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Primary high-grade myxofibrosarcoma in the anterior mediastinum: A case report and review of the literature

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ABSTRACT

Herein, we report on a case of a 70-year-old man with a primary high-grade myxofibrosarcoma (MFS) in the anterior mediastinum. A computed tomography (CT) scan of the patient's chest revealed a heterogeneous mass lesion. On magnetic resonance imaging (MRI), the mass lesion exhibited heterogeneous low signal intensity with focal high signal intensity on T1-weighted images, and high signal intensity with cystic lesions on T2-weighted images. There were no signs of adipose tissue or calcification in the chest CT or MRI findings. Tumor resection was performed for the diagnosis and treatment. The resected mass was composed of myxoid and solid areas. The myxoid areas revealed atypical spindle cells with abundant myxoid matrix. The solid areas showed atypical spindle cell proliferation with numerous mitoses and multinucleated atypical cells. MDM2 gene amplification was not found in the tumor using fluorescent in situ hybridization method. Thus, the tumor was diagnosed as myxofibrosarcoma. Postoperative radiation therapy was administered to the mediastinum. However, the patient died from locally recurrent disease 1-year after surgery. Our case confirms the existence of MFS in the mediastinum and shows its poor prognosis and rapid progression.

1. Introduction

Malignant mesenchymal tumors are a rare occurrence in mediastinal structures. To date, 36 cases of malignant fibrous histiocytoma (MFH), including one case of myxoid MFH, have been reported in the mediastinum [1–3]. It has been suggested that the majority of tumors previously diagnosed as MFH actually represent dedifferentiated liposarcoma (DDLS) [4]. Liposarcomas are also relatively common in the mediastinum. Therefore, the existence of MFH, including myxoid MFH, in the mediastinum was considered questionable. *In addition, MFH is now recognized as undifferentiated pleomorphic sarcoma because the tumor does not demonstrate convincing histiocytic differentiation* [5]. *MFH variants, including myxoid MFH, have been critically re-evaluated. Myxoid MFH is synonymous with myxofibrosarcoma (MFS; a term that more accurately reflects its fibroblastic lineage and myxoid properties)* [6].

Myxoid MFH, now recognized as *MFS*, has frequently been reported in soft tissues without adequate exclusion of DDLS as a differential diagnosis. To the best of our knowledge, only one case of myxoid MFH in the mediastinum has been described in the English literature, thus far [3], without cytogenetic or molecular analyses having been conducted. Adequate exclusion of DDLS is required for a diagnosis of myxoid MFH, especially since amplification of the *MDM2* and *CDK4* genes have proven useful alterations in confirming DDLS [7].

Herein, we report on a rare case of high-grade MFS (formerly recognized as myxoid MFH) in the anterior mediastinum, having excluded DDLS by means of fluorescence-based *in situ*

Abbreviations: CT, computed tomography; DDLS, dedifferentiated liposarcoma; FISH, fluorescence-based *in situ* hybridization; MFH, malignant fibrous histiocytoma; MFS, myxofibrosarcoma; MRI, magnetic resonance imaging

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hybridization (FISH) detection of *MDM2* gene amplification. Our case confirms the existence of MFS in the mediastinum and shows its poor prognosis and rapid progression.

2. Case presentation

A 70-year-old man presented at our clinic with a cough and pyrexia. The patient had a 12-year history of glaucoma. A mass lesion in the right pulmonary hilum was detected on a chest radiograph conducted by the family physician (Fig. 1A). The patient was admitted to the National Hospital Organization Kinki-Chuo Chest Medical Center for further evaluation. Physical examination was normal. Laboratory findings exhibited slight elevations in the levels of fibrin/fibrinogen degradation products, including D-dimer, soluble interleukin-2 receptor, C-reactive protein, and carcinoma antigen 125. Concentrations of alpha-fetoprotein and human chorionic gonadotropin were within reference limits.

A computed tomography (CT) scan of the chest revealed a heterogeneous mass lesion with infiltrative margins in the anterior mediastinum (Fig. 1B). On magnetic resonance imaging (MRI) the mass lesion exhibited heterogeneous low signal intensity with focal high signal intensity on T1-weighted images, and high signal intensity with cystic lesions on T2-weighted images (Fig. 1C and D). There were no signs of adipose tissue or calcification in the chest CT or MRI findings. Clinical differential diagnosis of the lesion included: thymoma with cystic change, thymic carcinoma, and malignant mesenchymal tumor.

Total resection of the tumor and thymus, and partial resection of the right lung, pleura, and pericardium was performed to diagnose and treat the lesion. The diagnosis in the intraoperative consultation with pathologists was malignant spindle cell neoplasia, supporting DDLS, owing to the proliferation of atypical spindle cells on a myxoid background. Post-operative macroscopic findings revealed a lesion measuring $120 \times 78 \times 30$ mm in size that exhibited multi-nodular growth with incomplete septa, and a fibrous variegated gross appearance with fleshy and gelatinous regions with necrosis and hemorrhage (Fig. 2A and B).

In hematoxylin and eosin-stained sections, the mass lesion was composed of 60% myxoid and 40% solid areas (Fig. 3A). The myxoid areas revealed atypical spindle cells with an abundant myxoid matrix (Fig. 3B and C), while the solid areas revealed solid sheets and cellular fascicles of atypical spindle cells with numerous mitoses (≥ 20 mitoses per 10 high power fields) and atypical multi-nucleated cells (Fig. 3D). Lipoblasts were not present in the tumor. In hematoxylin and eosin-stained sections, differential diagnosis of the lesion included: high-grade MFS, DDLS, and sarcomatoid carcinoma. A prominent vascular network was not evident from silver impregnation staining (Fig. 3E). Alcian blue staining exhibited mucin production in the background (Fig. 3F). Immunohistochemical analysis of the spindle cells showed positivity for cluster of differentiation 99 and focal positivity for smooth muscle actin. The spindle cells also stained negatively for cytokeratin and muscle actin monoclonal antibodies, epithelial membrane antigen, tumor protein p63, S-100 protein, B-cell lymphoma 2, desmin, mouse double minute 2 homolog, cyclin-dependent kinase 4, proto-oncogene c-Kit, anion exchanger 1/3, and cluster of differentiation 21/34/68. No amplification of the *MDM2* gene was detected using FISH. The latter, along with negative mouse

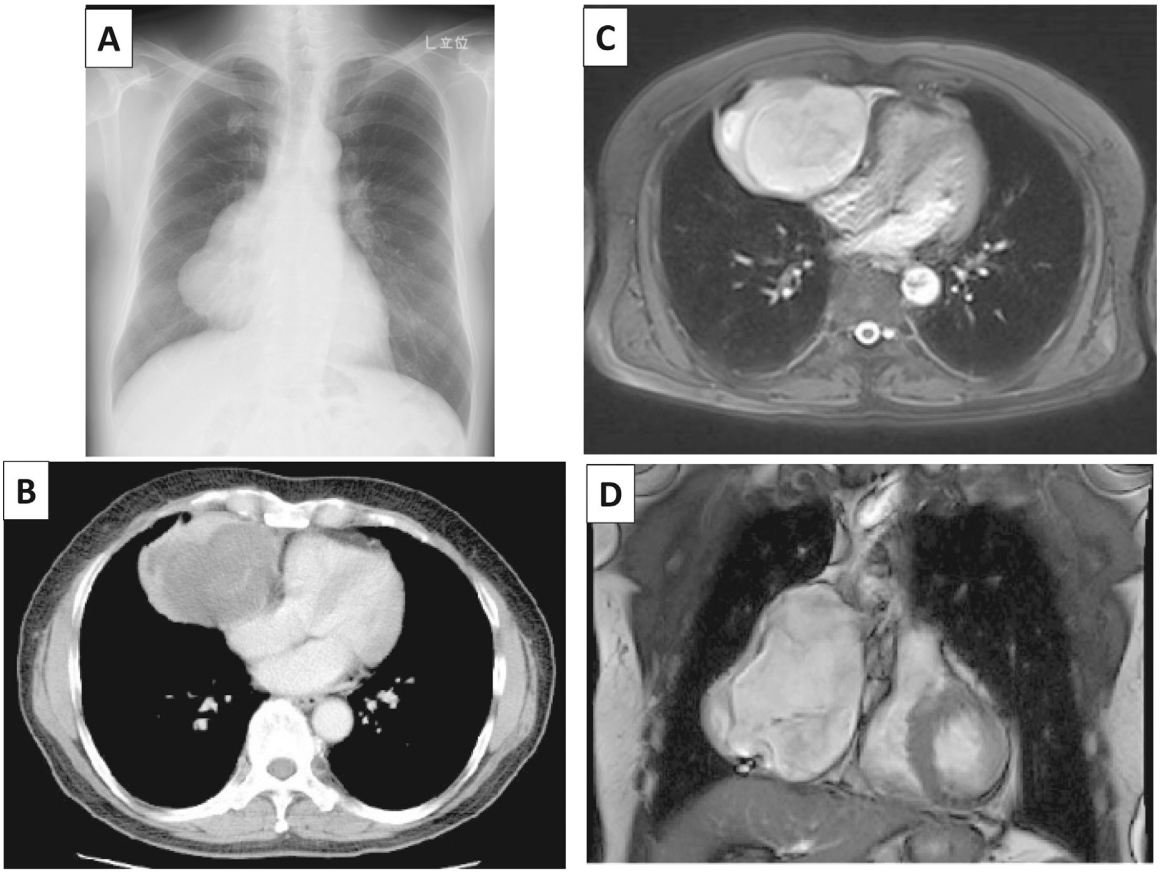

Fig. 1. Imaging findings of the mediastinal tumor: (**A**) chest radiograph revealing a mass lesion in the right pulmonary hilum; (**B**) computed tomography (CT) scan of the chest showing a heterogeneous mass lesion with infiltrative margins in the anterior mediastinum; and (**C-D**) magnetic resonance imaging revealing that the mass lesion exhibits a heterogeneous high signal intensity with cystic lesions on T2-weighted images. There were no signs of adipose tissue or calcification in the chest CT or MRI findings.