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Inflammatory Myofibroblastic Tumor of the Lung: Case Series

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ABSTRACT

Background: *Inflammatory myofibroblastic tumor is a rare occurrence in general practice. Its biologic nature, natural history and response to different treatment modalities are obscure.*

Materials and Methods: *We retrospectively reviewed clinical and pathological features of 5 patients with inflammatory myofibroblastic tumor of the lung observed between 1999 and 2006.*

Results: *Under-study patients were 3 women and 2 men with a median age of 32.6 years. All patients were symptomatic. Computed tomography (CT) scan demonstrated a mass in all cases. Four patients underwent surgery (tumor resection in 1, lobectomy in 1, bilobectomy in 1 and lobectomy with mediastinal mass debulking also in 1). Complete resection was achieved in 2 patients who are currently alive with no evidence of disease. One died due to progressive disease. Another is alive with disease after incomplete resection, and one refused any kind of surgery. There was no operative mortality. All patients were under follow-up (range, 5 to 60 months; median 39 months).*

Conclusion: *This study illustrates that some inflammatory myofibroblastic tumors behave aggressively and have a poor prognosis. It also confirms that radical resection is the treatment of choice for this malignancy.* ***(Tanaffos 2009; 8(1):68-74)***

Key words: *Inflammatory myofibroblastic tumor, Inflammatory pseudotumor, Lung tumor*

INTRODUCTION

Inflammatory myofibroblastic tumor (IMT) is a spindle cell proliferation with a characteristic fibro-inflammatory appearance (1). A wide variety of names has been applied to this tumor including plasma cell granuloma (created by Bahadori and Liebow in 1984), inflammatory pseudotumor, xanthomathous pseudotumor, fibrous histiocytoma and mast cell granuloma (2,3). This rare occurrence was initially recognized in the lungs, but now has been described in most organs and anatomic sites (1).

Although this tumor has been described as non-neoplastic, it includes a spectrum of lesions ranging from benign masses to frankly malignant sarcomas and represents an aberrant inflammatory response despite its gross and microscopic features as a spindle cell neoplasm (1, 4, 5). In pulmonary IMT a history of antecedent respiratory infection is some

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times elicited and progression from organizing pneumonia has been described (6, 7). It has been suggested that the lesions commence as a chronic interstitial pneumonia of viral etiology (6). There may be an association with Epstein-Barr virus, human herpes virus-8, and over production of IL-6 (8, 9, 10). Meanwhile, IgG4-positive plasma cells may also have a role in the development of IMT (11).

The age range stretches from the first year of life to the eighth decade but most patients are less than 40 years old and many are children (2, 6). Although it is an uncommon lesion in general practice (12), this lesion is one of the most common primary lung tumors seen in young people (13). Both sexes are equally affected and no significant racial or geographical differences have been noted. Approximately half the patients are asymptomatic with the lesion being discovered as an incidental radiological finding. Symptomatic patients complain of cough, hemoptysis, shortness of breath and chest pain, sometimes accompanied by systemic features, namely low-grade fever and weight loss that are possibly related to interleukin production by the lesion (3, 12).

Abnormal laboratory findings in some cases include microcytic hypochromic anemia and raised erythrocyte sedimentation rate (ESR) (3).

Chest roentgenograms typically disclose a solitary, sharply marginated, round or oval tumefactive mass, although the edges of the lesions are blurred and said to be more ill defined as they attain large sizes. Some of the proliferations can involve parietal pleural surfaces, suggesting the possibility of malignancy (12). Focal calcification and multiple nodules have also been reported (14). The differential diagnosis for a solitary mass of the lung should include IMT, particularly in an infant (15). The pathologic differential diagnosis of pulmonary IMT includes sclerosing pneumocytoma, plasmacytoma, localized organizing pneumonia, amyloid tumor, hyalinizing granuloma, malignant fibrous histiocytoma and spindle cell carcinoma (3, 16).

MATERIALS AND METHODS

We retrospectively reviewed the clinical data of five cases that were consulted by the oncology department between 1999 and 2006. The histological specimens were reviewed again by two pathologists and the diagnosis of inflammatory myofibroblastic tumor was confirmed. The clinical and paraclinical findings of the patients are as follows:

Case 1:

A 48- year-old female was evaluated for a 2-month history of progressive dyspnea and right-sided chest pain. On chest X-ray a right upper lobe mass with ipsilateral effusion was detected.

The mass was completely resected and no adjuvant treatment was recommended. Two years after surgery she developed breast cancer. She underwent modified radical mastectomy, and received 6 cycles of anthracycline-based chemotherapy. After 4 years and 8 months of follow-up, she is well without any evidence of disease.

Case 2:

A 50- year-old male with complaints of cough, sputum production, fever, dyspnea and weight loss for 2 months was referred to the pulmonary clinic. Upon workup, chest X-ray and CT scan demonstrated air space pulmonary consolidation with air bronchogram in the right upper lobe as well as right sided hilar and para-tracheal lymphadenopathy (Figure 1). Bronchoalveolar lavage (BAL) and CT guided biopsy failed to make a definitive diagnosis and the patient underwent thoracotomy. Due to the location of the mass, diffuse fibrosis and adhesive fibrotic bands between the upper and middle lobes, a bilobectomy was performed. After five years of follow up, the patient is alive with no evidence of recurrence.

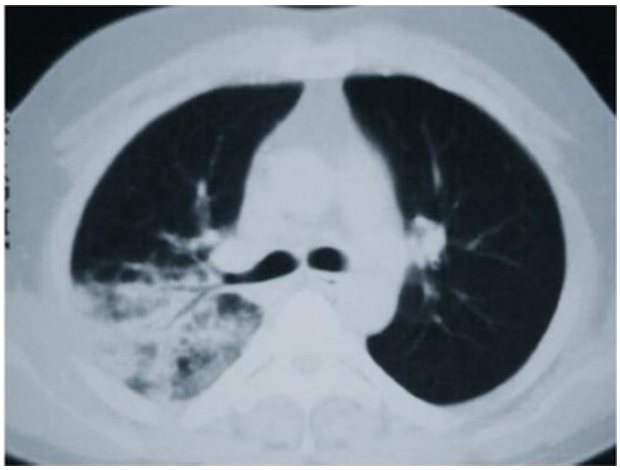

Figure 1. Case 2. CT scan (lung window) shows pulmonary consolidation in right upper lobe

Case 3:

A 32- year- old female with dyspnea and weight loss for 3 months demonstrated a mediastinal mass on chest X-ray. CT scan indicated a mediastinal mass with extension to the posterior mediastinum and right hilum (Figure 2). Right paratracheal calcification was also noted.

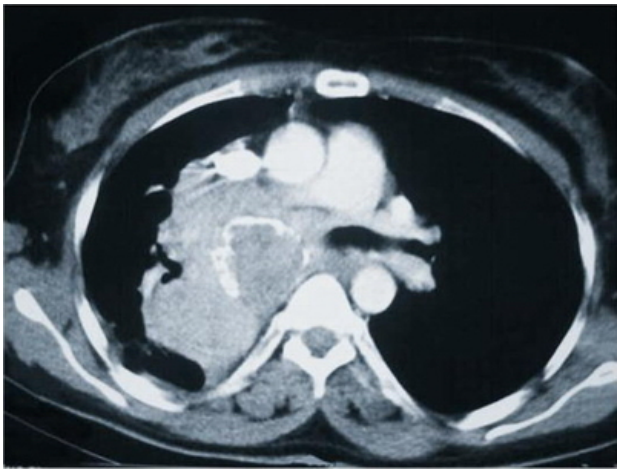

Figure 2. Case 3: CT scan (mediastinal window) shows large solid mediastinal mass that extends to the right lung. Calcification is also present.

The patient underwent a right lower lobe lobectomy and debulking of the mediastinal mass with residual disease left in the mediastinum. Radical surgery was not attempted because of extensive mediastinal involvement. She refused any adjuvant treatment. On follow up eight months after surgery, radiological recurrence of the tumor was detected and the patient became symptomatic 4 months later. This time she also complained of hoarseness and dysphagia. On bronchoscopy, the right main bronchus was 90% occluded by the tumor. The left main bronchus was also involved. Histological specimen reconfirmed the diagnosis of IMT. She was treated with laser therapy followed by localized radiotherapy.

Twenty-three months after the initial diagnosis, she is only under close observation, with stable pulmonary complaints.

Case 4:

A 14 -year-old female with a 5-month history of cough, sputum production, hemoptysis, and weight loss was admitted for further evaluation. On chest CT-scan, a large pleural-based calcified mass was detected in the right upper lobe with extension to the paramediastinal space (Figure 3). The patient underwent a right upper lobe resection and mediastinal lymphadenectomy.

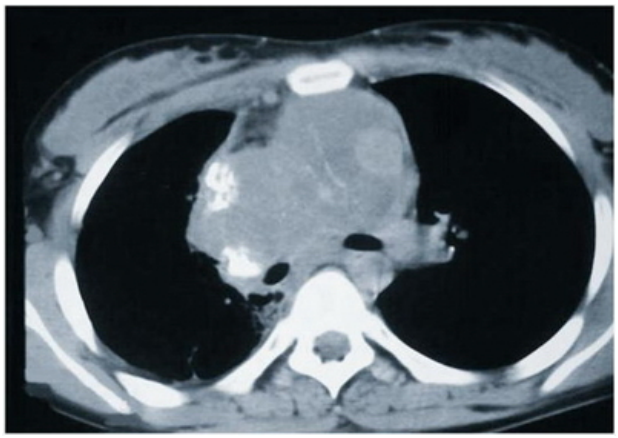

Figure 3. Case 4. CT scan (mediastinal window) shows large soft tissue mass in the medial part of the right upper lobe that invades in the mediastinum. Multiple irregular calcifications are noted within this mass.

After 2 years, the patient had a local endothoracic relapse. This time, CT scan demonstrated a large irregular, heterogeneous mediastinal mass with invasion to the superior vena cava (SVC) and

pulmonary artery. There was also another right lower lobe mass with extension to the pericardium and accompanied pericardial effusion. The abdominal CT revealed hepatomegaly and ascites.

Surgery was not attempted due to diffuse involvement. Meanwhile, she rapidly developed SVC syndrome and cardiac tamponade. The patient underwent pericardial window insertion and was referred for mediastinal radiotherapy. The patient underwent eight courses of CHOP chemotherapy with partial response. Two months after termination of chemotherapy, she showed progressive disease and was treated with salvage chemotherapy (ICE regimen).

She did not respond to chemotherapy and succumbed 4 years and 3 months after the first diagnosis.

Case 5:

A 19- year-old male with intermittent dyspnea for 1 year and one episode of hemoptysis was discovered to have a left hilar mass on chest CT scan. On bronchoscopy, the left main bronchus had a polypoid mass, which was biopsied and reported as an IMT.

The patient was scheduled for surgery, but he refused any form of surgical intervention. After five months of follow-up, the mass is stable in size on chest X-ray.

DISCUSSION

IMT is a tumor with no sex predilection that can occur in any age group, but over half the patients are less than 40 years of age (17). Among our five cases, 3 were women and 2 were men. Since pediatric thoracic surgeries are not routinely performed in our hospital, the age range was between 14 and 50 years with a median of 32.6 yrs. Contrary to other case reports, the patients were all symptomatic in our series (3, 18). Four out of five cases complained of dyspnea (80%).

Other symptoms included sputum production (60%), cough (40%), hemoptysis (40%) and weight loss (60%). Routine laboratory examination was done for all patients. Only one patient was reported to have an elevated ESR and two had hypochromic microcytic anemia, which did not appear to correlate with the extent or prognosis of the disease. There was no specific abnormal finding in laboratory studies.

The standard procedure, for both diagnosis and treatment, is surgical resection. The extent of resection is generally minimized to preserve lung function (4, 14, 17).

Bronchoscopy is rarely successful as a diagnostic procedure because endobronchial inflammatory tumors account for less than five percent of cases (18, 19). In our series, only one patient was diagnosed by bronchoscopy and the remaining four were diagnosed by tumor resection and/or lobectomy.

The radiological appearance of the pulmonary myofibroblastic tumor is typically a solitary, slow-growing circumscribed mass of variable size with a lobulated or speculated border (Case 1). The tumor can present as multiple masses and sometimes as diffuse or lobar pneumonitis (Case 2). Local invasion (Case 4), primary involvement of the mediastinum (Case 3), and hilar structures (Case 5) are unusual manifestations (20). Involvement or compression of a proximal bronchus can cause atelectasis (21). Commonly heterogeneous or homogenous enhancement is noted on CT-scan. Calcification is unusual, occurring more frequently in pulmonary and mediastinal IMT of children (Cases 3 and 4) (22, 23). Cavitation is a rare finding in this disease (18); hence, CT-scan results have been characterized as variable and nonspecific. In our series, CT-scan did not lead to a specific diagnosis and all patients were suspected of lung cancer or

carcinoid tumor as the initial diagnosis. At the time of presentation or follow up, no patient had extra-thoracic involvement. Metastatic or progressive disease outside the thoracic cage has been reported for primary pulmonary IMT. This could be due to originally sarcomatoid lesions or a sarcomatous transformation in the tumor (4) (Figure 1-3).

Except for one case, all patients underwent surgery. Tumor resection, lobectomy, bilobectomy, and lobectomy with mediastinal mass debulking were each performed in one case. In our series, complete resection was achieved in two patients, and was not feasible in two other patients. There was no operative mortality.

The final diagnosis was made based on the resected specimen in four cases. Generally, all of these tumors were composed of spindle cell proliferation arranged in fascicles with variable degrees of lympho - plasmocytic infiltration on H & E staining slides (Figure 4). The diagnosis of all IMTs of the lung presented in this study was always supported not only by their morphologic characteristics but also by their immunophenotypic features (Table 1).

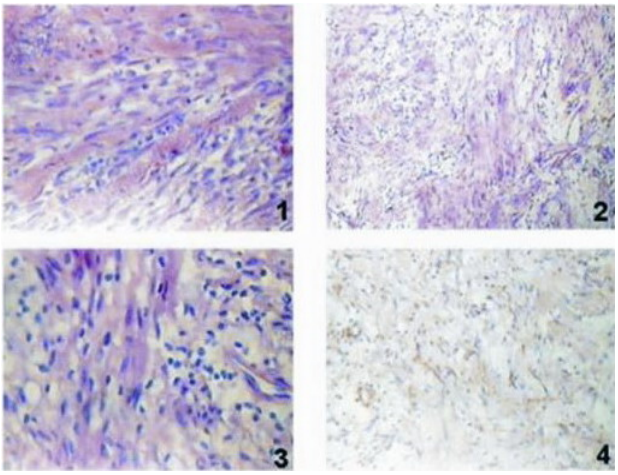

Figure 4. Bland looking spindle cell proliferation with collagenous stroma, containing lympho-plasmocytic inflammatory cells (1,2,3, in H& E staining). Immunohistochemistry staining revealed SMA positivity of spindle cells (4).

Table 1. The pathological characteristics of five patients with "Inflammatory Myofibroblastic Tumor" of the lung. SMA: Smooth muscle actin, EMA: epithelial membrane antigen

Case	Specimen	Immunohistochemistry stainings		Subclassification
1	Right upper lobe mass	CD34 (-) EMA (-) Cytokeratin (-)	SMA (+) Desmin (-)	Fibrohistiocytic
2	Lobectomy	Cytokeratin (-) EMA (-) CD68 (+)	Desmin (-) SMA (+) CD 34 (-)	Lymphohistiocytic
3	Right lower lobectomy and mediastinal mass	Cytokeratin (-) EMA (-) CD34 (-) S_{100} (-)	CD68 (+) Focal Desmin (+)Focal Actin (+) Focal SMA (+)	Fibrohistiocytic
4	Mediastinal mass and lobectomy	Cytokeratin (-) EMA (-) S_{100} (-) Desmin (-)	Actin (+) CD68 (+) CD34 (-) SMA (+)	Fibrohistiocytic
5	Rigid bronchial biopsy	SMA (+) Actin (+) Vimentin (+) Cytokeratin (-)	EMA (-) Desmin (-) CD34 (-) CD68 (+)	Fibrohistiocytic

The histologic types according to the Matsubara and associates criteria were "fibrohistiocytic" in four cases and "lymphohistiocytic" in one case (24). The immunohistochemical investigations showed generally positive staining for smooth muscle actin and negative results for cytokeratin, epithelial membrane antigen, desmin and CD34. Variable degrees of positivity for CD68 and/or muscle specific actin were also evident. These findings can exclude other morphological differential diagnoses. The above mentioned immunophenotypic features are consistent with the myofibroblastic differentiation in these tumors. We did not test cytoplasmic anaplastic lymphoma kinase (ALK), but it has been reported that expression of ALK in pulmonary examples favors a neoplastic basis (3) (figure 4).

All patients were under regular follow-up (range 5

to 60 months; median: 39 months). The two patients with complete resections are currently alive with no evidence of recurrence for more than 4 years (cases 1 and 2). One is alive with evidence of stable disease after 23 months (case 3). One patient died as the result of disease progression (case 4). She showed an extensive mediastinal and RLL relapse with SVC, pulmonary artery and pericardial invasion.

In our study, two cases received palliative mediastinal radiotherapy and only one case underwent chemotherapy.

CONCLUSION

In recent years, IMT of the lung with considerable biologic aggressiveness and unfavorable evolution has been described with increasing frequency.

Some series have shown that a significant number of patients with IMT of the lung have a poor prognosis which confirms the need for radical resection in treatment of this unusual entity (4). Death is secondary to local relapse with infiltration of the mediastinal organs or rarely due to distant metastases. It seems that incomplete resection is the major prognostic factor for both complications and mortality. The prognosis of patients who undergo radical resection is excellent (4).

In conclusion, in this study IMT shows an aggressive behavior supporting the theory that at least some of these tumors are true neoplasms. Our study confirms that not only surgery is the treatment of choice for IMT but also the radicality and completeness of surgery are the most important prognostic factors. Patients seem to need prolonged follow-up. Effectiveness of non-surgical treatments such as radiotherapy, laser therapy and chemotherapy is controversial.

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