimize surgical management reducing intra and perioperative complications.

Data to support the usage of radiotherapy and chemotherapy in the treatment of SFTPs, which are widely used in thoracic cancers, is insufficiently available [19-23]. Thirty nine case series identifying 82 patients with giant SFTP have been reported in the literature between 1980 and 2014 [17, 24-28]. All cases reported in these series underwent surgical excision. In only 15 patients a preoperative vascularity study was performed. In this subgroup (eight women and seven men), mostly benign tumors were found with an average weight of tumor between 500-4500 g. Age at diagnosis ranged from 38 to 72 years.

The most common symptoms at presentation were dyspnea (87%), chest pain (67%) and chronic cough (60%). Pleural effusion, syncope and osteoarthrodystrophy were less frequent. In all reported cases a CT-guided percutaneous biopsy was performed preoperatively using fine needle aspiration biopsy (FNAB) or Tru-Cut biopsy, although preoperative diagnosis was not always achieved [17,18]. Angiography with collateral embolization was the preferred technique in 14 cases: micro-coils, polyvinyl alcohol granules, spongiosis granules or intravascular plugs were used to reduce vascular supply alone or in combination. CT-angiogram was carried out only once; to improve safety of the procedure and decrease intraoperative bleeding total circulatory arrest was made using cardiopulmonary by-pass. Interestingly, some authors [17] have pointed out that the low-flow cardiac arrest is not useful in management of blood loss due to possible difficulties in recognition of bleeding sources.

In the Pinedo et al. series [24] five subjects underwent preoperative embolization; one case reported paresis of lower right limb from medullary ischemia without further consequences resulting in 16.7% procedure linked intraoperative complication rate. Average intraoperative bleeding was 1908.3 ml. In contrast, blood leakage was lower in Guo et al. series [25] (average value 800 ml); this difference was probably related to timing of surgery after embolization; average delay to surgery was 7 vs 1 day. Other perioperative complications noted were pleural effusion, air leaks and re-dilatation pulmonary edema.

Based on the immunohistochemistry data available, cytokeratins SMA, EMA, S100 and Desmin had a 0% positivity whilst a positivity of 25% was found for BCL2, 62.5% for vimentin and 100% for CD34. In one case D 99 was tested (positive) and CD31 (negative). Malignant lesions, determined by the number of mitosis (4 per microscope field 10X), marked pleomorphism, high cellularity, necrosis and intralesional haemorrhage, accounted for 19% of

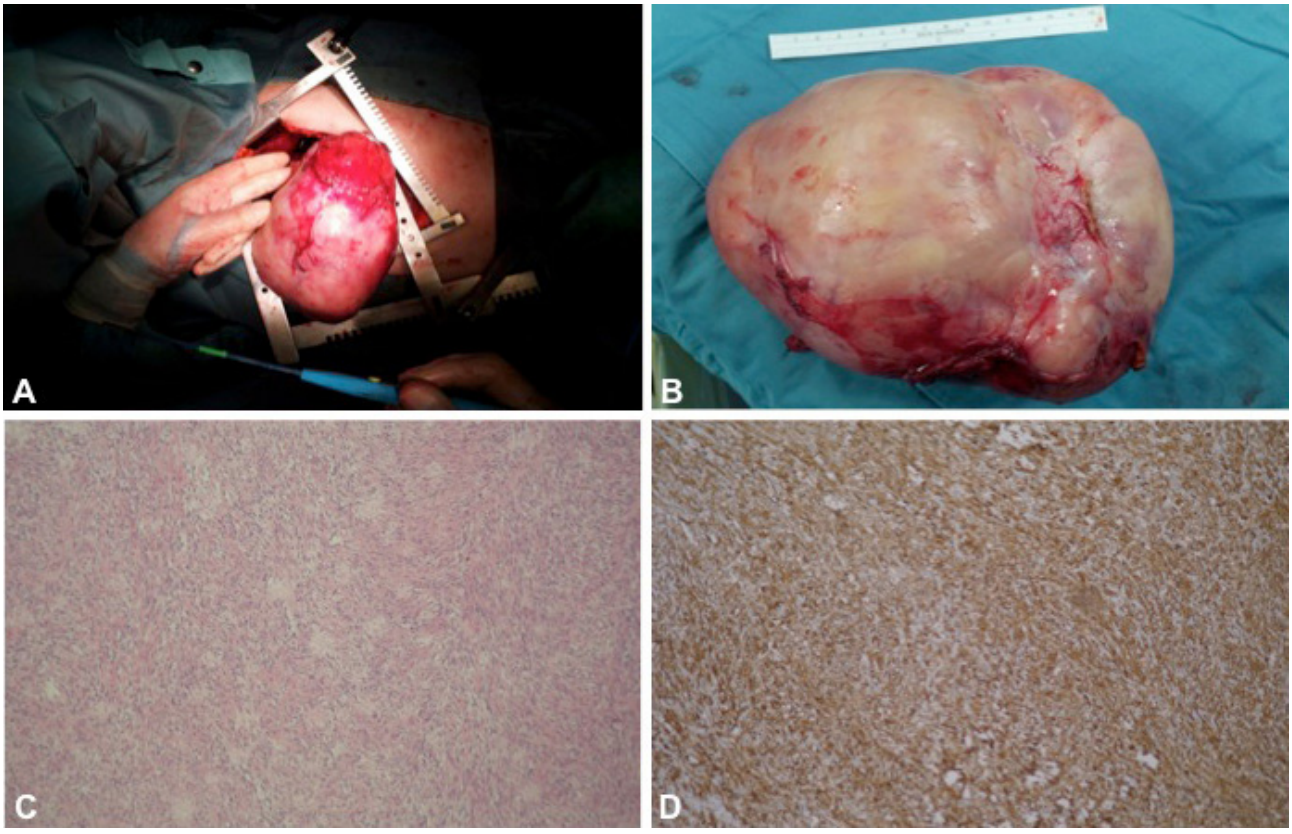

Figure 2: Giant solitary fibrous tumor of the pleura: Surgical excision (A); Surgical specimen removed (B); H&E Staining, Original Magnification x 200 (C); Immunochemistry CD34 staining, Original Magnification x 200 (D).

cases. Amongst 15 cases collected from the literature only one patient in Pinedo et al. series had recurrence resulting in 6.7% overall relapse. Perioperative mortality was 1/15 (6,7%); the only death in this series occurred when low-flow cardiac arrest rather than preoperative embolization was employed. Table 1 summarizes the demographic, clinical and therapeutic features of the cases reported in these series.

2 Case report

A 76-year old female with a medical history of bilateral keratokonus, presented with a 3-month history of increasing breathlessness and left sided chest pain. Radiographic study showed an extensive opacity in the left hemithorax that displaced the contralateral mediastinum. Chest CT scan (Fig. 1) showed the presence of an abnormal solid mass occupying the left hemithorax (craniocaudal diameter of 15 cm.) with defined margins and consensual pleural and pericardial effusion.

Pre-surgical histological samples were obtained through true-cut under CT guidance. Tissues were composed of spindle cells with a thin fibrovascular stroma and scattered myxoid-like areas in the absence of necrosis and appreciable mitotic index; immunohistochemistry was positive for vimentin, CD34, and CD99 BLC2. Hematological routine exams showed no relevant abnormalities. Respiratory functional study showed a severe restrictive ventilatory pattern causing a mild hypoxemia.

The patient underwent angiography, which showed multiple arterial streams, the mass supplied by two bulky collaterals originating from left side subclavian artery and by a peripheral branch of the internal left mammary artery. During the procedure embolization of the collateral vessels originating from the subclavian was performed using Amplatzer Vascular Plug system device IV 5mm in the first collateral and Amplatzer Vascular Plug IV and 4 mm in the second. The collateral deriving from the left internal mammary artery was embolized by implantation of spiral-controlled detachment Cook 3-PDA-5.

Forty-eight hours following embolization the patient underwent surgical resection: a left lateral thoracotomy approach was employed with dual access to the pleural cavity through the 3rd and 6th intercostal space. The tumour was partially adherent to the parietal pleura, via

a large pedunculated and highly vascularized appendix, from where it appeared to originate. Cautious mobilization manoeuvers demonstrated strong adhesions to the upper lung lobe, which was partially torn, and the mediastinum and lower lobe from which it was excised by apical sub-segmentectomy.

The tumor was partially attached to the adventitia of the aortic arch from which it was also excised. A large lymph node station 9 was finally removed. (Fig. 2). The surgical procedure was completed without complications in the peri- and post-operative period. In our case, despite the delay, as opposed to the recommendations in the literature, which suggests a maximum time of 24 hours between collaterals embolization and surgical resection, has not led to the feared risk of bleeding. Imaging and functional reassessment, carried out 90 days after surgery, showed re-expansion of the lung parenchyma and an improvement of all functional parameters (FEV1pre-FEV1po: 41% vs 78% thth; CVpre-CVpo 39% vs 75 th % th; VO2peak pre-VO2peak po: 38% vs 50% th).

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

Informed consent: Informed consent has been obtained from all individuals included in this study.

3 Discussion

Solitary fibrous tumors of the pleura are rare primary tumors with heterogeneous clinical onset, which have represented, over the years, a complex disease entity. Clinical diagnosis is challenging as symptoms may mimic both benign and neoplastic lung disease. Immunohistochemistry techniques and electronic microscopy determine its mesenchymal origin, differentiating it from other diseases of the pleura [11-13].

A precise definition of giant fibrous tumor has not been clarified. Although molecular profiling technologies to assess DNA, RNA, protein and metabolites have led to better understanding of molecular basis of cancers [29-50], research on SFTP has been limited. Complete surgical resection is the mainstay of treatment, which significantly impacts prognosis [51-53]. Local recurrence can occur in malignant cases, but is very rare in solitary benign tumors; it may be a result of an incomplete or conservative surgery, lack of identification of a tumor during the operation or a growth of a synchronous neoplasm independent from that removed [51,52].

Video Assisted Thoracoscopic Surgery (VATS) is indicated for lesions less than 5 cm of diameter. Size of the tumor, relationship with adjacent structures and identification of the vascular peduncle may be challenging also in surgical resection. The blood supply of the tumor is most often guaranteed by collateral branches from phrenic artery, the intercostal arteries, and internal mammary and bronchial arteries [51,52]. Unlike other techniques [54], using micro-coils, polyvinyl alcohol granules or spongiosis granules, the embolization technique used in our case involves implantation of vascular plugs. These consist of a steel wire with strands-filaments of dacron and are able to occlude a vessel through the formation of thrombus and have been shown to reduce procedure time and radiation exposure.

4 Conclusion

Our experience suggests that preoperative embolization has an important role in management of giant chest tumors. Difficulties in diagnosis and therapeutic management of SFTP highlight the importance of a multidisciplinary approach to this disease including pulmonologist, thoracic surgeon, interventional cardiologist, radiologist and pathologist. This integrated approach represents the optimal strategy to ensure best diagnostic and prognostic outcomes for patients suffering from this type of pathology.

Conflict of interest statement: Authors state no conflict of interest.

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