Inflammatory Pseudotumor of the Lung in Adults

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Background. **Thoracic surgeons have limited experience of inflammatory pseudotumors of the lung owing to their rare occurrence in routine clinical practice.**

Methods. **We retrospectively investigated the clinicopathologic features of 18 patients with inflammatory pseudotumor of the lung observed between 1992 and 2002.**

Results. **There were 13 men and 5 women. Median age was 57 years. Eight patients (44%) were symptomatic. Computed tomographic scan showed a solitary nodule (≤3 cm) in 12 patients, bilateral nodules in 1, and a mass in 5. Two patients had undergone prior incomplete resections. Lobectomy was performed in 5 patients, bilobectomy in 1, segmentectomy in 1, and wedge resection in 11. Complete resection was achieved in 13 patients (72%). There was no operative mortality. Follow-up was complete in all patients (range, 13 to 134 months; median, 63 months). Overall 3-year and 5-year survival rates were 82% and 74%, respectively. Thirteen patients are currently alive with no evidence of disease, 1 is alive with disease, 1 died of unrelated causes, and 3 had a relapse and died. Completeness of resection and lesion size less than or equal to 3 cm were associated with a better survival ($p < 0.001$ and $p = 0.007$, respectively). Multivariate Cox analysis confirmed the association between completeness of resection and better survival, which is independent of other clinicopathologic variables ($p = 0.02$).**

Conclusions. **This series shows that a significant number of patients with inflammatory pseudotumor of the lung have a poor prognosis and confirms the need for radical resection in the treatment of this unusual entity.**

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Inflammatory pseudotumor of the lung, also known as plasma cell granuloma or inflammatory myofibroblastic tumor, is a rare occurrence. This is supported by the fact that only four major studies [1–4] with more than 10 patients appeared in the literature between 1990 and 2003. Because of its rarity, the precise biologic nature, natural history, and response to treatment of inflammatory pseudotumor of the lung have yet to be completely defined. In particular, it is not clear whether inflammatory pseudotumor is an uncontrolled inflammatory process or a true neoplasm. Its natural history is, moreover, extremely variable, ranging from benign lesions with a favorable evolution to large masses with local invasion, distant metastases, and a poor prognosis [1–10]. Its variable cellular composition seldom enables diagnosis to be made preoperatively with transthoracic fine-needle aspiration or bronchoscopic biopsy, and the lesion is generally resected to rule out cancer [4, 11]. Surgical resection is the treatment of choice not only to exclude malignancy but also to achieve cure [4, 8, 12, 13]. However, very scant data are available in the literature on the results of both surgical treatment and other therapies, such as chemotherapy, radiotherapy and corticosteroids, which are very occasionally used to cure these rare pulmonary lesions in nonoperable patients.

To contribute to a better understanding of the clinical significance of inflammatory pseudotumors of the lung and of the criteria for treating them, we retrospectively analyzed 18 cases of inflammatory pseudotumor of the lung to ascertain their clinical, imaging, histopathologic, and evolutive features.

Patients and Methods

We retrospectively reviewed the tumor registry of the San Raffaele University Hospital, Milan, covering an 11-year period (January 1992 through December 2002) and the consultation files of one of the authors (E.B.) to identify all the patients with a histologic diagnosis of inflammatory pseudotumor of the lung. Because pediatric thoracic operations are not routinely performed in our hospital, patients reviewed were all older than 18 years of age. Histologic specimens were reviewed again by three pathologists (G.A., E.B., and N.R.), confirmed as inflammatory pseudotumor, and subclassified according to criteria of both Matsubara and colleagues [11] and the World Health Organization [14], on the basis of hematoxylin and eosin-stained sections. Immunohistochemical studies were performed on 4-μm-thick formalin-fixed paraffin-embedded tissue sections using a standard heat-induced epitope retrieval method, a standard avidin–biotin peroxidase complex detection technique, and an

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automated immunostainer (Autostainer, DAKO Cytomation, Copenhagen, Denmark). Representative sections from all cases were incubated with monoclonal antibodies against smooth muscle actin, CD34, desmin, epithelial membrane antigen, CD68, vimentin, and anaplastic lymphoma kinase-1 (ALK-1). Patients' charts were reviewed for age, sex, medical and surgical history, preoperative work-up, type of treatment, length of hospital stay, morbidity, and mortality. Computed tomography (CT) scans of the chest were reviewed for tumor morphology, tumor location, tumor size, enlarged mediastinal lymph nodes, pleural effusion, mediastinal invasion, and chest wall invasion. On the basis of the CT appearance, pulmonary lesions were classified as nodules (≤3 cm in diameter) or masses (>3 cm in diameter). Follow-up data were obtained from the patients' hospital visit or telephone interview. Operative mortality was defined as any death during hospitalization or within 30 days from surgery. Late mortality was defined as any subsequent death.

Differences between patients who died and those who did not were tested for significance with the χ^2 or Fisher's exact tests for discrete variables, and with the Student's t test for continuous variables. Survival rates of patients grouped according to selected variables were compared by log-rank statistics. Survival plots were reconstructed according to the Kaplan-Meier method. Potential predictors of outcome were identified by χ^2 analysis of selected dichotomous variables. Simple Cox regression analysis was used to estimate the odds ratios for the variables evaluated at baseline. On the basis of the univariate analysis, multivariable Cox regression analyses were performed to adjust for potential confounders using a forward stepwise method to introduce significant covariates into the model. Reported p values are two-sided. Results of analyses were considered significant at a level of p less than 0.05. All confidence intervals were calculated at the 95% level.

Results

We identified 18 patients (13 men, 5 women; age range, 18 to 75 years; mean, 57 ± 3 years) with a diagnosis of inflammatory pseudotumor of the lung. Eight patients (44%) were symptomatic, which included cough in 4, chest pain in 2, fever in 1, and hemoptysis in 1. In the remaining 10 asymptomatic patients (56%) inflammatory pseudotumor was an incidental finding on examination of chest radiographs. Five patients (28%) had a history of prior lower respiratory tract infection or pneumonia. Computed tomographic scan of the chest performed on all patients revealed a solitary nodule (≤3 cm) in 11 patients, a nodule with invasion of the mediastinal pleura in 1, bilateral nodules in 1, a pulmonary mass (>3 cm) in 2, a mass with bilateral nodules in 1, a mass with chest wall invasion in 1, and a mass with invasion of the mediastinal pleura in 1 (Fig 1). No patients had enlarged (short axis > 1 cm) mediastinal lymph nodes at CT scan. The location of the lesions at CT scan was right upper lobe in 2 patients, left upper lobe in 3, right lower lobe in 3, left lower lobe in 5, medium lobe in 3, and bilateral in 2. Bronchoscopy, performed preoperatively in 13 patients and intraoperatively in the remaining 5, was always negative for bronchial lesions. Transthoracic fine-needle

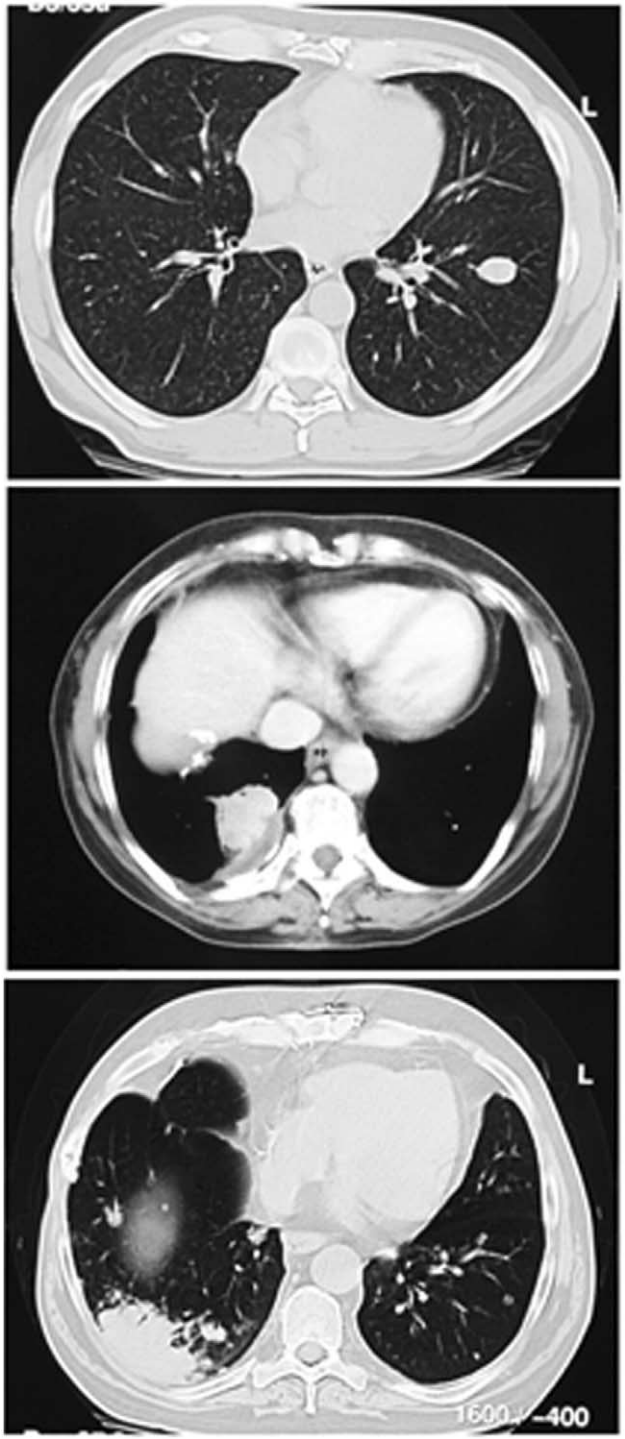

Fig 1. Computed tomographic scans of the examples of the inflammatory pseudotumors of the lung. (Top) A solitary noncalcified nodule is observed in the left lower lobe. (Middle) A well-circumscribed mass is found in the right lower lobe with thickening of the adjacent pleura. (Bottom) A large mass is seen in the right lower lobe with bilateral nodules.