ELSEVIER

INTERNATIONAL JOURNAL OF SURGERY

www.theijs.com

Localized (solitary) fibrous tumors of the pleura: An analysis of 15 patients

Valerio Perna[a,*], *Francisco Rivas*[a], *Ricardo Morera*[a], *Josep Saumench*[a], *Ricard Ramos*[a], *Ivan Macia*[a], *Anna Ureña*[a], *Ignacio Escobar*[a], *Rosa Villalonga*[b], *Juan Moya*[a]

[a]*Hospital Universitario de Bellvitge, Thoracic Surgery Department, Feixa Llarga s/n, L'Hospitalet de Llobregat, Barcelona 08907, Spain*
[b]*Hospital Universitario de Bellvitge, Anesthesiology Department, Barcelona, Spain*

ARTICLE INFO

Article history:
Received 13 April 2008
Accepted 23 April 2008
Published online 1 May 2008

Keywords:
Pleura
Fibrous tumor
Surgery
Adjuvant/neoadjuvant therapy

ABSTRACT

Background: Localized fibrous tumors of the pleura (LFTPs) are rare neoplasms, which are considered to originate from submesothelial connective tissue. The aim of this article is to present 15 new cases because of their different clinical behaviors and to discuss the treatment of choice of such neoplasms.

Methods: The records of 15 consecutive patients with LFTP operated at our Institution between 1995 and 2006 were retrospectively reviewed. Diagnostic procedures, clinical courses, and outcomes of these patients were studied. Total excision through a thoracotomy was performed in all patients. Neoplasms were considered to be malignant if one or more of the following histologic features were present: increasing mitotic activity; high cellularity with crowding and overlapping of nuclei; necrosis; and pleomorphism.

Results: No operative mortality was reported. The mean follow-up time was 76 months. Malignant transformation was seen in 1 patient 26 months after resection of a benign tumor. Six cases were pathologically considered to be malignant: 2 patients developed local recurrence. One of these underwent redo-surgery and required pneumonectomy; in the other one surgery is not indicated because at the time of diagnosis the patient was 85 years. Currently, all patients are alive and 13 disease-free.

Conclusions: For histologically benign tumors, because of the risk of recurrence and malignant transformation, complete surgical resection is indicated and long-term follow-up is recommended in all patients. For malignant cases, complete surgical resection may be insufficient for the cure: further study should be performed to identify reliable prognostic factors to indicate and evaluate the effectiveness of systemic treatment.

1. Introduction

Localized fibrous tumors of the pleura (LFTPs) are rare, slow-growing neoplasms with about 900 cases reported in the literature to date.[1] LFTPs can usually be distinguished from malignant mesothelioma by their radiographic features, gross appearance (often pedunculated), immunohistologic characteristic (negative for cytokeratin expression and positive for CD34), and ultrastructural characteristic. Thirteen percent of reported tumors had aggressive clinical behavior with local infiltration and local recurrence or distant metastasis. The remaining 87% had benign clinical behavior and were resected completely, including adjacent structures if necessary, which is generally believed to be sufficient treatment.[2] The aim of

* *Corresponding author*. Tel.: +34 627717119.
E-mail address: v.perna@hotmail.com (V. Perna).
1743-9191/$ – see front matter © 2008 Surgical Associates Ltd. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.ijsu.2008.04.005

this article is to present 15 new cases operated at our Institution because of their different clinical behaviors and to discuss the treatment of choice of such neoplasms.

2. Material and methods

The records of 15 consecutive patients with LFTPs (3 men, 12 women) operated at our Institution between 1995 and 2006 were retrospectively reviewed. The mean age was 51.5 years (range, 29–82 years). We reexamined pathologic slides, and malignant LFTP was diagnosed when one of following criteria was satisfied[3]: increasing mitotic activity (>4 mitoses per 10 high-power fields); high cellularity with crowding and overlapping of nuclei; presence of necrosis; and mild, moderate, or marked pleomorphism. To differentiate the cell origin of resected tumors, we performed immunostaining for a panel of cell markers including vimentin, CD34, cytokeratin, and S-100.[4,5] History taking, a physical examination, a routine blood test, standard chest radiography, electrocardiography, and a thoracic computed tomographic (CT) scan were available for all patients. Fiberoptic bronchoscopy was performed in 12 patients. In all of them, extrinsic compression of segmental bronchi was observed, but no endobronchial lesion was detected. CT guided aspiration biopsy was performed in 9 patients: in 4 patients, histologic examination revealed benign appearing spindle cells and this suggested diagnosis of benign pleural fibrous tumor; in 1 patient the specimen suggested sclerosing hemangioma of the lung; in 4 patients specimens were not significant. Chest pain (in 2 patients), dyspnea (in 3 patients), cough (in 1 patient), and hemoptysis (in 2 patients) were the symptoms. Eight patients were symptom-free. No patient had asbestos exposure. Two patients showed associated disease: breast carcinoma and endometrial squamous cell carcinoma. Operative mortality was defined as death within 30 days of an operation or during hospitalization. Recent patient status was determined by using the clinical records of outpatient clinics or by telephone interview.

3. Results

Surgical excision was performed by posterolateral thoracotomy in all patients. There was no operative morbidity or mortality. The largest mass excised in our patients was $23 \times 20 \times 18$ cm and 3000 g (Fig. 1). Four of the cases were based on the visceral pleura and 11 arose from the parietal pleura. Three tumors were pedunculated on visceral pleura-based pedicles. Among tumors arising from the visceral pleura, one showed a prevalent intrapulmonary growth (the so-called inverted fibroma). For tumors related to the visceral pleura, the resection was performed by wedge resection. One

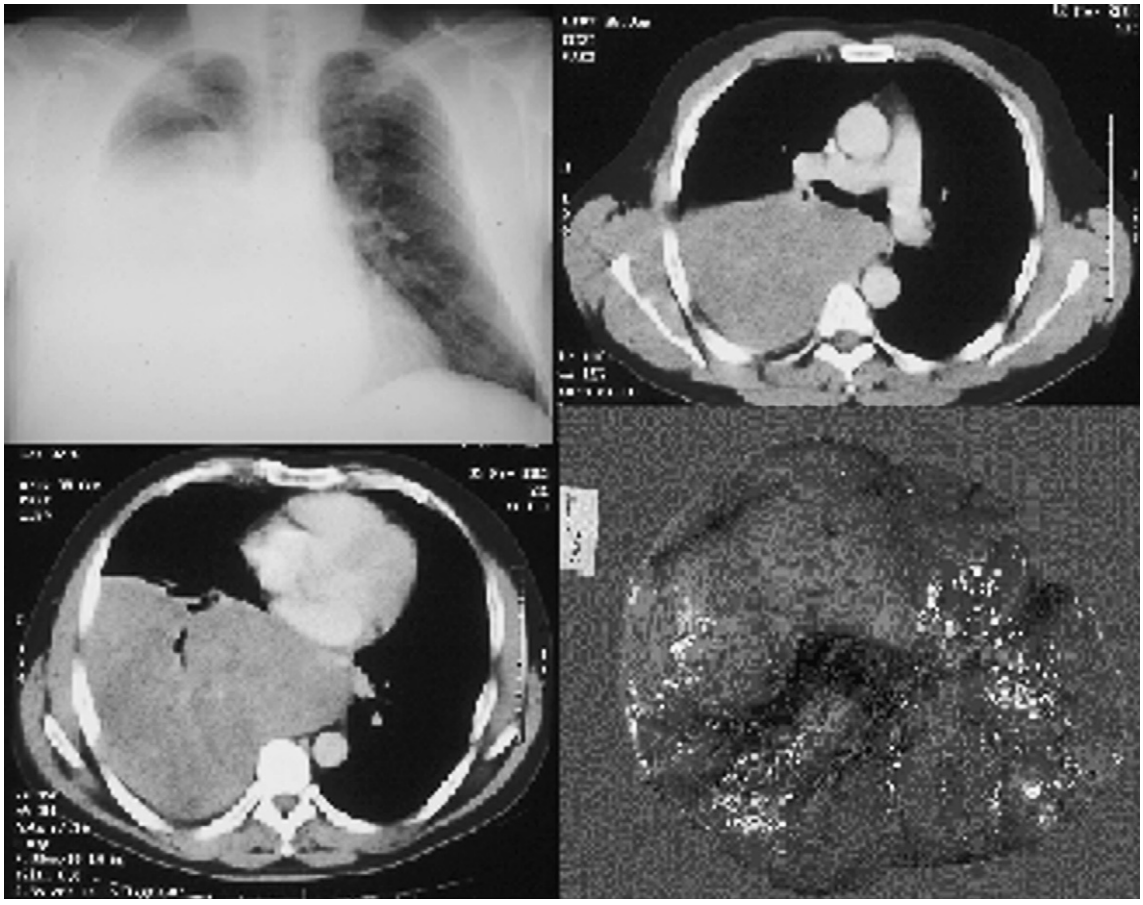

Fig. 1 – Chest roentgenogram (top left). Computed tomogram revealing a broad-based mass on the parietal pleura (top right and bottom left). Gross morphologic image of the mass (bottom right).

lobectomy was performed due to an intraparenchymal extension of the tumor (inverted fibroma). Tumors arising from the parietal pleura, even if not invading the chest wall, obliged the surgeon to be more accurate during resection particularly in the control of possible bleeding related to the extrapleural dissection. Chest-wall resection was required in 2 cases. Complete tumor resection as evidenced by pathologic examinations was obtained in all cases. There were 9 pathologically benign LFTP cases, and 6 malignant LFTP cases. Details about malignity criteria are reported in Table 1. All tumors stained positively for CD34 and vimentin but negatively for keratin, and S-100. No adjuvant therapy was used. The mean follow-up time for benign LFTP was 73.2 months and that for malignant was 78.6 months. Among malignant LFTP cases, 2 developed local recurrence. One of these underwent redo-surgery and required pneumonectomy; in the other one surgery is not indicated because at the time of diagnosis the patient was 85 years. Malignant transformation was seen in 1 patient 26 months after resection of a benign tumor. Rethoracotomy revealed multiple pleural and lung metastasis. The patient received postoperative radiotherapy and is currently alive (follow-up 19 months).

4. Comment

LFTPs are uncommon, representing less than 5% of all neoplasms involving the pleura.[6] LFTPs show no gender predilection.[7] In our series, there was a marked female predilection (12 female and 3 male) and, according to the literature, no cases were observed in childhood.

The usual presentation is an asymptomatic mass discovered incidentally on a chest radiograph.[8] Symptoms, if any, tend to be more common in larger lesions with malignant histological features and include either local symptoms, such as chest pain, cough, dyspnea, and more rarely hemoptysis (in our series, 2 cases), or systemic symptoms, such as weakness, nocturnal sweating, chills, weight loss, digital clubbing, hypertrophic osteoarthropathy, and hypoglycemia.[9] In our series, there was no correlation between symptoms and the presence of malignancy (Table 2). When symptoms are present regressing completely after surgical resection,[10] as observed in our patients.

CT guided aspiration biopsy is not a reliable diagnostic tool[11]; in fact, only 4 of 9 cases (45%) were identified by CT guided aspiration biopsy. Surgical resection for diagnosis and treatment is acceptable if the patient is operable, because operative morbidity and mortality are very small.

The great majority of LFTPs have a benign clinical outcome with a long-term disease-free survival in around 90% of the cases. The single best predictor of a benign course was the complete excision with microscopically free surgical margins.[12] Intraoperative examination of the surgical margins is therefore mandatory. Approximately 10% of the benign LFTPs recur with malignant change rarely supervening (<0.5%).[2] In our series, malignant transformation was seen in 1 patient 26 months after resection of a benign tumor. Probably it was the first case in the literature with multiple pleural and lung metastases and it was impossible to perform a complete resection.

Table 1 – Malignity criteria among the 6 malignant tumors

Criterion of malignity	No. of tumors
Increasing mitotic activity	4
High cellularity	2
Presence of necrosis	4
Pleomorphism	3

Table 2 – Malignant versus benign LFTP

	Malignant	Benign
Male	0	3
Female	6	6
Mean age	63.5	50.3
Visceral pleura origin and pedunculated morphology	2	1
Parietal pleura origin and sessile morphology	4	7
Presence of symptoms	1	6

In our study, 4 out of the 11 tumors with an origin from the parietal pleura and a sessile morphology had malignant histological features; in the same way, 2 out of the 4 tumors with an origin from the visceral pleura and a pedunculated morphology had malignant histological features (Table 2). Among malignant LFTP cases, developed local recurrence a tumor with an origin from the parietal pleura and a sessile morphology and a tumor with an origin from the visceral pleura and a pedunculated morphology: our data partially confirm the findings of other authors[1,12] of a more aggressive behavior of LFTP with an origin from the parietal pleura and a sessile morphology.

Tumor size has been reported as being a prognostic factor,[13] since larger LFTPs tend to have malignant histological features and a worse prognosis. In our study, 4 out of the 9 tumors with benign histological features and 4 out of the 6 tumors with malignant histological features were over 10 cm in diameter; we also classified a 23 cm tumor as benign, which indicates that large size is not necessarily a marker of malignancy.

We observed the expression of CD34 and vimentin in all tumors, which confirm the role of these markers in diagnosing LFTP.[14]

Surgical treatment is associated with favorable results, with 10-year survival rates varying from 75%[14] to 94%.[3] We observed a 5-year survival rate of 100% and a 5-year disease-free survival rate of 80%, which is in accordance with previous reports.[3,12,14]

The role of adjuvant treatments for LFTP has been only partially investigated, although radio and chemotherapy have shown to be effective in treating selected patients.[15] For malignant cases, complete surgical resection may be insufficient for the cure: preoperative or postoperative systemic therapy should be considered in selected patients who have the highest risk of recurrence.

However, as observed in part in our series, currently there are no reliable prognostic factors that allow selecting this type of patients.

In conclusion, although LFTPs are considered histologically benign tumors, because of the risk of recurrence and malignant transformation, complete surgical resection is indicated and long-term follow-up is recommended in all patients. Further studies are required to identify reliable prognostic factors and multicenter trials to evaluate the effectiveness of preoperative or postoperative systemic therapy.

Conflict of interest
None to declare.

Funding
None.

Ethical approval
Not required.

REFERENCES

1. Sung SH, Chang JW, Kim J, Lee KS, Han J, Park SI. Solitary fibrous tumors of the pleura: surgical outcome and clinical course. *Ann Thorac Surg* 2005;**79**:303–7.
2. Altinok T, Topçu S, Tastepe AI, Yazici U, Çetin G. Localized fibrous tumors of the pleura: clinical and surgical evaluation. *Ann Thorac Surg* 2003;**76**:892–5.
3. Magdeleinat P, Alifano M, Petino A, Le Rochais GP, Dulmet E, Galateau F, et al. Solitary fibrous tumors of the pleura: clinical characteristics, surgical treatment and outcome. *Eur J Cardiothorac Surg* 2002;**21**:1087–93.
4. Hanau CA, Miettinen M. Solitary fibrous tumor: histological and immunohistochemical spectrum of benign and malignant variants presenting at different sites. *Hum Pathol* 1995;**26**:440–9.
5. Flint AQ, Weiss SW. CD-34 and keratin expression distinguishes solitary fibrous tumor (fibromesothelioma) of pleura from desmoplastic mesothelioma. *Hum Pathol* 1995; **26**(4):428–31.
6. Akman C, Cetinkaya S, Ulus S, Kaynak K, Oz B. Pedunculated localized fibrous tumor of the pleura presenting as a moving chest mass. *South Med J* 2005;**98**(4):486–8.
7. Cardillo G, Facciolo F, Cavazzana A, Capece G, Gasparri R, Martelli M. Localized (solitary) fibrous tumors of the pleura: an analysis of 55 patients. *Ann Thorac Surg* 2000;**70**: 1808–12.
8. Chong S, Kim TS, Cho EY, Kim J, Kim H. Benign localized fibrous tumour of the pleura: CT features with histopathological correlations. *Clin Radiol* 2006;**61**(10):875–82.
9. Balduyck B, Lauwers P, Govaert K, Hendriks J, De Maeseneer M, Van Schil P. Solitary fibrous tumor of the pleura with associated hypoglycemia: Doege–Potter syndrome: a case report. *J Thorac Oncol* 2006;**1**(6):588–90.
10. Rena O, Filosso PL, Papalia E, Molinatti M, Di Marzio P, Maggi G, et al. Solitary fibrous tumour of the pleura: surgical treatment. *Eur J Cardiothorac Surg* 2001;**19**(2):185–9.
11. Santos RS, Haddad R, Lima CE, Liu YL, Misztal M, Ferreira T, 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.
12. Carretta A, Bandiera A, Melloni G, Ciriaco P, Arrigoni G, Rizzo N, et al. Solitary fibrous tumour of the pleura: immunohistochemical analysis and evaluation of prognostic factors after surgical treatment. *J Surg Oncol* 2006; **94**(1):40–4.
13. England DM, Hochholzer L, McCarthy M. Localized benign and malignant fibrous tumors of the pleura. A clinicopathologic review of 223 cases. *Am J Surg Pathol* 1989; **13**:640–58.
14. Brozzetti S, D'Andrea N, Limiti MR, Pisanelli MC, De Angelis R, Cavallaro A. Clinical behavior of solitary fibrous tumors of the pleura. An immunohistochemical study. *Anticancer Res* 2000; **20**:4701–6.
15. Veronesi G, Spaggiari L, Mazzarol G, De Pas M, Leo F, Solli P, et al. Huge malignant localized fibrous tumor of the pleura. *J Cardiovasc Surg* 2000;**41**:781–4.