Institutional report - Thoracic general

Clinical spectrum of pulmonary inflammatory myofibroblastic tumor

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Abstract

We retrospectively describe clinicopathological characteristics of five patients with surgically resected pulmonary inflammatory myofibroblastic tumor (IMT), and discuss in the light of present-day concepts regarding this disease entity. During the past 15 years, five patients with an age ranging from 21 to 74 years underwent surgery for IMT of the lung, and the resected lesions were studied histologically and immunohistochemically. Three asymptomatic patients referred as X-ray suspicious lung cancer, one patient complained of recurrent hemoptysis, and one presented with fever and dyspnea. The three patients were treated by lobectomy, and one segmentectomy and one wedge resection, two of whom were diagnosed as pulmonary sarcoma by frozen section at surgery. The tumor size ranged from 1.5 to 5.5 cm in diameter and histologically characterized by myofibroblasts that are mixed with chronic inflammatory cells, including plasma cells, lymphocytes, and histiocytes. There was no recurrence in these patients, and all of them are in good health. Complete surgical resection can be chosen for both diagnostic and therapeutic for IMTs, which remains the best treatment.

Keywords: Inflammatory myofibroblastic tumor (IMT); Inflammatory pseudotumor; Rare pulmonary neoplasm

1. Introduction

Inflammatory myofibroblastic tumors (IMTs) are challenging lesions with respect to classification, differential diagnosis, and biologic potential [1, 2]. They present histologically, presenting spindle cell proliferation with a distinctive fibroinflammatory and even pseudosarcomatous appearance [2]. IMT has been described by various terms because of its variable cellular components, which include plasma cell granulomas [1, 3], inflammatory pseudotumor [1, 4], xantogranuloma [5], and fibrous histiocytoma [6].

The term ‘pseudotumor’ came about because of its propensity to mimic clinically and radiologically a malignant process. However, the pathogenesis whether IMT is an inflammatory reactive lesion or neoplasm is still controversial. Recent detailed studies [1, 6] suggested that IMT is a neoplasm with benign or low-grade malignancy. The exact incidence of this disease is unclear. Furthermore, little information has been reported regarding the natural history, clinical presentation, and effective treatment. Diagnostic dilemma exists in the fact that even the frozen section did not reach the differential diagnosis. The purpose of this retrospective analysis is to describe five additional cases of pulmonary IMT and to review those previously reported in the light of concept regarding the disease entity and clinical significance.

2. Materials and methods

We retrospectively reviewed the charts of five patients (0.15%) who were diagnosed as inflammatory myofibroblastic tumors (IMTs) among 3486 general thoracic procedures that were performed at our institution between 1992 and 2006. Clinical characteristics as well as clinicopathological features, and including case presentation were documented.

Clinical characteristics of the five cases are presented in Table 1. Preoperative work-up included laboratory examinations, bronchofiberscopy, transthoracic fine needle aspiration cytology (FNAC), chest X-ray, and computed tomographic (CT) scans. For pathological examination in each case, the tissue was fixed in 10% buffered formalin, and embedded in paraffin. The sections were cut then stained with routine hematoxylin and eosin as well as immunohistochemistry. Follow-up was complete for all patients ranging from 18 months to 7 years.

3. Results

The following five case reports illustrate some important features of IMTs in terms of surgical management and outcome.

3.1. Patient 1

A 74-year-old female presented with an abnormal shadow 1.5 cm in size in the left lung field when she underwent an annual check-up following an implantation of a cardiac...
pacemaker. Since the bronchofiberscopy did not reach a diagnosis, exploratory video-assisted thoracic surgery (VATS) wedge resection was employed. The frozen section revealed being compatible with organizing pneumonia. Final histologic diagnosis was IMT, and the patient was followed-up for seven years without relapse. This case was similar to the organized pneumonia type according to the classification by Matsubara et al. [7].

3.2. Patient 2

A 50-year-old female was transferred to our hospital with recurrent hemoptysis of 50–100 ml, occurring two or three times per week. Chest CT showed the endobronchial tumor (Fig. 1a), and bronchofiberscopy revealed a protruding mass in the right lower lobe with a total obstruction of the B7, however, repeated biopsies did not reach a definite histological diagnosis. Then, a right lower lobectomy with bronchoplasty was employed, and the frozen section revealed a possible highly malignant sarcoma during the surgery. There was no lymph node metastasis, and the final diagnosis was IMT with lymphohistiocytic type was obtained from the resected specimen. Immunohistochemistry revealed a strong staining for anaplastic lymphoma kinase (ALK) (Fig. 1b,c). The patient is doing well 54 months after surgery.

3.3. Patient 3

A 31-year-old female was admitted to our hospital with suspicious diagnosis of lung cancer, radiologically presenting with an irregular margin mass with pleural indentation in chest CT. Then a VATS exploration and diagnostic left S6 segmentectomy was employed, and a frozen section revealed a suspected sarcoma. However, there was no lymph node metastasis by intraoperative sampling of the lymph nodes. Further extensive resection was not performed because of the previous experience in patient 2, of which clinical and histological features mimicked. The final diagnosis was IMT with a histologically fibrous histiocytic pattern. Immunohistochemistry revealed a weak staining for ALK. This case was similar to the lymphocyte predominant type [7]. The patient is doing well 45 months after surgery.

3.4. Patient 4

A 55-year-old female was admitted to our hospital for close examination for a lung tumor 2 cm in size in the right middle lobe (Fig. 2a). Transbronchial lung biopsy (TBLB) revealed organized pneumonia without malignancy. Then the patient was followed up in the outpatient clinic. Just two months later in the outpatient clinic, repeated chest X-ray revealed a large tumor 5 cm in size, invading into the chest wall (Fig. 2b). The surgery was achieved by right middle lobectomy and combined chest wall resection (4th and 5th ribs). The final histological diagnosis was IMT that was similar to the organized pneumonia type [7]. Immunohistochemistry revealed a negative staining for ALK. The patient is doing well 41 months after the surgery.

3.5. Patient 5

A 58-year-old female was transferred to our hospital with coughing and fever. Chest X-ray revealed a irregular mass 5 cm in size. Bronchofiberscopy did not reach a histological diagnosis, however, positron emission tomography (PET) confirmed an abnormal metabolic activity with a high standardized uptake value (SUV) of 8.4 in the lesion, suggestive of malignancy (Fig. 3). Therefore, a left upper lobectomy was employed, and frozen section revealed a suspicious diagnosis of IMT. Immunohistochemistry revealed a strong staining for ALK. The patient is doing well 24 months after surgery. This case was similar to the histiocytoma type (44%), and fibrohistiocytic type [7]. Three patients were asymptomatic and referred because of radiologically suspicious lung cancer, and one patient complained of a cough and the other patient presented with recurrent hemoptysis, and dyspnea. The three patients were treated by lobectomy, one segmentectomy, and one wedge resection (Table 1). Intraoperatively two patients were diagnosed as pulmonary sarcoma by frozen section, and one organizing pneumonia. The resected tumor size ranged from 1.5 to 5.5 cm in diameter. Histologically, a variety of inflammatory and spindle cells were observed. Three of five patients (60%) showed ALK, abnormalities were found in five patients, which further supported a diagnosis of IMT. Despite a short follow-up period, there was no recurrence in these patients, and all of them are in good health without recurrence at the time on writing.

4. Discussions

Inflammatory myofibroblastic tumors (IMTs) or inflammatory pseudotumor, the name implies its propensity to mimic clinically and radiologically a malignant process. Initially, IMTs arise through a non-neoplastic process due to an unregulated growth of inflammatory cells, and this down-regulation remains unknown [1, 4]. The incidence reported in the literature ranged from 0.04 [4] to 1.2% [8, 9] of all

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### Table 1

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/sex</th>
<th>Symptom</th>
<th>Location/size</th>
<th>Preoperatives/frozen</th>
<th>Surgery</th>
<th>Subtype</th>
<th>ALK</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>74/F</td>
<td>None</td>
<td>LUL/1.5 cm</td>
<td>−/OP</td>
<td>Wedge resection</td>
<td>OP type</td>
<td>−</td>
<td>7 years alive</td>
</tr>
<tr>
<td>2</td>
<td>50/F</td>
<td>Hemoptysis</td>
<td>RLL/3.5 cm</td>
<td>−/sarcoma</td>
<td>Sleeve lobectomy</td>
<td>LP type</td>
<td>+ + +</td>
<td>54 months alive</td>
</tr>
<tr>
<td>3</td>
<td>31/F</td>
<td>None</td>
<td>LLL/1.6 cm</td>
<td>−/sarcoma</td>
<td>Segmentectomy</td>
<td>FH type</td>
<td>+</td>
<td>49 months alive</td>
</tr>
<tr>
<td>4</td>
<td>55/F</td>
<td>None</td>
<td>RML/5.5 cm</td>
<td>OP/OP</td>
<td>Lobectomy CW</td>
<td>OP type</td>
<td>−</td>
<td>41 months alive</td>
</tr>
<tr>
<td>5</td>
<td>58/M</td>
<td>Fever cough</td>
<td>LUL/4.8 cm</td>
<td>−/FH</td>
<td>Lobectomy</td>
<td>FH type</td>
<td>+ + +</td>
<td>24 months alive</td>
</tr>
</tbody>
</table>

OP, organizing pneumonia; LP, lymphoplasmacytic; FH, fibrous histiocytic; ALK, anaplastic lymphoma kinase activity; LUL, left upper lobe; RLL, right lower lobe; LLL, left lower lobe; RML, right middle lobe; CW, chest wall resection.
Fig. 1. Chest CT image showing the protruding endobronchial tumor in the right lower lobe (a). The histological diagnosis of the frozen section was inconclusive, and the diagnosis of IMT with lymphohistiocytic type was obtained by the resected specimen (b). Immunohistochemistry revealed a strong staining for anaplastic lymphoma kinase (ALK) that was characteristic of this disease (c).

lung tumors. In addition to the rarity in pulmonary tumors, the important issue exists in that they can demonstrate characteristics that mimic malignant lesions, such as invasion of pleural mediastinal and chest wall structures seen in patients 4 and 5.

Histopathologically, the lesions may range from a primarily myofibroblastic or fibroxanthomous appearance to one that has a heavy infiltrate of plasma cells, which may be the reasons why they were named later as plasma cell granulomas [3], inflammatory pseudotumor [1, 4], xanthogranuloma [5], and fibrous histiocytoma [6]. Namely, they include a spectrum of myofibroblastic proliferation with varying infiltrate of inflammatory cells as a histologic feature.

IMTs occur at any age, however, they are a relatively common lung mass in pediatric patients compared to adults. There was no sex predilection [2, 4, 5], half of the
patients have been reported asymptomatic, and the tumor is seen as an incidental finding in the chest X-ray that was seen in patient 1, 3, 4. Symptom related to bronchial obstruction and hemoptysis that was seen in patient 2, and patient 5 presented with respiratory symptom of cough and fever. In particular, rapid growing in size was observed in Case 4. Others were non-specific constitutional symptoms, and no consistent identifiable risk factors. On the chest X-ray, usually solitary, well demarcated mass, sometimes irregular in the periphery [10, 11], and positive uptake in the FDG-PET [12] similar to the malignancies. In one report from Korea [11], IMTs were more commonly derived from tracheobronchial airways, than those in the peripheral origin.

Matsubara et al. [7] classified this entity into three subtypes by analyzing 32 cases of clinicopathologic findings of inflammatory pseudotumor of the lung, i.e. organizing pneumonia type (44%), fibrous histiocytoma type (44%), and lymphoplasmacytic type (12%). Organizing pneumonia type has intraalveolar lymphohistiocytic inflammation which converts to intraalveolar fibrosis peripherally and interstitial fibrosis centrally because of a proliferation of fibroblasts. Fibrous histiocytoma type has a predominant proliferation of spindle cells and histiocytes in storiform pattern, with loss of alveolar architecture. Lymphoplasmacytic type has a predominance of lymphocytes and plasma cells with little fibrosis [7]. There is considerable histologic overlap among the three types. This concept derived from the idea that IMT was inflammatory origin. On the other hand, Colby and associates [13] removed the type of organizing pneumonia from this entity, and classified into fibrohistiocytic subtype and plasma cell granuloma subtype. The former consists of spindle cells (myofibroblasts and fibroblasts), collagen, macrophage, foamy macrophages, and Touton giant cells. The latter consists of spindle myofibroblasts and inflamatory cells with abundant plasma cells. Immunohistochemical studies demonstrate vimentin, muscle specific actin, and focally desmin within the cytoplasm of the spindle cells indicating myofibroblastic differentiation [13].

Based on the findings of the published reports [1–4, 10], IMT is a benign, non-metastasizing proliferation of myofibroblasts with a potential for recurrence and persistent local growth, similar in some respects to the fibromatoses at the present stage. In the clinical setting that IMT decreased in size with corticosteroid therapy [14], and IMT associated with IgG4 – positive lung tumor suggest IMT is inflammatory or immunoopathologic disease process, namely non-neoplastic, was postulated.

On the other hand, demonstration of ALK and p80 as well as the evidence of crucial gene or chromosomal rearrangement of 2p23 that occur in IMT [15] is strongly suggestive of neoplasm nature. Moreover, as to the clinical behavior, local recurrence or distant metastasis have been reported [1, 4], thus a complete surgical resection is mandatory. We diagnosed them as malignant pulmonary sarcoma in two patients by frozen section during surgery, may due to the closely similar histological features compared to sarcoma, except that the IMTs lacked mitoses and invasiveness [7, 13].

As already stated, IMT are difficult to diagnose pre- or intraoperatively [1, 2, 4], fine needle aspiration cytology (FNAC) sometimes shows a mixtures of inflammatory cells, and fibroplastic proliferation with mitoses may mimic mesenchymal neoplasms. The differential diagnosis ranged from fibrohistiocytic neoplasms, lymphoma, primary lung cancer or sarcoma, and fibrosis. As we experienced in patient 4, the indeterminate nodule was once diagnosed as organized pneumonia of benign nature, however, the lesion rapidly increased in size associated with invasion to the chest wall, which showed a characteristic biological behavior of IMT. Thus, we recommended complete resection for diagnosis and treatment for this disease and prevention of recurrence, since the patient management otherwise does not change [2, 4, 9].

According to the literature reviews, the prognosis of patient wit IMT who undergo a complete resection was excellent, however, local and distance recurrence as well as tumor deaths were reported. A collective review showed a 5 year and 10-year survivals of 91 and 77% [8], which alternatively suggestive of prognostic nature of low-grade malignancy.

In conclusions, a IMT is a rare benign lesion that is characterized by myofibroblasts proliferation mixed with chronic inflammatory cells, which should be distinguished from malignant tumors by surgical resection.
References


