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Case Report

Primary well differentiated liposarcomas in the mediastinum: two cases and a review of the literature

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Abstract: Well differentiated liposarcoma is a malignant mesenchymal tumor which occurs extremely rarely in the mediastinum, comprising less than 1% of all mediastinal tumor cases. The tumor is indistinguishable radiologically from other neoplasms occurring in the mediastinum including lipoma, teratoma and thymoma. Therefore, histological examination is the most important tool in the diagnostic process. Here, we report two cases of well differentiated liposarcoma in the mediastinum of Asian female. Both of the lesions were radiologically diagnosed as benign tumors, but the histological findings, including significant variation in cell size, focal nuclear atypia in adipocytes, and scattered lipoblasts, supported the diagnosis of well differentiated liposarcoma. Upon reviewing the literature, we have summarized the clinical presentation, prognosis, and treatment of liposarcoma in the mediastinum. We found that Computed tomography (CT) scans are the imaging modality of choice for the diagnosis of such lesions, but ultimately, histological examination is required for a definitive diagnosis.

Keywords: Liposarcoma, mediastinum, diagnosis, computed tomography, histological

Introduction

Atypical lipomatous tumor (ALT)/well differentiated (WD) liposarcoma is an intermediate (locally aggressive) malignant mesenchymal neoplasm, typically occurring in the lower extremities and retro peritoneum. And accounting for 10-16% of all sarcomas, it is the most common type of soft-tissue sarcoma [1]. When this tumor occurs in the mediastinum, obtaining a wide margin surgically is nearly impossible, resulting in a high propensity for recurrence, so the diagnosis of "well differentiated liposarcoma" is recommended. Primary liposarcoma in the mediastinum is extremely rare, comprising less than 1% of all mediastinal tumor cases [2]. It shares radiographic features with other mediastinal tumors and can be misdiagnosed as the more commonly occurring lipoma, teratoma or thymoma. The two cases we report were initially diagnosed as benign tumors by the radiologist due to the density of the adipose tissue on the computed tomography (CT) scan and because of the patient's lack of worrisome clinical features, such as weight loss Histologically, the tumor cells displayed significant variation in cell size with focal adipocyte nuclear atypia and scattered lipoblasts, suggestive of the diagnosis of well differentiated liposarcoma.

Case presentation

Case one is a 33-year-old female patient who presented to the hospital with dyspnea, post-exercise orthopnea, as well as an occasional cough producing white phlegm. Case two is a 55-year-old Asian female who presented to the hospital with a three year history of dyspnea and three month history of a cough productive of white phlegm. Their visit to the hospital was prompted by worsening of symptoms. No other neurological deficits were identified in both two patients. Both of the two patients had no history of trauma or cranial nerve abnormalities. Both of the two patients declared for no family history of malignant tumor.

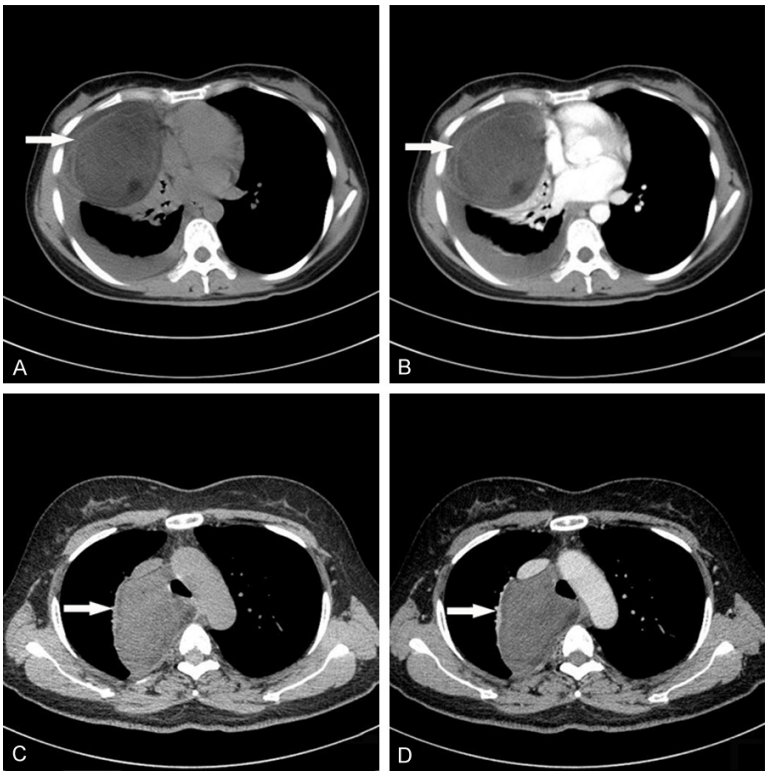

Figure 1. Computed tomography (CT): (A) In case one, the lesion marked with a white arrow is a large heterogeneously dense shadow in the mediastinum near the aortic arch. (B) In case one, the lesion presented as a heterogeneous density with a focal fat shadow and no distinct enhancement after contrast administration; the lesion is marked with a white arrow. (C) In case two, a distinct heterogeneously dense shadow with clear boundaries in the mid aspect of the posterior mediastinum is seen with no enhancement (D), the lesion is marked with a white arrow.

Materials and methods

The patients underwent computed tomography (CT) and magnetic resonance imaging (MRI) examinations. Pathology examination was performed, the resected tissues were embedded in paraffin blocks and sectioned, H&E staining was done according to the standard protocol. This study was prospectively performed and approved by the institutional Ethics Committees of China Medical University and conducted in accordance with the ethical guidelines of the Declaration of Helsinki. Written informed consent was obtained from the patient for the publication and accompanying images.

Result

Case one

The contrast-enhanced CT scan of her thorax revealed a large mediastinal mass near the right lung characterized by a heterogeneous density with local fat shadow but no distinct enhancement following contrast administration (**Figure 1A**, **1B**). Radiologically, the differential diagnosis for the lesion included lipoma, teratoma or thymoma. The tumor was surgically resected and submitted for pathologic evaluation. On gross examination, the lesion measured 10 x 8 x 7 cm, was well-circumscribed, lobulated in shape with no macroscopic evidence of invasion into surrounding tissue. The cut surface of the tumor was white-yellow, firm, and there was no grossly apparent necrosis or hemorrhage. Microscopically, adipocyte-like tumor cells showed significant variation in size and nuclear atypia. Scattered lipoblasts could also be seen among the mesenchymal cells. The histological appearance was most consistent with WD liposarcoma (**Figure 2A** and **2B**). Clinical follow-up based on review of the patient's electronic medical record showed no recurrence by CT examination at 3 and 6 months after surgical treatment.

Case two

A 55-year-old Asian female presented to the hospital with a three year history of dyspnea and three month history of a cough productive of white phlegm. A contrast enhanced CT scan of the thorax demonstrated a large heterogeneously dense, non-enhancing mass, with a clear boundary, located in the midline of the posterior mediastinum (**Figure 1C**, **1D**). The lesion was surgically resected and gross examination revealed a 15 x 10 x 7 cm well-circumscribed, encapsulated, white-yellow, and firm mass. Microscopically, lipoma-like tumor cells with atypical features including enlarged, irregular nuclear and scalloped/signet ring-like lipoblasts were easily identified. Ultimately, the mass was pathologically classified as liposar-

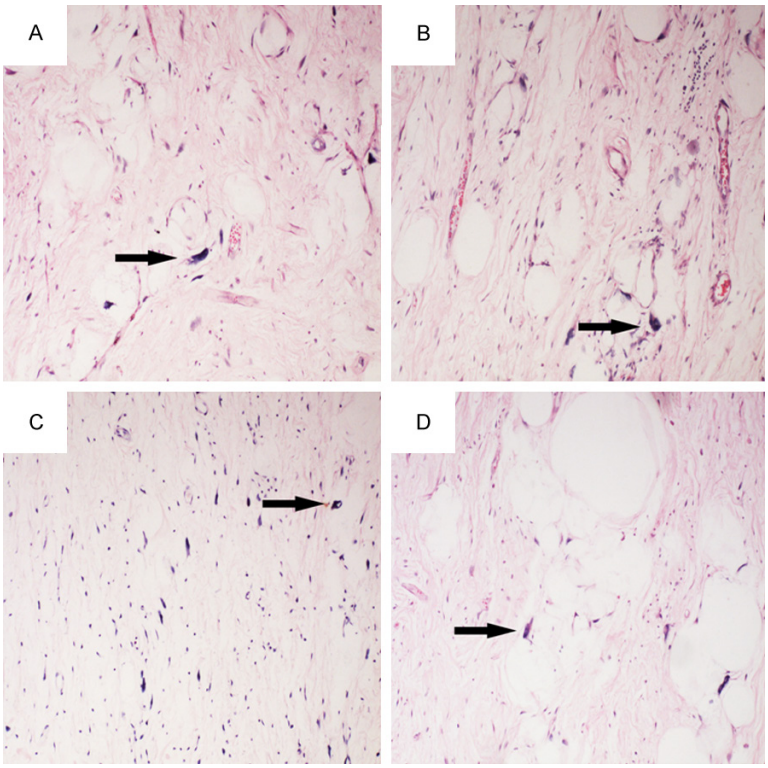

Figure 2. Histopathological examination. (A, B) Case one shows lipoblasts scattered in a background of mesenchymal cells. Lipocytes with nuclear atypia are seen and the lipoblasts are marked with a black arrow; (C, D) Case two exhibited abundant stromal cells (C) and adipocyte-like tumor cell (D), marked with a black arrow.

coma (**Figure 2C** and **2D**). Review of the patient's electronic medical record revealed no radiological evidence of recurrence by CT examination at 3, 6, and 12 months following treatment.

Discussion

ALT/WD liposarcoma accounts for about 40-45% of all liposarcomas and therefore represents the largest subgroup of aggressive adipocytic neoplasms. These lesions primarily occur in middle aged adults with a second peak incidence in the sixth decade. Liposarcoma arises from primitive mesenchymal cells and commonly occurs in the lower extremities and retroperitoneum, with an extremely rare rate of occurrence in the mediastinum. Liposarcomas may also arise from subcutaneous tissue and, more infrequently, from the skin [3-5]. **Table 1** illustrates the demographics, presenting symptoms, treatment, and follow-up data of 20 patients with this rare entity. The majority of cases published in the literature occured in patients older than 40, with a mean age range of 43-58 years. There is no apparent difference in the incidence rate between genders [6, 7]. Both of our patients were women. One of our patients presented at the age of 33, which is younger than the mean age published in the literature; and the other presented at 55, coinciding with the typical mean age. Presenting symptoms vary depending on the location and size of the lesion. Mediastinal liposarcomas commonly grow to a large size and by exerting a mass effect on surrounding organs, they result in clinical symptoms such as shortness of breath, chest pain, and tachypnea [8], as was seen in our cases. Some patients are asymptomatic and their lesions are detected incidentally on imaging, making the diagnosis more difficult [9]. Radiologic investigation is the primary diagnostic approach, specifically CT scan of the thorax. The detected of a heterogeneous low-density shadow similar to that of fat with clear boundaries and no obvious parenchymal enhancement should raise the possibility of a liposarcoma. The radiographic diagnosis of liposarcoma can be challenging due to its similarities with other lesions, including lipoma, teratoma and thymomas by CT.

Histopathological examination is required for a definitive diagnosis. Grossly, liposarcomas are typically large, well-circumscribed, and lobulated masses. Rarely, an infiltrative growth pattern may be seen. Color varies from yellow to white depending on the proportion of adipocytic fibrous/myxoid components present, respectively, Necrosis is commonly apparent in larger lesions. The tumors in our cases were encapsulated and well-circumscribed with a white-yellow cut surface, no obvious necrosis.

ALT/WD liposarcoma can be subdivided morphologically into four main subtypes: adipocytic (lipoma-like), sclerosing, inflammatory, and

Table 1. Clinical features and prognosis of 20 cases mediastinal liposarcoma

NO.	Sex	Age	Location	Symptoms	Treatment	Follow-up
1	F	17	Anterior mediastinum	Shortness of breath, chest discomfort and unusual heart murmur.	Complete surgical excision followed by adjuvant chemotherapy and radiation therapy.	NA
2	M	27	Posterior mediastinum	Chest tightness and shortness of breath	Complete surgical resection and radiotherapy	2 months, no recurrence
3	F	28	Anterior mediastinum	Asymptomatic	Complete surgical excision	NA
4	F	29	Posterior mediastinum	Cough, dyspnea, tachycardia	Complete surgical excision	24 months, no recurrence
5	F	32	Posterior mediastinum	Cough and dyspnea	Complete surgical excision	25 months, no recurrence
6	M	38	Posterior mediastinum	Breathlessness	Complete surgical excision	6 months, no recurrence
7	M	39	Posterior mediastinum	Chest pain	Complete surgical excision	14 months, no recurrence
8	M	44	Posterior mediastinum	Chest distress and abdominal distention	Complete surgical resection and radiotherapy	4 months, no recurrence
9	F	45	Anterior mediastinum	Gastroesophageal reflux, fatigue	Complete surgical excision	24 months, no recurrence
10	F	46	Anterior mediastinum	A palpable neck mass	Complete surgical excision	8 months, no recurrence
11	M	47	Posterior mediastinum	Constant cough, chest distress, and slight dysphagia	Complete surgical excision	25 months, no recurrence
12	M	49	Posterior mediastinum	No symptoms	Complete surgical excision	12 months, no recurrence
13	F	50	Posterior mediastinum	Chest pain	Complete surgical excision with negative margins	15 months, no recurrence
14	M	59	Posterior mediastinum	Left flank pain and cough	NA	7 months, no recurrence
15	M	60	Posterior mediastinum	No symptoms	Complete surgical excision	4 months, no recurrence
16	M	63	Anterior mediastinum	Dyspnea, hoarseness	Complete surgical excision	22 months, no recurrence
17	M	63	Posterior mediastinum	dyspnea, chest pain	Complete surgical excision	6 months, no recurrence
18	F	74	Posterior mediastinum	Dyspnea with strenuous activity	Thoracoscopic resection	3 months, no recurrence
19	M	77	Anterior mediastinum	Dyspnea and recent onset of chest pain without fever or weight loss.	Complete surgical excision	24 months, no recurrence
20	M	87	Posterior mediastinum	Cough, chest pain	Complete surgical excision	Death from unrelated causes

Notes: Abbreviations, F: female, M: male, NA: not mentioned.

spindle cell [10-13]. The presence of more than one morphological pattern in the same lesion is common, particularly in retroperitoneal tumors. The two cases we report were of the adipocytic type, characterized by a proliferation of relatively mature adipocytic call, focal nuclear atypia, and scattered lipoblasts. Immunohistochemistry and molecular testing play a very minor role in the diagnosis of ALT/WD liposarcoma because of their classic morphological features. MDM2 amplification studies were not performed on our cases because the characteristic histological appearance did not warrant further testing.

The most important prognostic factor for ALT/WD liposarcoma in the mediastinum is extent of resection with clear margins. Overall survival rates associated with radical surgery are superior to conservative surgical approaches. According to the literature, patients that underwent conservative surgery and received adjuvant radiation and chemotherapy did not exhibit an improved prognosis or rate of relapse, compared to those who did not receive adjuvant treatments. Furthermore, there was no significant difference between overall survival and disease-free survival when comparing parameters such as gender and age [13]. Fortunately, both of our patients tolerated radical resections and negative surgical excision margins were confirmed intraoperatively by frozen section. At the time this manuscript was submitted, the most recent follow-up data indicated both of our patients were free from disease recurrence at six and twelve months, respectively by CT scan.

In conclusion, liposarcomas are rare tumors in mediastinum. CT scan is the imaging modality of choice, but distinguishing these lesions from radiographically similar lipomas, teratomas, and thymomas is challenging. Therefore, histological examination is the most reliable approach for obtaining a definitive diagnosis.

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Disclosure of conflict of interest

None.

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References

[1] Conesa X, Seijas R, Ares O, Huguet P and Perez-Dominguez M. Multicentric liposarcoma. Acta Orthop Belg 2011; 77: 9-14.

[2] Kashu Y, Yukumi S, Tsunooka N, Tanigawa K, Arakane M, Nakagawa H and Kawachi K. Successful resection of a massive mediastinal liposarcoma that rapidly extended into the entire left thoracic cavity: report of a case. Surg Today 2012; 42: 68-71.

[3] Winchester DS, Gardner KH, Lehman JS and Otley CC. Superficial liposarcoma: a retrospective review of 13 cases. J Am Acad Dermatol 2016; 74: 391-393.

[4] Fukai R, Fukumura Y and Suzuki K. A dedifferentiated liposarcoma of the anterior mediastinum. Int J Clin Oncol 2009; 14: 174-177.

[5] Zhao C, Zhang F, Zhang X, Tu S, Wu Z, Li X, Xiang Y, Zheng C and Zeng Q. Recurrent primary mediastinal liposarcoma: a case report. Oncol Lett 2016; 11: 3782-3784.

[6] Eisenstat R, Bruce D, Williams LE and Katz DS. Primary liposarcoma of the mediastinum with coexistent mediastinal lipomatosis. AJR Am J Roentgenol 2000; 174: 572-573.

[7] Thompson WM, Kende AI and Levy AD. Imaging characteristics of gastric lipomas in 16 adult and pediatric patients. AJR Am J Roentgenol 2003; 181: 981-985.

[8] Oaks J and Margolis DJ. Spindle cell lipoma of the mediastinum: a differential consideration for liposarcoma. J Thorac Imaging 2007; 22: 355-357.

[9] Ferrozzi F, Tognini G, Marchesi G, Spaggiari E and Pavone P. Gastric tumors with fatty components. CT findings and differential diagnosis. Radiol Med 2000; 100: 343-347.

[10] Ishibashi F, Moriya Y, Tamura H, Matsui Y and Iizasa T. Differential diagnosis of primary intrapulmonary thymoma: a report of two cases. Surg Case Rep 2015; 1: 56.

[11] Kaneuchi Y, Hakozaki M,Yamada H, Tajino T, Watanabe K, Otani K, Hojo H, Hasegawa T and Konno S. Primary dumbbell-shaped epidural myxoid liposarcoma of the thoracic spine: a case report and review of the literature. Oncol Lett 2016; 11: 1421-1424.

[12] Dei Tos AP, Mentzel T, Newman PL and Fletcher CD. Spindle cell liposarcoma, a hitherto unrecognized variant of liposarcoma. Analysis of six cases. Am J Surg Pathol 1994; 18: 913-921.

[13] Chen M, Yang J, Zhu L, Zhou C and Zhao H. Primary intrathoracic liposarcoma: a clinicopathologic study and prognostic analysis of 23 cases. J Cardiothorac Surg 2014; 9: 119.