

Sarcomatous transformation in an Inflammatory Myofibroblastic Tumor of lung: a rare finding in a young male

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Citation

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Abstract

Inflammatory myofibroblastic tumor (IMT or pseudotumor) of lung mimic as malignant lesion. Cough, fever, dyspnea and hemoptysis are the usual presenting symptoms. History of previous pulmonary disease is present in about 30% of the cases and significant proportions of cases remain asymptomatic. Although it is generally acknowledged that IMT involve a non-neoplastic process characterized by unregulated growth of inflammatory cells, the existence of genuine involvement of neighboring structures or its rapid recurrence arise the possibility of it being a neoplasm. Although rare, IMT can undergo sarcomatous transformation. Here in we present a young male diagnosed as a case of malignant fibrous histiocytoma (MFH) in a background of inflammatory pseudotumor (IMT). We emphasize the need to take multiple sections at the periphery of the suspected for IMT lesion. Secondly morphologically a biphasic pattern with benign and malignant appearing components in a case of IMT, such sarcomatous transformation needs to be ruled out.

INTRODUCTION

Inflammatory myofibroblastic tumor (IMT) is an umbrella term that encompasses nonspecific or not otherwise classifiable chronic inflammatory and expansive lesions, which are reactive in nature.¹ IMT most commonly involves the lung and the orbit. It constitutes less than 1% of all lung tumors. It is the most common lung tumor in patients less than 16 years of age. Clinical demonstration of recurrences, metastases, morphological features of aggressive behavior, including angioinvasion and extrapulmonary extension into adjacent structures, and cytogenetic evidence of acquired chromosomal abnormalities question this umbrella term IMT.²

Patients with pulmonary IMT present with cough, dyspnea, fever, chest pain, and hemoptysis. History of previous pulmonary disease is present in about 30% of the cases and significant proportions of cases remain asymptomatic.³ Laboratory abnormalities reported include anemia, elevated erythrocyte sedimentation rate, thrombocytosis, and polyclonal hypergammaglobulinemia. Radiologically, the nodule is often well circumscribed with either smooth or lobulated margins. In 20% of the cases, IMT appear as an ill-defined mass with infrequent calcification or cavitations. The tumor size ranges from 1.2 to 15cm. On microscopic

examination based on the predominant histopathology features, the lesions can be divided into three histological types (1) Organizing pneumonia pattern; (2) Fibrous histiocytic pattern; (3) lymphohistiocytic pattern.² The myofibroblast is eventually recognized as the principal cell type along with typically large number plasma cells and other inflammatory cells. Inflammatory MFH may form one end of the spectrum in this myofibroblastic lesions.⁴

Literatures do describe Sarcomatous transformation in an IMT.¹ Tumor composed of fibroblasts and myofibroblasts pose significant challenges in differential diagnosis in such cases of sarcomatous transformation. Here in we report a case of primary pulmonary Malignant Fibrous Histiocytoma in a young male. Undoubtedly, this tumor should be called pleomorphic fibrosarcoma which is included in the new World Health Organization classification.⁵ The designation of tumors with overlapping morphologic features between IMT and inflammatory fibrosarcoma and unpredictable clinical behavior remains controversial. Moreover, histological appearance does not predict behavior.²

CASE REPORT

Asymptomatic right lung opacity was discovered on chest x-ray examination in a 21-year old south-Indian male, during

an episode of cold. Computed Tomography scan showed solid and partly cystic mass, measuring 6x 5.7x 5.5 cm in right paracardiac region of diaphragm. He was referred to our hospital for mass excision with clinical diagnosis of Congenital Pulmonary Airway malformation/ extrapulmonary sequestration. His total leukocyte count was 11,100/cumm. Erythrocyte sedimentation rate was within normal range. Many abnormal vascular channels from the mass draining into inferior veinacava were seen intraoperatively. Artery arising at L1 level from abdominal aorta supplying the lesion was also noted. Excised mass was sent for histopathological examination. Grossly tumor was partly encapsulated. Pleural surface showed focal nodularity with marked areas of congestion. Cut surface was yellowish-white, partly nodular and soft to firm in consistency. Central area of cystic degeneration (4x3cm) with hemorrhage and necrosis was noted (Fig 1). Few cystic spaces with mucus plugs and hemorrhage were seen. Part of attached normal lung was also noted.

Microscopically it showed highly cellular and focally cystic lesion. The lesion was seen blending with adjacent lung focally with endobronchial spread (Fig.2a.). Few emboli noted. Tumor cells showed biphasic pattern with benign and malignant appearing components. Benign looking tumor cells were seen arranged in hemangiopericytomatous pattern with few cystically dilated vascular spaces. Areas showing short fascicles and vague storiform pattern were also noted (Fig.2b.). Tumor cells were seen entrapping bronchioles and bronchi with benign looking epithelium. Areas showing marked pleomorphism with scattered giant cells were also seen (Fig.2c.). Occasional osteoclast-like giant cell were noted. Admixed with these cells were mixed inflammatory cells composed of eosinophils, lymphocytes, plasma cells and mast cells. Large areas showing collection of foamy macrophages were seen with focal fibro-xanthomatous look. Mitotic rate around 3-5/10 Hpf was noted. Central area of necrosis was noted (<10% tumor area). No heterologous or hamartomatous areas were seen. Focal area with calcification noted. Immunohistochemistry showed strong focal positivity in SMA (<25% tumor cells, Fig.2d). CK, Desmin, S-100 and CD34 were negative. Based on these findings a diagnosis of MFH was given (with inflammatory/ angiomatoid variant).

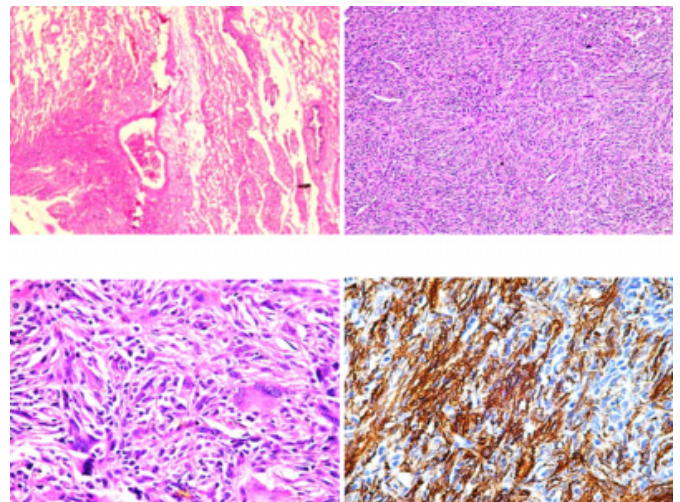
Figure 1

Figure 1: Gross photograph, showing central area of cystic degeneration with focal hemorrhage & necrosis.



Figure 2

Figure 2: (a).Lowpower view showing tumor blending with adjacent lung tissue.(4X, H&E). Fig.2(b)Areas showing short fascicles & vague storiform pattern.(4X, H&E). Fig.2(c) Areas showing pleomorphism with scattered giant cells. (40X, H&E). Fig.2(d)High powerview showing sStrong focal positivity for smooth muscle actin.(40X, IHC).



DISCUSSION

MFH is one of the most common soft tissue sarcoma of adulthood. It accounts for 20-25% of all sarcoma. It is very rare tumor of lung and only a few cases have been reported in the literature. MFH tends to be over diagnosed, careful attention to strict definition of a storiform pattern with pleomorphism is essential. Its etiology is unknown. Clinically, the patients usually present with chest pain, cough and hemoptysis. Chest x-ray usually shows single

mass but there are reports of more than one mass lesion in the literature.⁶ Our case there was solitary pulmonary lesion at the right paracardiac region.

Grossly MFH cut surface appears white to pale yellow, can present as hemorrhagic cysts which can be deceptive. Necrosis is rule rather than exception. Histopathologically, six types of MFH are described, of which most common one is storiform-pleomorphic type.⁵ In our case it had overlapping features of inflammatory/angiomatoid variant. Inflammatory MFH is a highly aggressive lesion that was initially misdiagnosed as reactive. Importantly, the inflammatory cells consist predominantly of neutrophils, although scattered lymphocytes and benign foamy histiocytes are also present. In our case, tumor cells were admixed with mixed inflammatory cells composed of eosinophils, lymphocytes, plasma cells and mast cells. Large areas showing collection of foamy macrophages were noted with focal fibro-xanthomatous look, typical of inflammatory pseudotumor. However aggregates of lymphoplasmacytic cells with germinal center or a typical large number of plasma cells were not noted. Although benign looking areas with short fascicles and vague storiform pattern was noted, stroma lacked sclerotic collagenous component (on masson's trichrome stain). Focal SMA-positive spindle cells with pale eosinophilic cytoplasm were noted. No morphological features suggestive of smooth muscle tumor were noted.

The designation of tumors with overlapping morphologic features between IMT and inflammatory fibrosarcoma and unpredictable clinical behavior remains controversial. Literatures suggest that, the cases originally described as inflammatory fibrosarcoma are generally considered to belong to inflammatory myofibroblastic group of lesions. Molecular findings show that the IMT demonstrates a fusion of the TPM3 or TPM4 (tropomyosin) gene to the ALK (anaplastic lymphoma kinase) gene.⁵ Nearly 40 to 60% of cases are immunoreactive with the ALK antibodies ALK1 or p80. According to Gal et al., factors associated with poor prognosis in IMT include metastases, necrosis greater than 15% of the total microscopic surface area of tumor examined, local recurrence, advanced stage at surgery, bizarre giant cells, mitosis of 3/50 Hpf or greater, high cellularity and poor circumscription. In our case last four factors were present with focal tumor emboli. Nascimento et al.,⁸ found 10% of sarcoma of the lung to have a dominant

endobronchial component. Our case had also a focal endobronchial component.

Surgery is the primary mode of therapy for both IMT as well as MFH. Early and complete surgical resection of the mass provides cure and prevents local recurrence.²⁶ Role of radiation therapy and chemotherapy has not been clearly defined. In conclusion, IMT can undergo sarcomatous transformation rarely. Morphologically a biphasic pattern with benign and malignant appearing components in a case of IMT, such a sarcomatous transformation needs to be ruled out. We emphasize the need to take multiple sections at the periphery of the lesion. Factors associated with poor prognosis in IMT according to Gal et al., may help in designating final terminology.

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References

1. Batsakis JG, el-Naggar AK, Luna MA, Goepfert H. "Inflammatory pseudo-tumor": what is it? How does it behave? *Ann Otol Rhinol Laryngol* 1995; 104: 329-31.
2. Ng SB, Tan PH, Tan RK. Unusual lung mass in a 21-year-old man. *Arch Pathol Lab Med* 2002; 126: 1127-29.
3. Pettinato G, Manivel JC, De Rosa N, Dehner LP. Inflammatory myofibroblastic tumor (plasma cell granuloma): clinicopathological study of 20 cases with immunohistochemical and ultrastructural observations. *Am J Clin Pathol* 1990; 94: 538-46.
4. Meis JM, Enzinger FM. Inflammatory fibrosarcoma of the mesentery and retroperitoneum. A tumor closely simulating inflammatory pseudotumor. *Am J Surg Pathol* 1991; 15: 1146-56.
5. John SJ, Brooks. Disorders of soft tissue. In: Stancy E. Mills, Darryl Carter, Joel K. Greenson, Harold A. Oberman, Victor Reuter, Mark H. Toler, editors. *Sternberg's Diagnostic surgical pathology*. 4th ed. Philadelphia: Lippincott William & Wilkins; 2004. p137-22.
6. Findik S, Erkan L, Kandemir B. A case report: Primary malignant fibrous histiocytoma of the lung. *Turkish Respiratory Journal* 2001; 2: 44-46.
7. Gal AA, Koss MN, McCarthy WF, Hochholzer L. Prognostic factors in pulmonary fibrohistiocytic lesions. *Cancer* 1994; 73: 1817-24.
8. Nascimento AG, Unni KK, Bernatz PE. Sarcoma of the lung. *Mayo Clin Proc* 1982; 57: 355-59.

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