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CLINICAL CASE REPORT

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Mediastinal Desmoid Tumor With Remarkably Rapid Growth

A Case Report

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Abstract: Desmoid tumors (DTs) are a group of rare and benign soft tissue tumors that result from monoclonal proliferation of well-differentiated fibroblasts. Since DTs tend to infiltrate and compress adjacent structures, the location of DTs is one of the most crucial factors for determining the severity of the disease. Furthermore, DTs can further complicate the clinical course of patients when the growth is remarkably rapid, especially for DTs occurring in anatomically critical compartments, including the thoracic cavity.

The authors report a case of a 71-year-old man with a known mediastinal mass incidentally detected 4 months ago, presenting dyspnea with right-sided atelectasis and massive pleural effusion. Imaging studies revealed a 16.4 × 9.4-cm fibrous mass with high glucose metabolism in the anterior mediastinum. The mass infiltrated into the chest wall and also displaced the mediastinum contralaterally. Interestingly, the tumor had an extremely rapid doubling time of 31.3 days.

En bloc resection of the tumor was performed as a curative as well as a diagnostic measure. Histopathologic examination showed spindle cells with low cellularity and high collagen deposition in the stroma. Immunohistochemical staining was positive for nuclear β-catenin. Based on these pathologic findings, the mass was diagnosed as DT. After surgery, there has been no evidence of recurrence of disease in the patient.

This patient presents a mediastinal DT with extremely rapid growth. Notably, the doubling time of DT in our case was the shortest among reported cases of DT. Our experience also highlights the benefits of early interventional strategy, especially for rapidly growing DTs in the thoracic cavity.

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Abbreviations: CT = computed tomography, DT = desmoid tumor, HU = Hounsfield unit, MRI = magnetic resonance imaging, PTNB = percutaneous transthoracic needle biopsy.

INTRODUCTION

Desmoid tumors (DTs), also known as aggressive (deep) fibromatosis or musculoaponeurotic fibromatosis, are a heterogeneous group of rare and benign soft tissue tumors caused by monoclonal proliferation of well-differentiated fibroblasts.[1] These tumors are rare entities that account for only 0.03% of neoplasms and less than 3% of soft-tissue tumors.[2] Previous studies have reported that the estimated annual incidence of DTs is 1 to 4 per million population.[3]

Although DTs do not metastasize, they tend to infiltrate and/or compress adjacent organs, manifesting diverse clinical symptoms. Thus, the location is an important factor that determines the clinical course of DTs.[4] Several therapeutic strategies for DTs have been suggested, including close observation, hormonal therapy, radiation, and curative surgery.[5] The treatment of choice in different clinical situations, however, remains controversial. Specifically, given that the incidence of DTs in the thoracic cavity is uncommon and that mediastinal DTs are quite rare with only approximately 20 patients reported in the English literature, critical factors that clinicians should take into account when they decide the treatment strategy for mediastinal DTs are not well understood.

Herein, we describe a case of a rapidly growing DT in the anterior mediastinum with a calculated doubling time of 31.3 days, the shortest among reported cases of DTs. The rapid growth of DT complicated the clinical course of the patient, causing massive pleural effusion and atelectasis, chest wall invasion, mediastinal shifting, and compression of the diaphragm. The mediastinal DT was completely removed through surgery, and there has been no evidence of recurrence of the disease in the patient.

CASE REPORT

A 71-year-old man visited our emergency department because of 1-week history of dyspnea with productive cough and right chest pain that aggravated with daily activities. He was an ex-smoker with 50 pack-year smoking history. He had undergone aortic repair because of aortic valve regurgitation caused by aneurysm of the aortic root and ascending aorta 2 years before this presentation. Four months before admission, a regular check-up none-enhanced chest computed tomography (CT) scan had shown a 7.4 × 3.4-cm mass in the anterior mediastinum incidentally but no further evaluation was made because of patient refusal (Fig. 1A).

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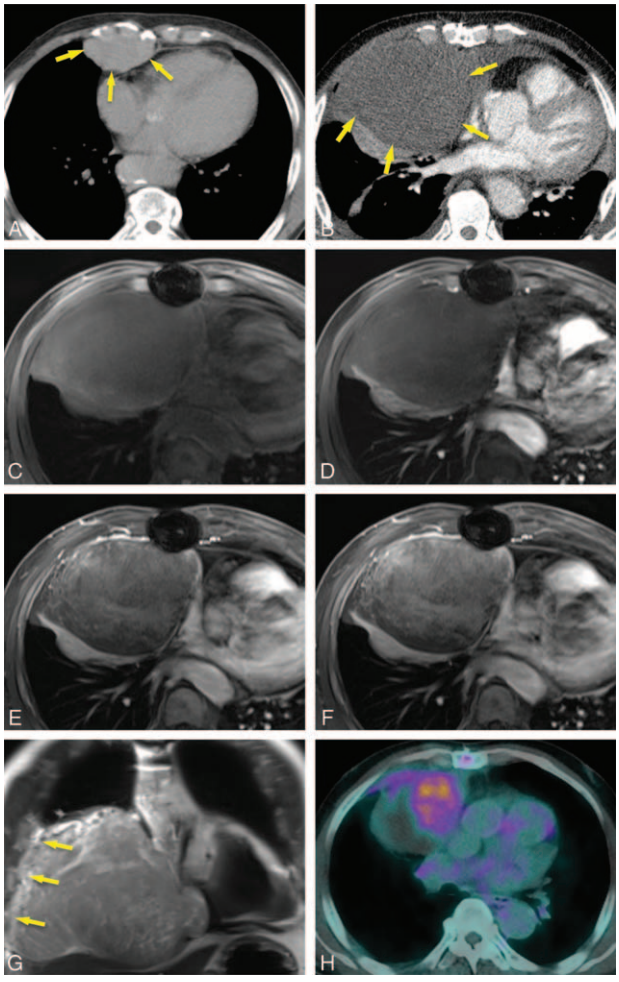

FIGURE 1. (A) Initial axial image of chest CT (none-enhanced) taken at a local clinic displays a tumor (arrows) in the anterior mediastinum. (B) Axial image of chest CT (contrast-enhanced) taken at admission to our clinic 4 months after initial detection of the mass demonstrates extremely rapid growth of the anterior mediastinal tumor (arrows). The tumor shifts the mediastinum to the opposite side and compresses the right heart. The tumor mainly consists of soft tissue matter with a radiodensity of 27 HU on none-enhanced CT. When iodine-based contrast medium was administered, the tumor was enhanced to only 33 HU, implying hypovascularity. (C) Pre-contrast; (D) Arterial; (E) Portal; (F) Delayed-phase dynamic gadolinium-enhanced chest magnetic resonance imaging (T1-weighted image) reveals a delayed enhancement pattern, indicating a fibrous tumor. (G) Coronal image of gadolinium-enhanced magnetic resonance imaging (T2-weighted image) shows infiltration of the tumor into the chest wall (arrows) and displacement of the right diaphragm to the abdominal cavity by the tumor. (H) 2-deoxy-2-[18F]-fluoro-D-glucose positron emission tomography-CT displays elevated glucose metabolism (maximum standardized uptake value = 5.68). CT = computed tomography, HU = Hounsfield unit.

His breathing was shallow, and breathing rate was slightly increased (respiratory rate = 25/min), but other vital signs were within the normal range. Laboratory data revealed that platelets, white blood cells, and differential cell counts were all within the normal range. Arterial blood gas analysis exhibited respiratory alkalosis with metabolic compensation, and arterial oxygen saturation was 96% on pulse oximetry in ambient air. On physical examination, there were decreased breath sounds on the right lower chest, and percussion revealed dullness over that area. Chest x-ray showed pleural effusion on the right hemithorax. Subsequent pleural fluid examination demonstrated neutrophil-dominant (68%) exudate according to Light criteria [pleural fluid protein [4.8 g/dl] to total serum protein (6.4 g/dl) ratio was 0.75]. Subsequent CT scan displayed a 16.4 × 9.4-cm tumor in the anterior mediastinum (Fig. 1B). The tumor had a homogeneous attenuation of 27 Hounsfield units (HU) on nonenhanced CT, and the tumor had 33 HU after enhancement, indicating that the tumor possessed dominantly soft tissue components with hypovascularity. A shift of the mediastinum to the opposite site of the mass and compression of the right-side heart were also evident (Fig. 1B), but there was no evidence of hemodynamic compromise in the patient on echocardiography. Moreover, passive atelectasis was visible in the right upper and middle lobes. There were no enlarged lymph nodes in the thoracic cavity. Because the most frequently occurring masses in anterior mediastinum are thymoma, lymphoma, and teratoma, the radiologic features of the mass on CT scan of our case were very unusual and atypical. In fact, thymoma and lymphoma have been reported to have mild to moderate enhancement, and teratoma often exhibits heterogeneous contents of fat, fluid, and soft tissue, as well as calcification.[6] To further characterize the mass and to evaluate whether the mass was involved in the major vascular system, chest magnetic resonance imaging (MRI) was applied to the patient. The mass showed high signal intensity on T2-weighted images and low signal intensity on T1-weighted images. In addition, the dynamic contrast-enhanced MRI exhibited inhomogeneous enhancement in portal and delayed phases, suggesting that the mass can be a fibrous tumor (Fig. 1C to F). T2-weighted MRI also demonstrated tumor infiltration into the left chest wall at the fifth to seventh rib locations and displacement of the right diaphragm to the abdominal cavity by the tumor (Fig. 1G).

Interestingly, the calculated volume of the tumor by the simple sum-of-area technique, revealed that the tumor had increased from $302.5 \pm 11.68\,cm^3$ to $4103.4 \pm 158.4\,cm^3$ over a period of 116 days (an approximately 13-fold increase in volume).[7] According to the formula to estimate doubling time, as previously described, the doubling time was 31.3 days.[8] Moreover, positron emission tomography showed uneven avid glucose uptake (maximum standardized uptake value = 5.68) (Fig. 1H).

For the pathologic diagnosis of the mass, percutaneous transthoracic needle biopsy (PTNB) was performed. The result, however, was inconclusive because of scant cellular components of the specimen. Thus, we planned surgical resection of the tumor for a curative as well as a diagnostic purpose. The surgical approach was a right thoracotomy. The tumor was readily visible when the thoracic cavity was opened. The largest diameter of the tumor was approximately 20 cm in the operation field. It was roundish, well-encapsulated, and overall soft on palpation. Gross findings exhibited severe adhesion of the tumor to the chest wall (Fig. 2A) such as the fifth to seventh ribs and the lower sternum, the pericardial space, and the medial portion of the diaphragm (Fig. 2B). The tumor compressed the right heart and the adjacent lung without invasion. En bloc resection of the mass consisted of partial resections of the fifth and the sixth ribs, the intercostal muscles, the pericardium, and the diaphragm (Fig. 2C and D). The mass was successfully resected, and histopathologic examination of the specimen revealed spindle cells with low cellularity and high collagen

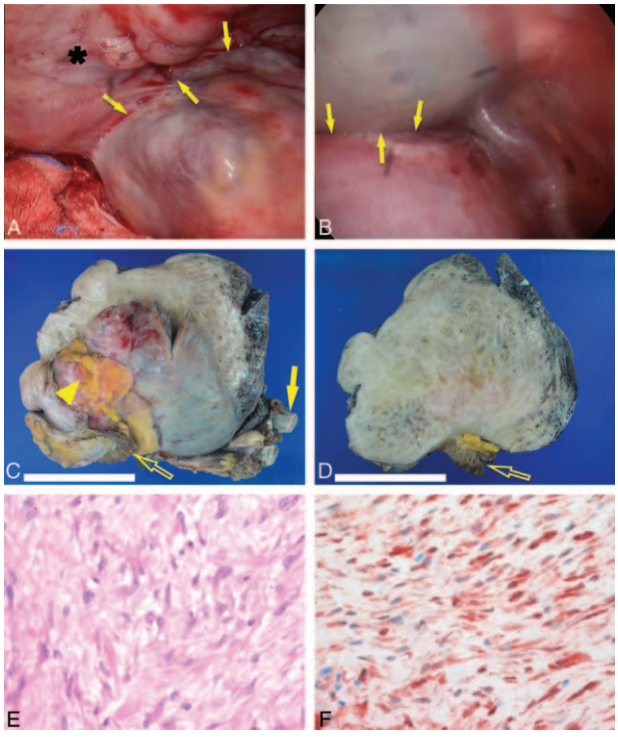

FIGURE 2. (A) Severe adhesion (arrows) between the tumor and the adjacent chest wall (asterisk) is present in the operation field. (B) The tumor shows severe adhesion (arrows) to the medial portion of the diaphragm. (C) The size of the tumor specimen is 22 × 20 × 11.3 cm. Surgical resection of the mass includes a part of the ribs and the intercostal muscles (arrow), the diaphragm (open arrow), and the pericardium (arrow head). White scale bar represents 10 cm. (D) Cross-section shows gelatinous appearance and a heterogeneous mixture of white and light green color of the tumor. Open arrow indicates partially resected diaphragm in this figure. White scale bar represents 10 cm. (E) Hematoxylin & eosin staining of the specimen demonstrates a relatively small number of spindle cells in a collagen-abundant stroma (×400). There are no features of malignant cells, such as nuclear hyperchromatia, nuclear atypia, high nuclear-to-cytoplasmic ratio, and mitosis. (F) Immunohistochemical staining with β-catenin demonstrates strong positive reactions in the nuclei of these cells (×400). Merged color of blue and red represents positivity for nuclear β-catenin staining.

deposition in the stroma without features of malignant cells, such as nuclear hyperchromatia, nuclear atypia, high nuclear-to-cytoplasmic ratio, and mitosis (Fig. 2E). Furthermore, immunohistochemial staining showed accumulation of β-catenin in the nucleus (Fig. 2F). Based on these pathologic findings, the mass was diagnosed as DT. The patient recovered after surgery without any complications, and there has been no evidence of recurrence of DT so far.

DISCUSSION

In this case, the patient presented an extremely rapid growing anterior mediastinal mass that had grown approximately 13-fold in volume within 116 days. The local effects of this rapid growing mass, such as chest wall invasion, mediastinal shifting, and compression of the heart, induced pleural effusion and atelectasis resulting in dyspnea, cough, sputum, and right chest pain. The mass was surgically resected and finally confirmed as an anterior mediastinal DT. Interestingly, the growth of DT in our patient was extraordinarily rapid compared to previously reported patients of DTs in the literature.

Previous studies have demonstrated that the location of DTs is one of the crucial factors for determining clinical course.[4] In particular, mediastinal DTs can be associated with fatal consequences because of their locally infiltrative nature. For example, several patients of mediastinal DTs have shown to display severe illnesses, including cardiac arrhythmia, circulatory collapse secondary to superior vena cava syndrome, and cardiac failure.[9–11] In our patient, compression of the right heart by an anterior mediastinal DT was evident without hemodynamic collapse. Other clinical manifestations associated with the location of DT in the thoracic cavity of limited space were massive pleural effusion, atelectasis, chest wall infiltration, and various mass effects, including mediastinal shifting and the compression of the diaphragm resulting in severe dyspnea, cough with sputum, and right chest pain. Hence, our experience also highlights the significance of anatomic location as one of the key factors for determining the severity of mediastinal DTs.

In addition, there is scarce data on the doubling time of mediastinal DTs. A previous report illustrated a dot-plot graph presenting the size of an anterior mediastinal DT over time in a patient; the maximal doubling time was more than 9 months.[12] In case of abdominal DTs, a previous case report showed a DT with a doubling time of 122 days, and another study of 23 patients with abdominal DTs reported that the mass doubled in less than 3 month at most.[13,14] In our patient, the doubling time was approximately 31.3 days. The volume of the tumor initially detected in the local clinic was approximately 300 cm^3. Because further evaluation was not made at that time, the mediastinal DT increased in volume to approximately 4000 cm^3. Notably, the doubling time of DT in our patient was the shortest among reported cases of DTs. Furthermore, the doubling time in this patient is noteworthy compared with several malignant tumors (pancreatic carcinoma, 18–255 days; nonsmall cell lung carcinoma, 8–1092 days; and small cell lung carcinoma, 54–132 days).[8] Taken together, the rapid growth of the DT in our patient may have played a key role in the complicated clinical course. Based on our experience, masses with rapid volumetric growth may cause serious complications in the thoracic cavity, a representative of closed anatomic compartments. Thus, an early invasive therapeutic strategy is likely to be beneficial for rapidly growing mediastinal DTs.

Obtaining tissue specimens through minimally invasive procedures, such as PTNB, enables clinicians to diagnose the disease promptly and allow patients to recover from procedure-associated morbidity early, thereby possibly yielding favorable outcomes in certain clinical situations.[15] As for DTs, however, the role of PTNB in preoperative diagnosis is yet to be defined.[16,17] In our patient, the result of PTNB was inconclusive because of a small number of cells in the specimen, and the mass was finally diagnosed as DT after surgical resection. In addition, the mass possessed characteristic findings of fibrous-dominant tumor with minimal contrast enhancement on preoperative radiologic images. Likewise, there were abundant fibrous contents with low cellularity in pathologic specimens, which makes the pathologic diagnosis somewhat inconclusive despite small biopsy such as PTNB. Based on our experience, early surgical resection rather than small biopsies might be a reliable diagnostic method, especially for soft tissue tumors having fibrous-dominant components on radiologic images.

In this report, we described an interesting case of a rapidly growing DT in the anterior mediastinum. The aggressive nature

of the DT in our patient was highlighted by calculating the doubling time that indicated extremely rapid growth. Considering that DTs commonly infiltrate and compress adjacent organs, its deleterious effects can be further intensified by rapid growth in the mediastinum. Our experience highlights DT as one of the differential diagnoses for rapidly growing mediastinal tumors and the benefits of early intervention of rapidly growing mediastinal DT.

ETHICAL REVIEW AND PATIENT CONSENT

The Institutional Review Board of Chonbuk National University Hospital stated that it was not necessary to achieve IRB approval for this case report, but that patient consent was required as the study dealt only with retrospective use of the patient's medical records and related images. Written informed consent was obtained from the patient before the publication of this case report and accompanying images.

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