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Case Report

Inflammatory myofibroblastic tumor of pericardium: a case report and review of the literature

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Abstract: Primary Inflammatory myofibroblastic tumors (IMTs) of pericardium are exceedingly rare. We reported a case of a 13-year-old female, who presented with abdominal pain and fever. Laboratory examination showed hemoglobin of 76 g/L and elevated C reactive protein of 136.85 mg/L. Computed tomography (CT) scan revealed an obvious circular isodense mass in the right pericardium. The mass was completely resected and the size was 6.2×5.2×5 cm with complete capsule. Microscopically, the tumor was composed of spindle-cells with predominantly scattered inflammatory cells. A panel of immunohistochemical staining revealed diffuse positivity for vimentin and anaplastic lymphoma kinase (ALK), and focal positivity for actin and smooth muscle actin (SMA) in the spindle cells, but negativity for Desmin, calretinin, MC, catenin-β, CD117, CD56, S-100, cytokeratin AE1/AE3, CD21, CD35, CD34, CD99 and bcl-2. Those spindle tumor cells exhibited low proliferating index of Ki-67 (2-3%). Post-operationally, no additional adjuvant therapy was performed. Twenty-five-month follow up was conducted and no evidence of recurrence or metastasis was noted.

Keywords: Inflammatory myofibroblastic tumor, pericardium, followed up

Introduction

Inflammatory myofibroblastic tumor (IMT) is a rare neoplasm from mesenchyme, which comprises of myofibroblastic and fibroblastic spindle cells with an inflammatory infiltration of plasma cells, lymphocytes, and/or eosinophils [1]. IMT occurs mainly in children and young adults, especially in females. The most frequent site is lung, but it also occurs in many extra-pulmonary positions [2, 3]. The heart is relatively less commonly involved for primary IMT. According to our knowledge, approximately 60 cases of IMT affecting the heart have been described in the English literature, and only one case occurred in pericardium [4]. We herein reported a case of a 13-year-old girl with IMT in pericardium and further performed a review of these cases. The objective of this study was to describe the clinicopathological features, and analyze the diagnosis and differential diagnosis of pericardium IMT.

Case report

A 13-year-old female presented with abdominal pain for half a month and with fever for a few days. Laboratory examination was conducted after admission. Blood count showed hemoglobin of 76 g/L and elevated C reactive protein of 136.85 mg/L. A chest computed tomography (CT) scan revealed a clear circular isodense mass in the right pericardium with large pericardial effusion (**Figure 1A**, **1B**). Whole-physical imaging examinations revealed there were no other tumors. During the operation, surgeon discovered that most of the mass had no adhesions to the heart and the basal part of the tumor was attached to the sulcus of the atria, which suggested that the tumor was originated from the pericardium, not the heart itself. Macroscopic pathology demonstrated the completely resected tumor measured 6.2×5.2×5 cm with complete capsule. It had a firm, tan-white, whorled cut surface with myxoid areas

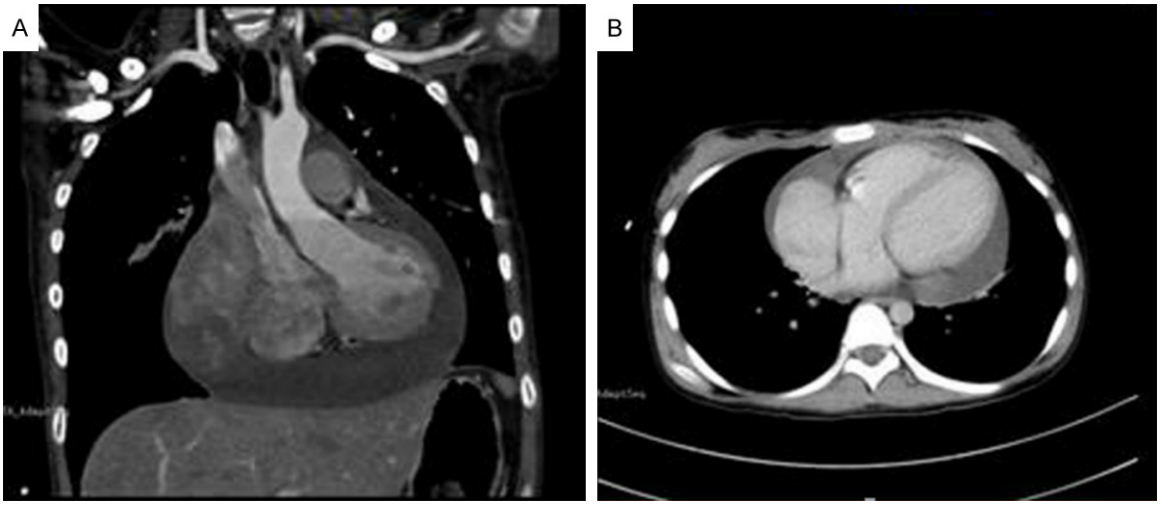

Figure 1. Radiological findings of the current patient by computed tomography (CT) before operation. (A, B) CT scan revealed a Clear circular isodense mass in right pericardium with large pericardial effusion (A: On Coronal section scan. B: On sagittal section scan).

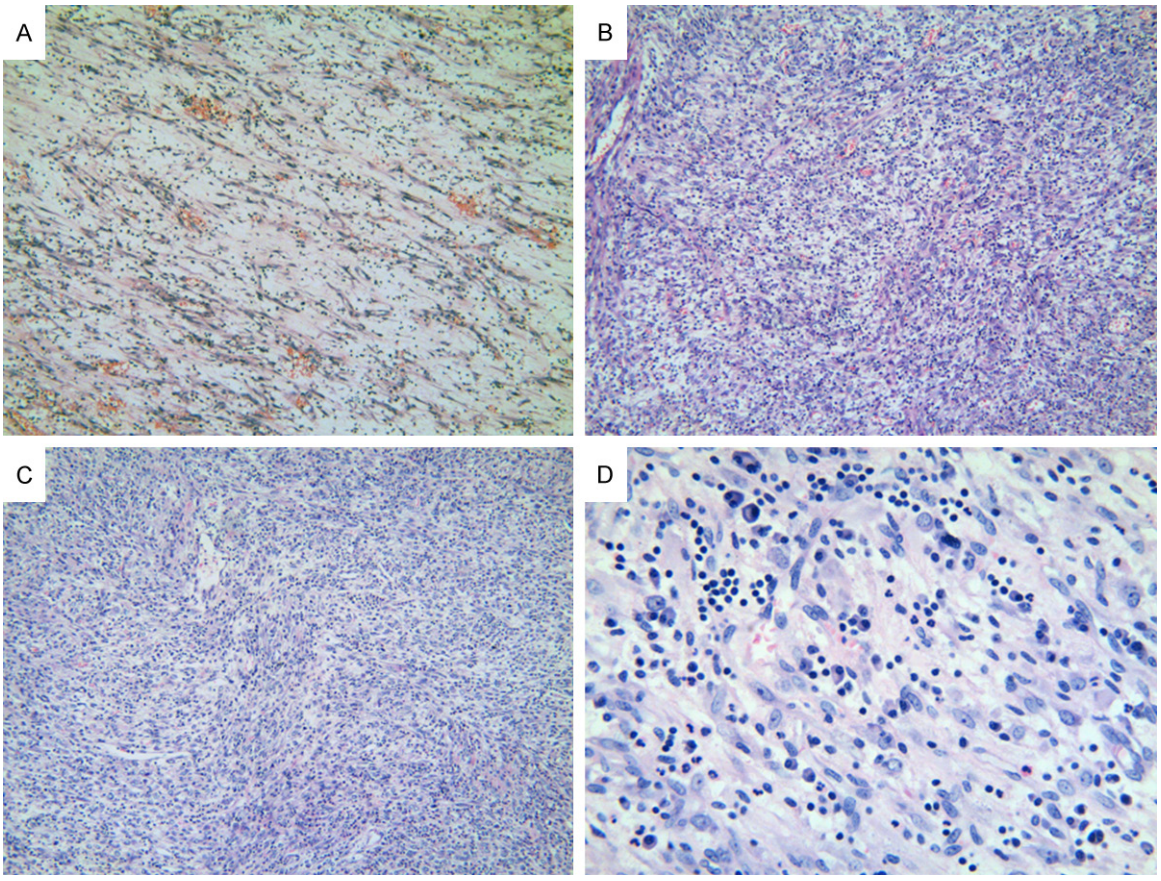

Figure 2. Histology examination of the pericardial inflammatory myofibroblastic tumor (IMT) with hematoxylin-eosin staining. A. Photomicrograph showing loosely arranged plump spindle cells with a prominent inflammatory infiltrate in an edematous or myxoid stroma with prominent vasculature background (magnification 100×). B, C. Photomicrograph showing compact fascicular spindle cells arranged the architectural growth patterns including fascicles or whorls with prominent inflammatory infiltrate (magnification 100×). D. Photomicrograph showing spindle cells were plump, fusiform or oval, with a vesicular nucleus containing obvious nucleoli and an eosinophilic cytoplasm and with a background of an inflammatory infiltration of plasma cells (magnification 400×).

and soft texture. No calcifications were found in the specimens. Microscopically, the tumor was composed of spindle tumor cells and with predominantly scattered inflammatory cells including plasma cells, lymphocyte and eosinophils. Spindle cells exhibited loosely in the edematous or myxoid areas. Numerous vessels could be observed in the mesenchymal background of tumor (**Figure 2A**). Meanwhile, it could be seen that compact fascicular spindle cells arranged into architectural growth patterns including fascicles or whorls with prominent inflammatory infiltration (**Figure 2B**, **2C**). Spindle cells were plump, fusiform or oval, with a vesicular nucleus containing obvious nucleoli and an eosinophilic cytoplasm and with a background of an inflammatory infiltration of plasma cells (**Figure 2D**). Typical mitotic figures were not observed. A panel of immunohistochemical staining revealed diffuse positivity for vimentin and anaplastic lymphoma kinase (ALK) (**Figure 3A**, **3B**), and focal immunoreactivity for actin and smooth muscle actin (SMA) (**Figure 3C-F**) in the spindle cells, but negative for Desmin, calretinin, MC, catenin-β, CD117, CD56, S-100, cytokeratin AE1/AE3, CD-21, CD35, CD34, CD99 and bcl-2. The tumor spindle cells exhibited low proliferating index of Ki-67 (2-3%) (**Figure 3G**, **3H**). Post-operationally, no additional adjuvant therapy was performed. No recurrence or metastasis was observed over the 25-month-follow-up.

Discussion

Primary heart tumors are extremely rare. The occurrence rate is approximately 0.02%. IMT constitutes <5% of primary heart tumors [4]. It arises predominantly in teenagers, with a mean age of presentation of about 17 years [3]. Most of the cardiac IMTs were located in right atrial or ventricular endocardium [3, 4]. To our knowledge, primary IMT of the pericardium has been occasionally reported only. The nonspecific symptoms of IMTs include an anemic appearance, fevers, abdominal pain or a palpable abdominal mass with non-specific laboratory discoveries [5]. The cardiac imaging is quite useful for the diagnosis of cardiac tumors [6]. The case reported in this paper presented with abdominal pain and fever symptoms. During the process of diagnosis and treatment, the heart mass was discovered in the pericardium by imaging examination and confirmed by the surgeon and pathology analysis.

Decisive diagnosis of IMTs is supported by pathological examination and immunohistochemical staining. Macroscopically, IMTs may be firm, fleshy or gelatinous with a white or tan cut surface. Calcification, hemorrhage, and necrosis are rare [7]. Histologically, the prominent feature under the microscope was that the hybrid plasma cells, lymphocytes and (or) eosinophils infiltrating into the area of the spindle cells. Because of these characteristics, the inflammatory myofibroblastic tumor was also named as inflammatory myofibroblastic tumor, plasma cell granuloma, inflammatory fibrohistiocytic tumor, xanthomatous pseudotumor, xanthogranuloma, or pseudosarcomatous fibromyxoid tumor [8-10]. The spindle cells were plump, fusiform or oval, which arranged in fascicles or whorls, some of the cells had obvious nucleoli and eosinophilic cytoplasm. Mitotic figures are rarely observed for IMTs. IMTs show fasciitis-like, compact spindle cell and hypocellular fibrous histologic patterns [7]. The first pattern is that plump or spindle myofibroblasts were loosely arranged in edematous myxoid background, in which infiltration of plasma cells, lymphocytes and abundant blood vessels in mesenchyme were observed. The second pattern is characterized by compact fascicular spindle cells arranged into the architectural growth patterns including fascicles or whorls with prominent inflammatory infiltration. The third pattern consists of a scar-like proliferation of plate-like collagen with lower cellularity and a relatively sparse inflammatory infiltration of plasma cells and eosinophils [1]. But spindle cells of the three patterns generally do not have obvious deformed nucleus or atypical mitosis. In this case, the first and the second patterns were visible.

An immunohistochemical examination revealed that the spindle tumor cells were positive for vimentin and SMA, and negative for desmin and CD34, suggesting that the spindle cells were myofibroblastic cells [10]. ALK was lately considered as a valuable marker for IMT, and the positive ratio of ALK in IMTs was stated to range from 50 to 70% by immunostaining [5]. ALK is a helpful marker for the diagnosis for IMT, however, negativity for the antibody could not exclude the possibility of IMT [11]. For the cases lack of ALK expression, fluorescence in situ hybridization (FISH) to detect the gene amplification may gain higher sensitivity compared to traditional Immunohistochemistry [11].

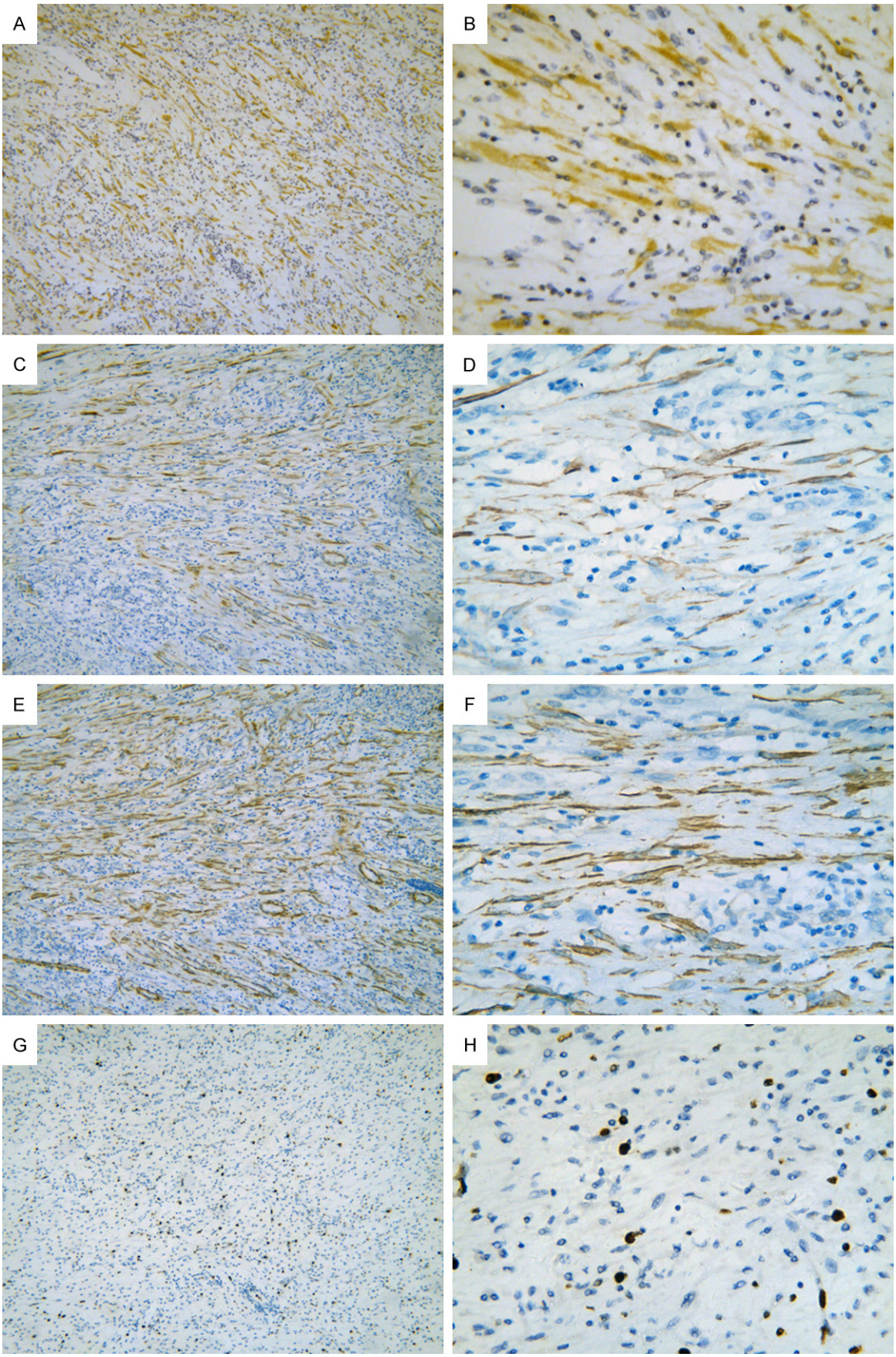
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Figure 3. Immunohistochemical examination of the pericardial inflammatory myofibroblastic tumor (IMT). (A, B) Immunohistochemical staining, positive for ALK (A magnification 100×, B magnification 400×). (C, D) Immunohistochemical staining, focal positive for Actin (C magnification 100×, D magnification 400×). (E, F) Immunohistochemical staining, focal positive for SMA (E magnification 100×, F magnification 400×). (G, H) Immunohistochemical staining showing the spindle tumor cells exhibited low proliferating index of Ki-67 (G magnification 100×, H magnification 400×).

In histology, the pericardial IMT of this report could be differentiated from other tumors with spindle cells such as low-grade sarcoma, follicular dendritic cell tumors, mesothelioma, peripheral nerve neurofibroma, fibromatosis and solitary fibrous tumor. In addition, owing to the prominent inflammatory cells, especially abundant plasma cells, IgG4-related diseases also need to be excluded [3, 12]. Immunostaining can help for the final diagnosis. The differential diagnosis of low-grade sarcoma with myofibroblastic differentiation was on the basis of lacking characteristics of obvious pleomorphism and atypical mitotic figures [2]. Follicular dendritic cell tumors also showed spindle cells, but the tumor cells could be marked with positive CD21, CD23, CD35 staining and absent ALK1 rearrangement. The morphology of mesothelioma is diverse, and tumor cells can be spindle. Immunohistochemically, calrentin and MC are positive, and CK5/6 and D2-40 also can be expressed, but ALK and SMA were negative for mesothelioma. Peripheral nerve neurofibroma, whose S-100 is strongly positive. But it is negative for SMA, Actin and ALK. For fibromatosis, their spindle cells are relatively sparse and inflammation is not obvious. Furthermore, atenin-β is often positive for fibromatosis. As solitary fibrous tumor is concerned, both hypocellular and hypercellular areas can be observed, which were separated by thick, hyalinized collagen with staghorn vessels. Immunohistochemistry of CD34, CD99 are usually positive, but smooth muscle actin and desmin are negative [13]. The differential diagnoses above could be excluded in the current case based on histological morphology and immunohistochemistry.

The molecular pathways and etiology of IMTs remain unknown. Recently, Lu et al [14] reported that IMTs had Up-frame shift 1 (UPF1; also called RENT1) mutations in 13 of 15 (86%) pulmonary samples. UPF1 mutations led to reduced nonsense-mediated RNA decay (NMD) magnitude, which provides evidence that disruption of NMD pathway has a contributory role in the majority of IMTs. UPF1 mutations and NMD activity may be beneficial diagnostic biomarkers for this disease. The World Health Organization (WHO) classification defines IMT as a mesenchymal neoplasm of intermediate biological potential, which may recur but rarely metastasize (<2%) [1]. Guidelines for the treatment of IMTs are not available. In most cases, complete surgical resection of the tumor is the best treatment for cardiac IMT [5]. Some studies recommend that the use of NSAIDs after the surgery should be a better option for treatment [15, 16]. Kovach et al [17] found that in patients with local tumor resection without radiotherapy or chemotherapy, there was a recurrence rate of 8%. Therefore, follow-up for the IMT patient is necessary. In our current case, the follow-up period of 25 months was conducted and no evidence of recurrence or metastasis was obtained.

In summary, the pericardium is one of the rarest sites of IMTs. Signs and symptoms are usually nonspecific. The cardiac imaging is extremely useful for the discovery of tumors. The diagnosis can be supported by histopathological analysis of the surgically removed specimens and immunohistochemical features are helpful for diagnosis. Differential diagnoses with other spindle cell tumors occurring in the heart is strongly necessary.

Disclosure of conflict of interest

None.

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