Thymic Dedifferentiated Liposarcoma Having a Leiomyosarcomatous Dedifferentiated Component

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(Received October 19, 2021; Accepted November 24, 2021)

We report an extremely rare case of 42-year-old man, diagnosed with thymic dedifferentiated liposarcoma (DDL) having a leiomyosarcomatous dedifferentiated component. The tumor was composed of atypical spindle cells. The morphological atypia was also observed around thymic adipose tissue. Immunohistochemically, the spindle cells were positive for desmin, smooth muscle actin, MDM2 and CDK4. MDM2 and CDK4 were also positive for the thymic adipose tissue. *MDM2* amplification was confirmed by fluorescence *in situ* hybridization. Although there are some reports of mediastinal leiomyosarcoma, DDL may be overlooked. For accurate diagnosis of mediastinal mesenchymal tumor, careful observation of thymic adipose tissue is required with immunohistochemical study.

Key words: Thymus, dedifferentiated liposarcoma, leiomyosarcoma, thymic adipose tissue

INTRODUCTION

Mesenchymal tumors are rare in mediastinum including thymic tissue. Some types of the mesenchymal tumors are reported: thymolipoma, lipoma, liposarcoma, solitary fibrous tumor, synovial sarcoma, vascular neoplasms, neurogenic tumors, and other rare mesenchymal tumors, and liposarcoma is the most common sarcoma among these tumors [1]. There have been some series studies regarding mediastinal liposarcoma [2–7]. Although these studies include some cases that are associated with thymus, there was no case of dedifferentiated liposarcoma (DDL) which has a leiomyosarcomatous dedifferentiated component and is associated thymus in these studies [2–7].

Binh MB *et al*. described mediastinal DDL having a leiomyosarcomatous dedifferentiated component in their study, but the tumor location, especially in relation to the thymus, was not described [4]. Boland *et al*. reported only one case of anterior mediastinal well-differentiated liposarcoma (WDL) with low-grade smooth muscle differentiation (lipoleiomyosarcoma) in 24 cases of mediastinum and thoracic liposarcoma [5]. Moreover, one case of WDL with smooth muscle component in anterior mediastinum is described [6]. However, thymic DDL having a leiomyosarcomatous dedifferentiated component has been not well known.

We report an extremely rare case of thymic DDL having a leiomyosarcomatous dedifferentiated component mimicking mediastinal leiomyosarcoma.

CASE REPORT

A 42-year-old man without a family history of malignancy had a history of clear cell renal cell carcinoma (38-year-old) and underwent follow up examination. Chest computed tomography revealed a tumor of 32 mm in diameter in the anterior mediastinum (Fig. 1). No apparent evidence of calcification or hemorrhage was noted. The lesion abutted the ascending aorta. Metastasis of renal cancer or thymoma was suspected, and the tumor was resected without pre-operative biopsy.

Macroscopic examination revealed a relatively well-circumscribed tumor of 30 mm in diameter (Fig. 2a). It was a white to tan mass with a whorled appearance (Fig. 2a). Hemorrhage, necrosis, and cystic change were not observed. Microscopically, the tumor was composed of bundles of eosinophilic spindle cells (Fig. 2b, c, 3a). Thymic tissue, including adipocytes and lymphoid tissue with Hassall's corpuscles, was observed around the spindle cell lesion (Fig. 2b). The tumor cell nucleus was elongated and blunt ended (Fig. 2c). Nuclear hyperchromasia and pleomorphism were noted focally (Fig. 2d). The spindle cells involved a vessel in a part of the tumor (Fig. 2e). Mitotic figures were observed at frequency of 4/10 hpf. Adipocytes in thymic tissue had atypia and hyperchromatic stromal cells were observed in fibrous septa (Fig. 2f). Coagulated necrosis and hemorrhage were not observed. Immunohistochemically, spindle cells were positive for desmin, smooth muscle actin, MDM2, and CDK4 (Fig. 3b–e), and negative for S100 protein, CD34, and c-kit. Due to the overexpression of MDM2 and CDK4,

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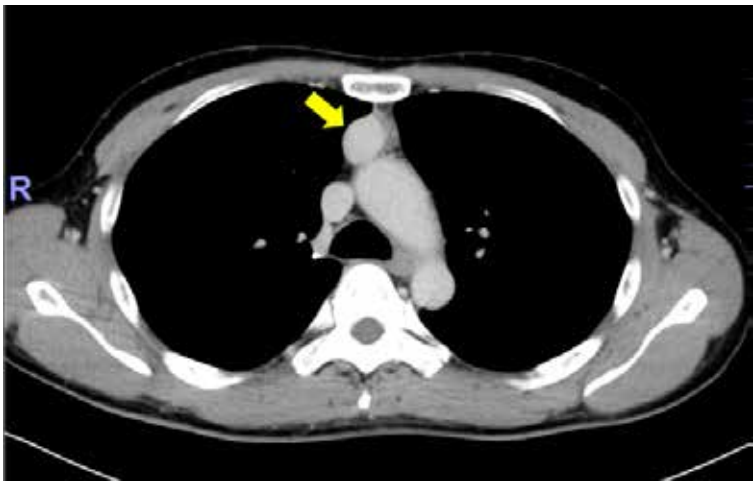

Fig. 1 Chest computed tomography reveal a tumor of 32 mm in diameter in the anterior mediastinum (arrow).

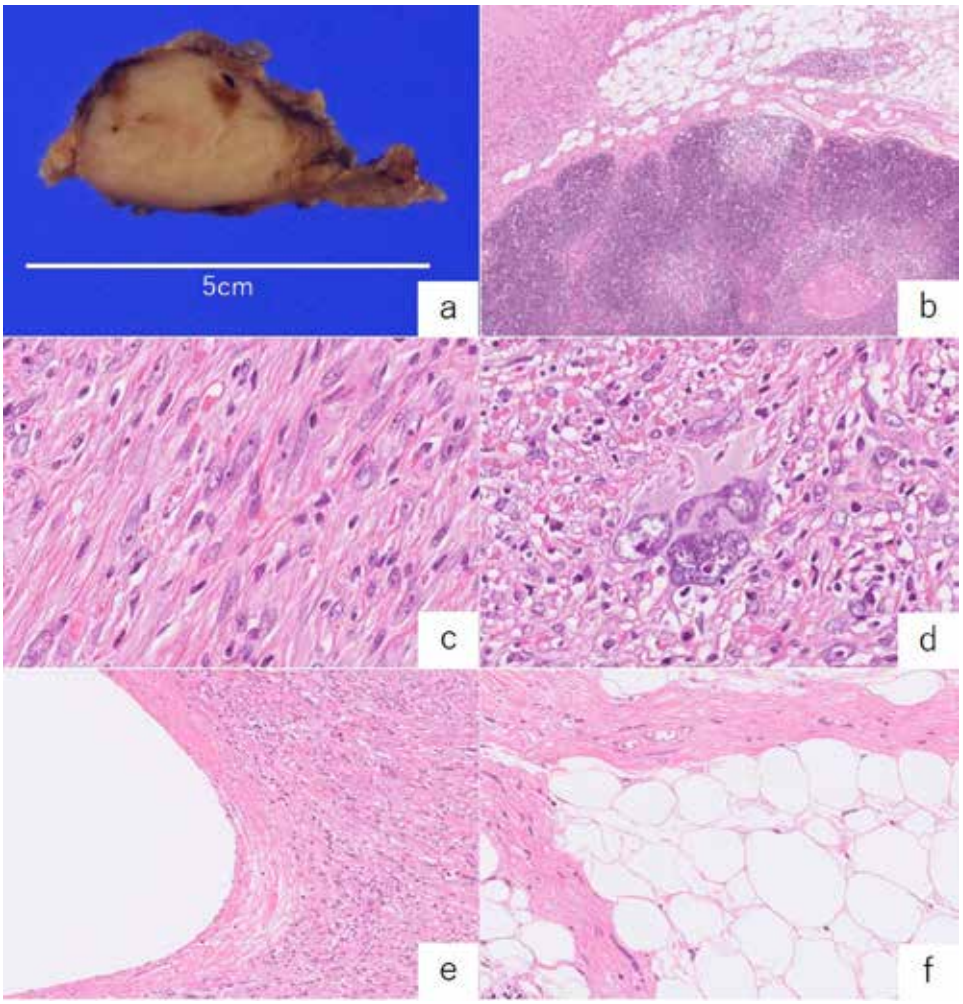

Fig. 2 (a) A relatively well-circumscribed white to tan tumor of 30 mm in diameter with a whorled appearance was observed.
(b) The tumor was composed of bundles of eosinophilic spindle cells. Thymic tissue, including fat and lymphoid tissue with Hassall's corpuscles, was observed around the spindle cell lesion. (HE, 2.5x)
(c) The tumor was composed of bundles of eosinophilic spindle cells. The tumor cell nuclei were elongated and blunt-ended. (HE, 20x)
(d) Nuclear pleomorphism was focally noted. (HE, 20x)
(e) The tumor cells involved a vessel. (HE, 10x)
(f) Adipocytes in thymic tissue had atypia and hyperchromatic spindle cells were observed in fibrous septa. (HE, 10x)

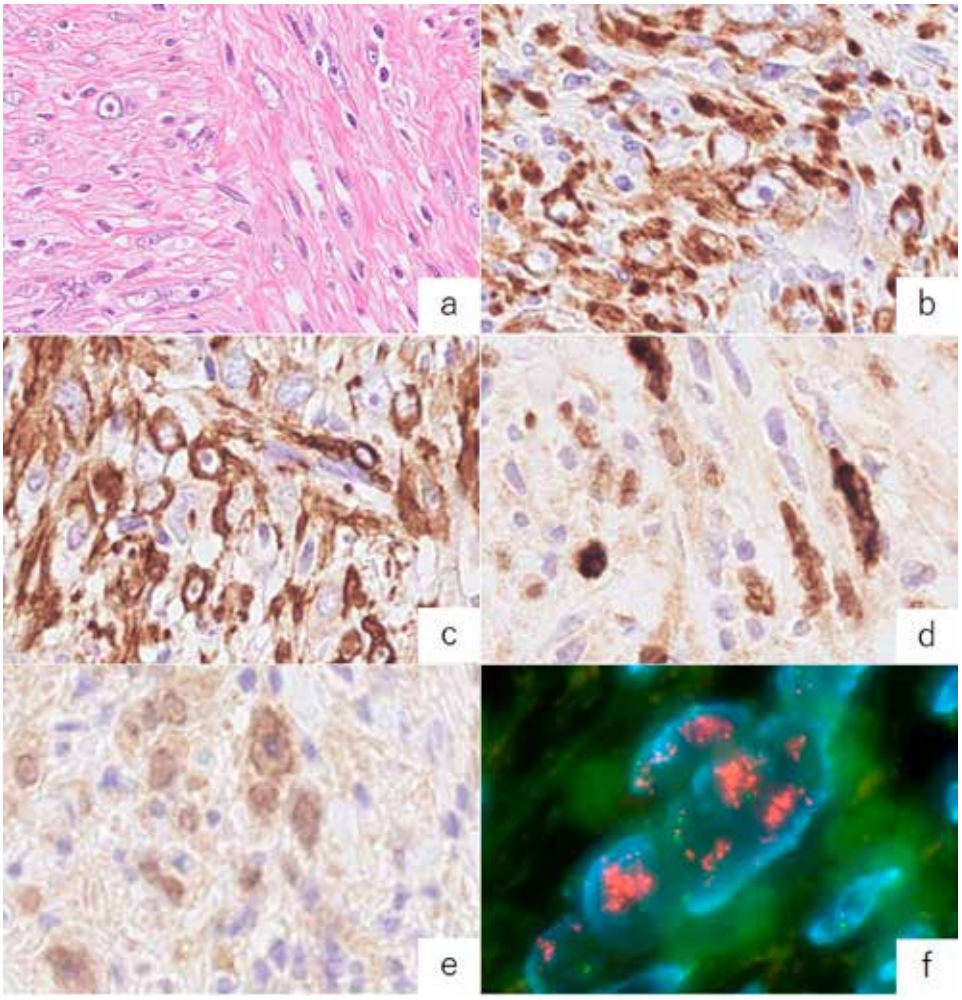

Fig. 3 (a) The tumor was composed of bundles of eosinophilic spindle cells. (HE, 20x)
(b) The tumor cells were positive for desmin.
(c) The tumor cells were positive for smooth muscle actin.
(d) The tumor cells were positive for MDM2.
(e) The tumor cells were positive for CDK4.
(f) *MDM2* FISH (red signal; *MDM2*, green signal; CEP12) revealed amplification of *MDM2* in tumor cells.

examination of *MDM2* amplification by fluorescence *in situ* hybridization (FISH) was performed and amplification was confirmed in spindle cells and atypical adipocyte (Fig. 3f). Although mediastinal leiomyosarcoma was listed in the differential diagnosis, the WDL component and *MDM2* amplification led to the final diagnosis of thymic DDL having a leiomyosarcomatous dedifferentiated component.

The patient has been treated by additional radiation therapy and has been well without recurrence or metastasis for 10 months after surgery. This patient has double malignant tumor in spite of his young age, but microsatellite instability analysis is negative by multiplex PCR fragment analysis.

DISCUSSION

According to the studies of mediastinum mesenchymal tumor, DDL arising from thymus is rare [2–7]. Although the association with DDL and thymus is unclear in some reported cases, our present case clearly showed DDL located in thymic tissue, including adipocytes and lymphoid tissue with Hassall's corpuscles, around the spindle cell lesion. It is necessary to clarify the location for making a diagnosis of DDL of thymic origin. Our reported case shows the spindle cell lesion occupies most of the tumor, however, a WDL component having atypia in thymic adipocytes and stromal cells in fibrous septa is recognized. These morphological findings lead to the final diagnosis of DDL by detecting overexpression of MDM2 and CDK4 by immunohistochemistry and *MDM2* amplification by FISH. Although the WDL component may not be identifiable in some DDL cases, histologically, it is important to observe the morphological findings in adipocyte, especially thymic adipose tissue.

Thymic DDL having a leiomyosarcomatous dedifferentiated component has been not well known. Although mediastinal DDL may have heterologous components, such as a rhabdomyosarcoma, leiomyosarcoma, or osteochondrosarcoma component, there has been no report of thymic DDL having a leiomyosarcomatous dedifferentiated component with a detailed pathological description [2–7]. Smooth muscle differentiation is a rare event in liposarcoma, and

may consist of either WDL with an intrinsic smooth muscle component, so-called "lipoleiomyosarcoma," or DDL having smooth muscle differentiation in the dedifferentiated zones [8]. In the present case, the leiomyosarcomatous differentiated component had sufficient cellular atypia to diagnose the tumor as not lipoleiomyosarcoma. Although Gómez-Román JJ *et al*. reported lipoleiomyosarcoma arising in aorto-pulmonary region, the tumor may be DDL having leiomyosarcomatous differentiated component [9]. Some cases of primary leiomyosarcoma of the mediastinum have been reported [10–12], but the possibility of DDL has not been examined. Our report recommends the evaluation of immunohistochemistry to detect mediastinal DDL with observing histological findings around tumor. Mediastinal leiomyosarcoma may develop from the vessels because the tumors histologically involve or attach to vessels [10]. Indeed, involvement of vessels was observed in the present case. We suggest that involvement or attachment to vessels reflects "tumor invasion", not "tumor origin".

Although myxoid liposarcoma is radiosensitive, WDL/DDL is not so radiosensitive [13]. But Miura *et al*. suggest that radiation therapy may be effective to control recurrent lesions in mediastinal DDL [7]. In this case, the tumor was localized in anterior mediastinum and surgical margin was positive for WDL component, so we chose radiotherapy for postoperative treatment, considering previous report with referring to Japanese Orthopaedic Association Clinical Practice Guidelines on the Management of Soft Tissue Tumors, 2nd edition.

The clinical feature of liposarcoma of mediastinum are as follows, median age is 58 years old, common symptoms are dyspnea and cough, some patients are asymptomatic [3]. Chen *et al*. studied primary intrathoracic liposarcoma and reported that poor disease-free survival and inferior overall survival were observed in the myxoid, pleomorphic and dedifferentiated types as compared to well-differentiated type [14]. However, the number of thymic DDL is small, and further studies are necessary to evaluate the clinicopathological features including treatment.

In conclusion, we report an extremely rare case of thymic DDL having a leiomyosarcomatous dedifferentiated component. For making accurate diagnosis, it is especially important to observe the surrounding adipose tissue with immunohistochemistry, because there is the possibility that thymic DDL has been reported as mediastinal leiomyosarcoma.

CONFLICT OF INTEREST

There were no conflicts of interest.

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