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Primary Extraskeletal Osteosarcoma in the Anterior Mediastinum: A Case Report and Review

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Extraskeletal osteosarcoma (ESOS) is a malignant soft tissue neoplasm producing osteoid, without any continuity with the bone or periosteum. Primary ESOS presenting in the mediastinum is an extremely rare, yet aggressive malignant tumor associated with a poor prognosis. We report a case of primary ESOS arising from the thymus in a 63-year-old male patient.

Key words: 1. Osteosarcoma
2. Mediastinum

Case report

In this study informed consent was obtained form the patient.

A 63-year-old man was referred to Seoul National University Hospital for further evaluation of a growing chest mass found during an abdominal aortic aneurysm work-up. The chest mass was first identified as an incidental finding 5 years previously and surgical resection was recommended. However, the patient was lost to follow-up. The patient had a history of hypertension and hyperlipidemia. His physical examination was unremarkable and a routine laboratory test showed no abnormal results. The patient's initial contrast-enhanced chest computed tomography (CT) taken 5 years previously showed a 2.6-cm, heterogeneously enhancing mass with no invasion of the adjacent vessels. However, the chest CT scan taken upon presentation to our department revealed a well-defined, 5.5-cm, heterogeneously enhancing mass in the anterior mediastinum that contained calcifications and encased the left brachiocephalic vein (Fig. 1).

The tumor was preoperatively diagnosed as a T3 advanced thymoma or thymic cancer, and robot-assisted total thymectomy via a subxiphoid approach was performed. Intraoperative findings revealed a tumor encasing the left brachiocephalic vein, internal thoracic vein and artery, and left phrenic nerve. The mass was completely excised with adequate resection margins by en bloc resection, and the vessels and nerve were sacrificed. Histology showed a grossly encapsulated tumor measuring 5.6 cm×5.0 cm×4.8 cm, with direct invasion of the brachiocephalic vein. There was no invasion of the phrenic nerve, internal thoracic vessels, or lymphatic system. No lymph node metastasis was identified. Hemorrhage and necrosis was detected from 20% of the tumor's cut surface, and calcification was present (Fig. 2). Histopathologic findings showed osteoid formation within the tumor and immunohistochemical studies showed a positive stain for vimentin, a focal positive stain for cytoker-

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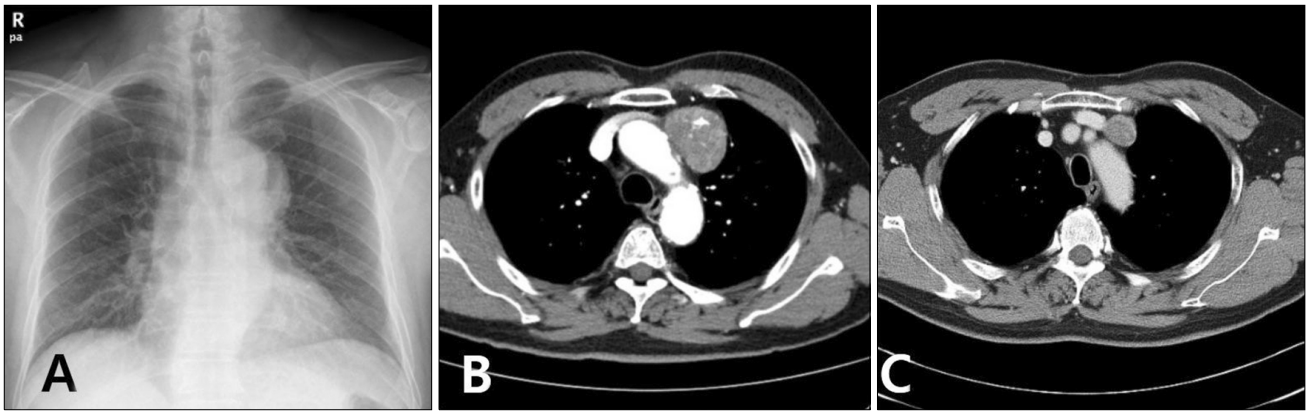

Fig. 1. Chest radiographs. (A) A chest X-ray showing a mass-like opacity at the anteroposterior window and (B) a chest CT axial view showing a 5.6-cm irregular mass with calcification encasing the left brachiocephalic vein, without any attachment to the bony thorax at the time of admission. (C) A CT axial view, taken 5 years previously, showing a 2.6-cm mass with no involvement of nearby vessels. CT, computed tomography.

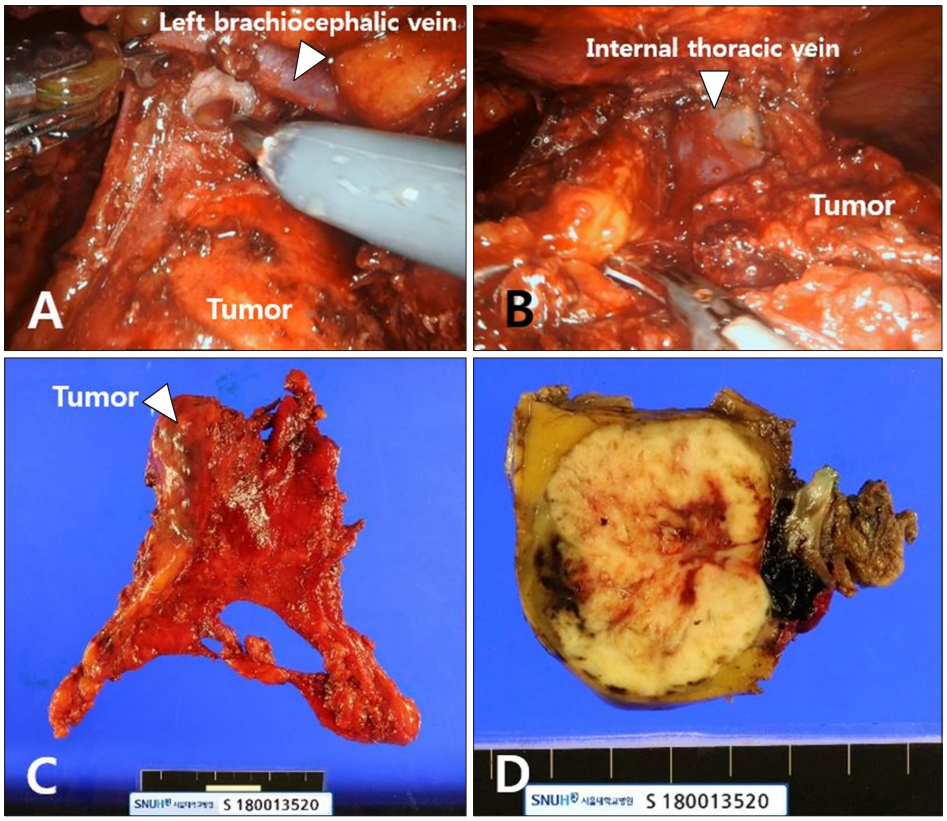

Fig. 2. Operative findings and gross findings of the mass. (A) Dissection of the left brachiocephalic vein (arrowhead). (B) Dissection of the internal thoracic vein (arrowhead). (C) Complete removal of the tumor (arrowhead). (D) A grossly encapsulated tumor, measuring 5.6 cm×5.0 cm×4.8 cm and exhibiting calcifications, hemorrhage, and necrosis on its cut surface.

atin, and negative stains for CD5, CD117, MUC1, and desmin (Fig. 3).

The pathological findings were consistent with osteosarcoma. The tumor showed no continuity with the thoracic bones, and no other extra-thoracic primary tumors were present. The tumor was diagnosed as a primary osteosarcoma of the thymus. The patient started radiotherapy 1 month after the operation and is scheduled to receive chemotherapy.

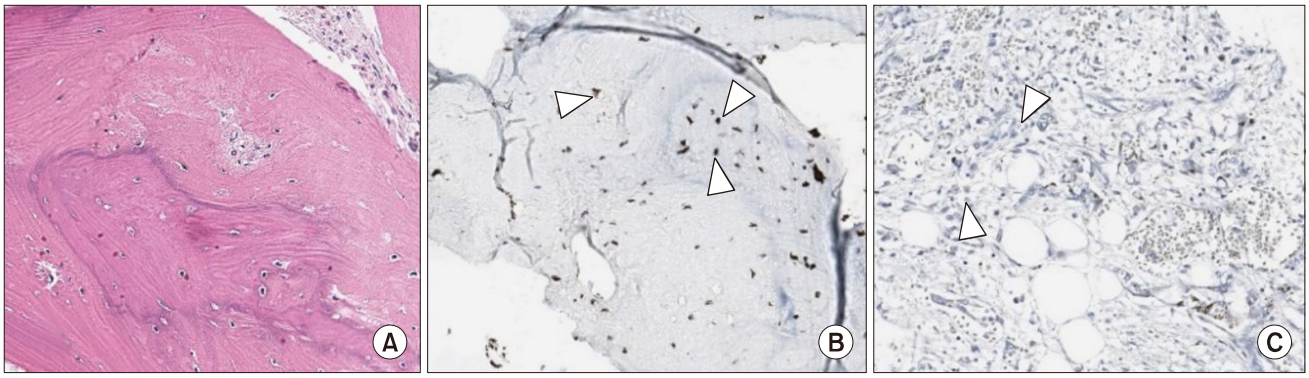

Fig. 3. Microscopic findings of the mass. (A) Osteoid formation, a definitive characteristic of osteosarcoma (H&E staining, ×20 magnification). (B) Positive staining for vimentin (×20 magnification; arrowheads). (C) Focal positive staining for cytokeratin (×20 magnification; arrowheads).

Discussion

Extraskeletal osteosarcoma (ESOS) is a malignant soft tissue neoplasm that produces osteoid, bone, or chondroid materials in places without direct attachment to bone or periosteum. ESOS is a rare malignant tumor, accounting for 1%–2% of all soft tissue sarcomas and 2%–4% of all osteosarcomas [1]. Unlike conventional osteosarcoma, which mainly affects teenagers and young adults, ESOS most commonly affects patients older than 30.

ESOS is difficult to diagnose due to its asymptomatic nature, and is usually found due to its mass effect. ESOS is diagnosed by the following criteria: (1) the presence of a uniform morphological pattern of sarcomatous tissue without the possibility of malignant mesenchymoma, (2) production of malignant osteoid or bone by the sarcoma, and (3) exclusion of a primary osseous tumor [2]. Because calcification or osteoid formation occurs in approximately 50% of patients with this tumor, the tumor may be best detected by chest CT. However, calcification is a common feature found in tumors with other etiologies, including thymomas [3]. Therefore, ESOS cannot be diagnosed based on a single chest CT scan showing malignant features accompanied by calcification. A definite diagnosis of ESOS requires histopathologic confirmation. ESOS shares the same histopathologic features as osteosarcoma originating from the skeletal system. It usually has a uniform sarcomatous pattern and produces osteoid. The immunophenotypes of ESOS, which are also similar to those of osteosarcoma, include expression of CD99, alkaline phosphatase, osteocalcin, and vimentin. In many cases, actin, desmin, S-100 protein, epithelial membrane antigen, and keratin are expressed as well [4]. Furthermore, a frozen biopsy during the operation may aid in diagnosing and obtaining an adequate resection margin. Obtaining an accurate and quick section of an osteosarcoma, however, is considered to be a challenge due to the calcified characteristics of the tissue.

The prognosis of ESOS remains poor, with a reported 5-year survival rate varying from 25% to 66%. Although little is known about the factors affecting survival in patients with ESOS, complete surgical resection is considered to be the optimal treatment to improve survival, since ESOS is not particularly sensitive to chemotherapy or radiotherapy [3,5]. The effectiveness of chemotherapy and radiotherapy is currently being debated, as a study has shown a favorable prognosis for ESOS [6].

Our case of a primary ESOS arising in the mediastinum is extremely rare. Only 10 cases have been reported in the international literature. Of the 10 patients, 6 were male and 4 were female. The median age was 47 years (range, 19–77 years) and the median size of the tumors was 9.25 cm (range, 5.5–16 cm). The outcome of ESOS arising from the mediastinum remains poor, with overall 1-, 2-, and 5-year survival rates of merely 44%, 22%, and 11%, respectively. The median overall survival was 4.0 months.

In conclusion, primary ESOS in the mediastinum is extremely rare, difficult to diagnose, and associated with a poor prognosis. In this case, the mass was ini-

tially considered to be a thymoma. However, physicians should be aware of the possibility of ESOS, and surgical resection should be considered as a primary choice in cases where ESOS is suspected.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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