Seminars in Diagnostic Pathology (2007) 24, 199-208

ELSEVIER

Seminars in
Diagnostic
Pathology

Unusual non-neoplastic lesions of the lung

Cesar A. Moran, MD,[a] Saul Suster, MD[b]

From the [a]Department of Pathology, M.D. Anderson Cancer Center, Houston, Texas; and the [b]Department of Pathology, Medical College of Wisconsin, Milwaukee, Wisconsin.

KEYWORDS
Pseudotumor;
Microlithiasis;
Transmogrification;
Calcification;
Tumor;
Lung

Many nonneoplastic conditions that may affect the lung are in reality rare or unusual manifestations of metabolic processes, inflammatory conditions, or unknown etiology. Because of their rarity, they can often be confused with malignant neoplasms. Familiarity with these conditions not only will expedite further treatment for these patients but also will avoid the process of more tests or unnecessary surgical procedures. The nomenclature for some of those conditions is still controversial. The clinical outcome of these conditions can be quite variable, with some patients surviving a long number of years and others eventually succumbing to the disease. We will limit our discussion in this review to four of these conditions, including inflammatory pseudotumor (inflammatory myofibroblastic tumor), placental transmogrification of lung, alveolar microlithiasis, and metastatic calcification. Although these lesions are not part of the gamut of neoplastic conditions affecting the lung, they are nonetheless important to recognize, as their outcome may not necessarily be an innocuous one.

Inflammatory pseudotumor

The term inflammatory pseudotumor (IPT) of the lung refers to a pulmonary growth that replaces normal lung parenchyma and which is believed to represent a sequel to an inflammatory process. Despite the "inflammatory" designation, the fact remains that IPT of the lung is a tumor with the potential to recur and invade adjacent structures, such as pleura, mediastinum, and diaphragm, and it may not necessarily be related to an inflammatory response such as a pneumonic process. The term inflammatory myofibroblastic tumor has been more recently employed as a substitute for the term inflammatory pseudotumor, and may more accurately reflect in purely descriptive terms its basic components without necessarily implying an inflammatory etiology. Although controversy continues to exist surrounding the current terminology of these lesions, the term used throughout this writing will be that of inflammatory pseudotumor.

Address reprint requests and correspondence: Cesar A. Moran, MD, Department of Pathology, M.D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030.

E-mail: cesarmoran@mdanderson.org.

0740-2570/$ -see front matter © 2007 Elsevier Inc. All rights reserved.
doi:10.1053/j.semdp.2007.06.006

Etiology

In the view of many authors, IPT represents an inflammatory response to a previous injury. The presence of myofibroblastic cells as a major component of these lesions, and the fact that a myofibroblastic proliferation is a prominent component in some reactive and inflammatory lung conditions such as diffuse alveolar damage has been proposed as an argument in favor of an inflammatory response.[1] In many cases, the clinical history is that of an upper respiratory tract infection or a resolving pneumonic process, in which patients have been treated symptomatically with antibiotics. Cases of IPT which expressed human herpesvirus-8 genes have been cited in support of an infectious etiology.[2,3] However, other authors believe that IPT may represent a true neoplasm, and some studies have demonstrated cytogenetic evidence supporting a clonal origin.[4] In addition, the fact that many of these lesions recur[5] may also lend some support to the theory that we may be dealing

with a true neoplastic process rather than a postinflammatory response. The etiology and pathogenesis of these lesions, however, remain unsettled.

Clinical features

It has been estimated that IPT represent less than 1% of all pulmonary tumors. However, the true incidence of these lesions may vary from author to author as a wide variety of lesions have been included under this designation.[5,6-36] Unfortunately, many other conditions have been included under the designation of IPT, including organizing pneumonia, sclerosing hemangioma, and pseudolymphoma, among others. In most cases, IPT may present as a solitary "coin lesion" in young adults, usually under 40 years of age. However, IPT is not restricted to younger patients as it has also been described in patients older than 40 years of age. Although it is common to obtain a history of cough, chest pain, and fever, IPT has also been described in patients who have been completely asymptomatic, and the lung abnormality was discovered on routine radiographic study. Occasionally, patients may present with more acute symptoms such as massive hemoptysis.[24] As with other intrapulmonary tumors, the symptoms of the patients will vary based on the location of the lesion, either centrally or peripherally. The tumors generally vary from 1 cm to more than 10 cm in greatest diameter.

Radiological features

The largest radiologic study of IPT of the lung was the one by Agrons and coworkers.[23] In that study, the authors analyzed 61 patients ranging from 17 to 61 years with a slight male predilection. Fifty-two patients had a peripheral solitary nodule or mass; in 11 of these patients, extrapulmonary involvement was evident in the hilum, mediastinum, and airway. The authors concluded that IPT is typically a solitary pulmonary lesion, which can involve extrapulmonary structures. In another study by Ishida,[15] the authors were able to document pleural involvement in 3 of 7 patients with IPT. Kim and coworkers[32] also described the radiographic features of 10 patients with IPT and identified 3 patients in whom the lesion was endobronchial. Rare cases of cystic lesions have also been described.[17]

Classification

A wide variety of overlapping and oftentimes dissimilar processes have been described under the designation of inflammatory pseudotumor. Although most pathologists would not include organizing pneumonia among cases of IPT, Matsubara and coworkers[36] described 32 cases of IPT of the lung in which the authors alluded to the possible progression of organizing pneumonia to fibrous histiocytoma to plasma cell granuloma. The authors concluded that most or all cases of IPT originate from organizing pneumonia, and that there is a considerable overlap of histological features among those three entities (organizing pneumonia-fibrous histiocytoma-plasma cell granuloma). One of the problems in classifying cases of organizing pneumonia as IPT, however, is the fact that some cases of bronchiolitis obliterans may have radiological evidence of an intrapulmonary nodule with air space consolidation,[37] similar to some of the cases diagnosed as IPT. If localized cases of bronchiolitis obliterans are included in this category of lesions, then essentially any unclassified "benign" inflammatory mass lesion in the lung will automatically be labeled as an IPT. For this reason, some authors have questioned the concept of IPT as an entity.[38] Bahadori and Liebow[7] preferred the term plasma cell granuloma to that of IPT; however, such nomenclature does not take into consideration the existence of lesions that are composed almost entirely of a fibrohistiocytic proliferation. Spencer[11] documented 27 cases of IPT in which he found that all the lesions had features of both plasma cell granuloma and histiocytoma, and proposed the pulmonary plasma cell–histiocytoma complex. However, Pettinato and coworkers[16] described 20 cases of what the authors designated as inflammatory myofibroblastic tumor and acknowledged that the lesions were composed of varying proportions of plasma cells, histiocytes, and spindle cells. Interestingly, 5% of their cases were multiple, and 5% showed involvement of the mediastinum and thoracic wall. On the other hand, other authors have focused more on lesions in which the histology is fibrohistiocytic. Buell and coworkers,[8] in a description of an endobronchial case of IPT, documented the presence of plasma cells and spindle cells, which by electron microscopy were akin to fibrocytic derivation. Gal and coworkers[22] analyzed the prognostic factors of fibrohistiocytic lesions of the lung and divided them into inflammatory pseudotumor, fibrohistiocytic type, borderline fibrohistiocytic lesions, and malignant fibrous histiocytoma. In their study, 15 lesions were coded as IPT and 3 were coded as borderline. Of interest, only 2 patients with IPT showed recurrences. Cerfolio and coworkers,[28] in a study of 23 patients with IPT, concluded that, regardless of the histology, the most important factor is whether the tumors are circumscribed or locally invasive.

The most commonly accepted classification of ITP is the one based on the predominant cellular component of the lesions. Based on their distinctive histopathological features, they have been divided into fibrohistiocytic type and plasma cell type. Regardless of the histology, it is important for prognostic purposes to carefully evaluate whether the tumors are invasive. In this regard, careful analysis of the radiological features and careful sectioning of the tumor become important parameters in the evaluation and final classification of these lesions.

Histological features

IPT of the lung may show essentially two distinct histopathological growth patterns: fibrohistiocytic type and plasma cell type (Figures 1-7). However, although there may