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Case report

Inflammatory myofibroblastic tumor of the lung with unique histological pattern and association with Sjögren's disease and systemic lupus erythematosus

Boris V. Shlopov, Samuel W. French *

Department of Pathology and Laboratory Medicine, Harbor-UCLA Medical Center, 1000 West Carson Street, Torrance, CA 90509, USA

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ABSTRACT

Inflammatory myofibroblastic tumor (IMT) of the lung is a rare condition. Radiological properties and clinical presentation of this disease can mimic malignant process. We present a case of IMT of the lung in a 58 year old female patient with a single lung nodule. Tumor was unencapsulated, firm, and well circumscribed. Microscopically tumor had multinodular structure with single or multiple small blood vessels in the center of each nodule surrounded in circular pattern by connective tissue containing spindle cells embedded into the thick layers of extracellular matrix. Extracellular matrix was identified as type I and type III collagen fibrils embedded into type IV collagen and laminin. The tumor was surrounded by T-, B-lymphocytes and polyclonal plasma cells. Histological organization of this lesion's stromal component was unique, but cell composition was similar to inflammatory pseudotumor of the lung. In addition, tumor tissue sections exhibited strong positivity for IgG, weak positivity for IgA, 1Cq, but were negative for IgM, and C3. Mutational analysis of the EGFR, KRAS genes and ALK locus rearrangement were performed and did not reveal any mutations. This is the first report of an IMT associated with Sjögren's disease, systemic lupus erythematosus and Non-Hodgkin lymphoma developing in the lungs. Patient was clinically followed up for 18 months and no recurrence of the tumor observed.

Introduction

Solitary pulmonary nodules are common radiologic findings, typically discovered incidentally in up to 0.2% of chest radiographs (Ost et al., 2003) or around 1% of computed tomography scans of the chest and neck (Alzahouri et al., 2008).

Solitary pulmonary nodules can have many causes. Primary lung cancer or metastatic cancer is usually the primary concern and represents from 11 to 23% of solitary pulmonary nodules (Swensen et al., 1997; Henschke et al., 1999). Origin of benign solitary pulmonary nodules also can include benign tumors, pseudotumors, bronchogenic cysts, hemangiomas, Castleman's disease, and Wegener's granulomatosis. In the southwestern part of the United States solitary granulomas are typically caused by *Coccidioides immitis*, in the upper Mississippi region by *Histoplasma capsulatum*, less commonly by Cryptococcus or blastomycosis. Rare causes of solitary pulmonary nodule may include a parasitic infection, most commonly a helminthic infection caused by the animal filarial parasite *Dirofilaria*, the intestinal ascarid, *Toxocara*, *Ascaris* or the human filarial parasite (Bielawski et al., 2001; Travis et al., 2002; Martínez et al., 2005; Sakai et al., 2006). These infections are prevalent in certain tropical and subtropical regions of the world. Most cases are diagnosed after a lung resection for a solitary pulmonary nodule presumed to be malignant.

Case report

A 58 year old female with a history of intrinsic lung disease and four month history of cough and left chest pain, was deemed to have pneumonia. The chest pain essentially resolved; however, the patient continued to have shortness of breath. A PET scan showed an increased uptake in the right lower lobe of the lung. Chest CT scan revealed a right lower lobe mass. Work up for tuberculosis was negative. Past medical history included systemic lupus erythematosus, hypothyroidism, Sjogren's syndrome and Non-Hodgkin lymphoma with status post chemotherapy in 1999. The patient had a wedge resection of the right lower lobe for the solitary pulmonary nodule.

Pathological findings

A single round, grey-white, 1.2 cm in diameter tumor was identified in the right lower lung lobe wedge resection specimen. Tumor was unencapsulated, firm, and well circumscribed. Microscopically it was represented by predominantly stromal component (Fig. 1A, B), and had multinodular organization with single or multiple small blood vessels in the center of each nodule (Fig. 1B, C). These small blood vessels were surrounded in concentric pattern by connective tissue containing spindle cells with inconspicuous

* Corresponding author. Fax: +310 222 8002.
E-mail address: sfrench@labiomed.org (S.W. French).

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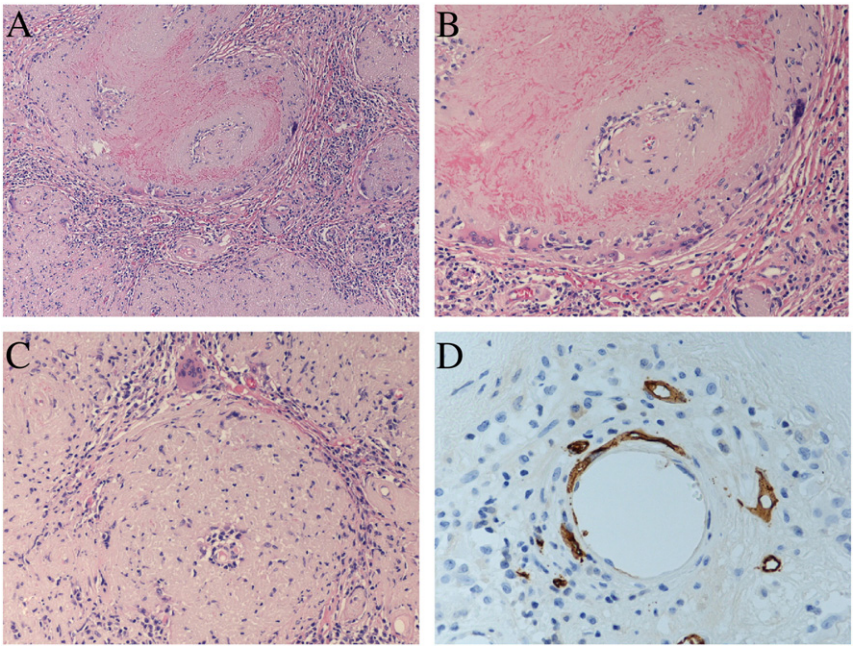

Fig. 1. A. Tumor represented by multiple nodules surrounded by mixed population of lymphocytes, plasma cells and giant cells. B. Individual nodule showing concentric pattern of connective tissue with partial hyalinization. C. Small blood vessel is surrounded in concentric pattern by connective tissue. D. Immunohistochemistry. CD34 marker showing blood vessel in the center of the lobule. (Hematoxylin and eosin stain. A, 100×, B–C, 200×, D, 400×).

nucleoli embedded into the thick layers of extracellular matrix. The periphery of each nodule was surrounded by lymphocytes, plasma cells, numerous multinucleated giant cells admixed with histiocytes and myofibroblasts (Fig. 2A, B). Giant cell reaction appeared to be present to the nodules of myofibroblasts. Immunohistochemical staining for CD3, CD5 and CD20 revealed mixed population of scattered T- and B-lymphocytes (Fig. 3A, B). Plasma cells stained with kappa and lambda light chains demonstrated polyclonal pattern with predominantly kappa positive plasma cells (Fig. 3C, D, E). Secondary and primary lymphoid follicles formations were observed at the periphery of the lesion. In addition, in the area adjacent to the tumor, we found focal changes consistent with extensive arteritis with recanalized thrombi and aneurismal dilatation. No cellular atypia or mitotic figures were found within the lesion.

Immunofluorescent study of the tumor revealed strong positivity for IgG, albumin, weak positivity for IgA, 1Cq and were negative for IgM, and C3 (Fig. 4A–F). TNF alpha and TGF beta cytokine level was undetectable by conventional immunohistochemistry. Steiner, Grocott's methenamine silver and periodic acid-Schiff stains did not reveal any microorganisms.

Electron microscopy study of the lesion revealed presence of myofibroblasts and fibroblasts producing thin collagen fibers embedded into the homogeneous extracellular matrix (Figs. 5 A, B, C). Immunohistochemical stain revealed myofibroblasts producing vimentin, laminin and smooth muscle actin but not desmin (Figs. 6 A, B, C). Collagen fibers were identified as type I and type III collagen, homogeneous extracellular material was predominantly represented by type IV collagen (Fig. 6D) and small amount of laminin. No elastic tissue was identified. Negative Congo Red stain helped to exclude pulmonary amyloidosis.

In addition, mutational analysis of the EGFR, KRAS genes and ALK locus rearrangement were performed to survey the most common lung tumor-associated genetic changes. Fluorescence in-situ hybridization analysis, using break-apart probes specific for ALK gene (2p23; Abbott Molecular), exhibited a normal pattern of hybridization. Mutation analysis of KRAS and EGFR did not reveal any mutations.

Histological organization of this lesion's stromal component was unique, but cell composition was similar to inflammatory myofibroblastic tumor of the lung. Patient was clinically followed up for 18 months and no recurrence of the tumor observed.

Discussion

Inflammatory myofibroblastic tumor (IMT) of the lung, also known as plasma cell granuloma, inflammatory pseudotumor, histiocytoma, fibroxanthoma and xanthogranuloma, is a rare entity.

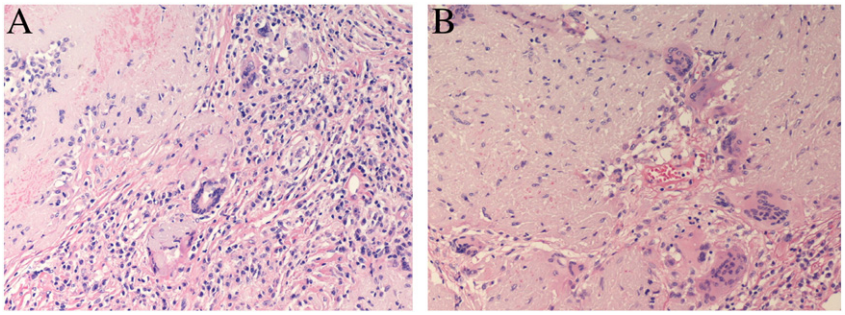

Fig. 2. A. Significant inflammatory component at the periphery of the tumor with giant cell formation. B. Numerous multinucleated giant cells. (Hematoxylin and eosin stain. A, B, 200×).