

**Case
Report**

Extraskelatal Osteosarcoma of the Pleura: Report of a Case

Hironobu Shiota, MD,¹ Tomohisa Yasukawa, MD, PhD,¹ Ayako Hirai, MD,¹
Masako Chiyo, MD, PhD,¹ Toshikazu Yusa, MD, PhD,¹ and Kenzo Hiroshima, MD, PhD²

Extraskelatal osteosarcoma is a rare malignant tumor occurring very rarely in the pleura. We herein report the case of 67-year-old man with asbestos exposure, who underwent biopsies of the large tumor from the chest wall, and diagnosed as a suspicious of fibrosarcoma. Surgical resection was done, and the pathological diagnosis was extraskelatal osteosarcoma arising from the pleura. The differential diagnosis is malignant pleural mesothelioma with osseous and cartilaginous which is also very rare and one of the histopathological subtypes with heterologous elements. Identification of epithelial components, labeling for cytokeratins in spindle cells and its' anatomical distribution may help to distinguish them. In the neoplasm arising from the parietal pleura, primary extraskelatal osteosarcoma of the pleura is very rare, but should be considered.

Keywords: extraskelatal osteosarcoma, pleura, asbestos exposure

Introduction

Extraskelatal osteosarcoma is rare, accounting for 1%–2% of all soft tissue sarcomas and 4% of all osteosarcomas,¹⁾ and extraskelatal osteosarcoma arising from the pleura is very rare. There have been only 8 reported cases of primary extraskelatal osteosarcoma of the pleura, including our case. In our case, it is difficult to distinguish malignant pleural mesothelioma with osseous and cartilaginous. We herein report a case of extraskelatal osteosarcoma of the pleura with occupational asbestos exposure, diagnosed by thoracoscopic biopsies, and treated by surgical resection and systemic chemotherapy after the operation.

¹Department of General Thoracic Surgery, Chiba Rosai Hospital, Ichihara, Chiba, Japan

²Department of Pathology, Tokyo Women's Medical University Yachiyo Medical Center, Yachiyo, Chiba, Japan

Received: March 5, 2012; Accepted: May 7, 2012

Corresponding author: Hironobu Shiota, MD. Department of General Thoracic Surgery, Chiba Rosai Hospital, 2-16 Tatsumidaihigashi, Ichihara, Chiba, 290-0003, Japan
Email: hironobu@med.uoeh-u.ac.jp

©2012 The Editorial Committee of *Annals of Thoracic and Cardiovascular Surgery*. All rights reserved.

Case Report

A 67-year-old man presented to another hospital in October 2008 for a comprehensive medical examination. Calcification was discovered in a portion of the right parietal pleura by chest CT. Since the patient had a history of asbestos exposure, it was followed up as calcified pleural plaques. In March 2009, the patient developed dyspnea on exertion and cough, and presented again to the same hospital. His chest radiography showed a massive right pleural effusion. In April 2009, the patient was referred to our hospital with a suspicion of malignant pleural mesothelioma.

His past medical history included cholelithiasis at age 45 yrs, and type 2 diabetes and hyperlipidemia at age 60 yrs. He had smoked 15 cigarettes a day for 46 yrs. His family history was non-contributory. He worked in the construction of electric power substations from age 28–60 and had a history of asbestos exposure. His present status was unremarkable except for the chest region with diminished breath sounds over the right middle and lower lung fields. The blood biochemistry test results on admission were normal except for a slightly high CRP at 1.1 mg/dL. Tumor markers CEA, CYFRA, Pro-GRP, and NSE were within their normal ranges.

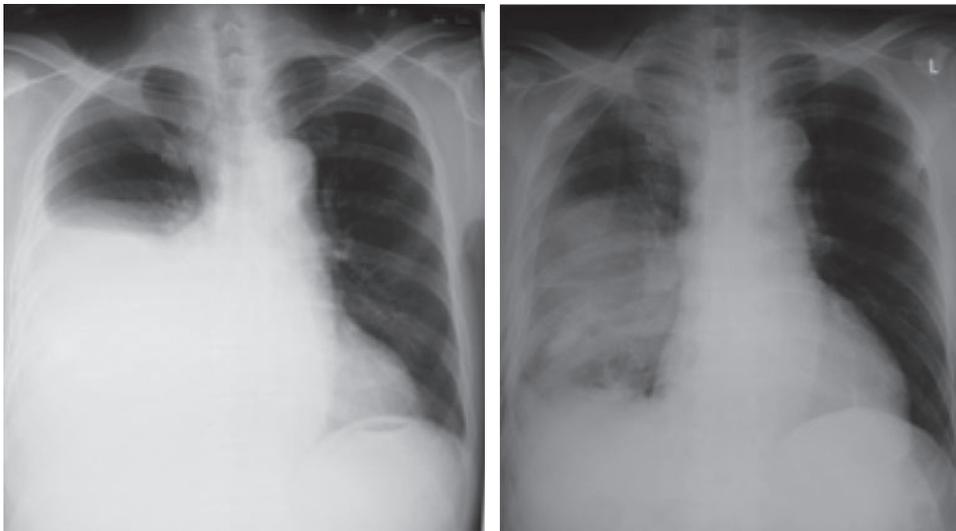


Fig. 1 (a) Chest X-ray shows right massive pleural effusion on admission day. (b) Large mass shadow with calcification was appeared at the right middle to lower lung field on chest X-ray after thoracic drainage.

In chest X-ray, a massive right pleural effusion was observed when the patient was admitted to our hospital, April 2009 (**Fig. 1a**). Chest X-ray after right tube drainage showed a mass and calcification in the right middle and lower lung fields (**Fig. 1b**). There was no abnormality in the chest X-rays taken on November 2006 and September 2007. In October 2008, Chest CT revealed calcification in a portion of the right parietal pleura (**Fig. 2a**). In March 2009, it revealed that the calcification became enlarged and irregular after approximately 5 months of follow-ups. Chest CT after right tube drainage showed a circular mass which was approximately 8×8 cm in the right thorax and the calcification was in this mass (**Fig. 2b**).

Examination of the pleural effusion revealed no pale yellow or turbid appearance. The specific gravity was 1.038, and the Rivalta test was positive. The culture results were negative and levels of CEA, ADA, and hyaluronic acid, were 0.8 ng/mL, 13.1 IU/L, 10200 ng/mL, respectively. Cytology of the effusion was classified as Class II and showed no malignancy. Thoracoscopic examination indicated a smooth fist-sized mass located in the posterior chest wall at the level of the seventh and eighth ribs. Multiple pleural plaques were seen in the parietal pleura. The mass was elastic and soft, and it easily bled and disintegrated. Biopsy was performed at 3 places for the parietal pleura and on a portion of the mass. Histopathologically, the diagnosis of the mass was a suspected fibrosarcoma, and no malignancy was found in the parietal pleura. Bone

scintigraphy showed a hot spot located consistently with the intrathoracic calcification, but no significant tracer accumulation was seen in other bones.

Because we did not deny the possibility of diffuse malignant pleural mesothelioma with heterologous elements, surgery was performed 10 d after biopsies by thoracotomy through the posterior sixth intercostal space. The mass was adhered firmly to the chest wall at the right seventh and eighth ribs. Thus, the mass was extirpated and the two ribs were also resected, and the chest wall defect was filled with Composix mesh.

In the examination of the extirpated specimen, the mass was $12 \times 10 \times 8$ cm, elastic, soft, and solid. Macroscopically, there was no continuity with the ribs (**Fig. 3a**). There were no bony lesions or continuity between the ribs and tumor (**Fig. 3b**). A pathological examination showed highly atypical spindle cells arranged in an interlacing pattern. Mitotic counts ranged from four to six per 10 high power fields. There were isolated areas with the cells differentiating into cartilage and bone (**Fig. 3c–3d**). These findings led to the diagnosis of osteosarcoma arising from pleura.

In the postoperative course, right pleural effusion was controlled by intrathoracic administration of mitomycin C for 3 d and OK-432 for a day and by pleurodesis, because we concerned about the tumor dissemination after thoracoscopic biopsies. Four courses of two-agent chemotherapy were performed

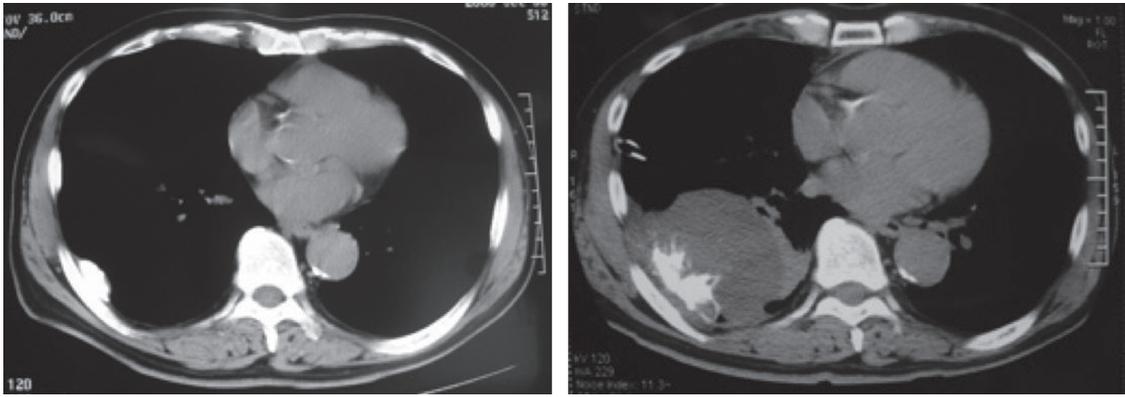


Fig. 2 (a) Chest CT shows the calcification in a portion of the right parietal pleura, in October, 2008. (b) Chest CT after right thoracic drainage showed that there was a round mass which was approximately 8 × 8 cm in the right thorax and the calcification became enlarged and irregular after approximately 5 months of follow-ups, in March, 2009.

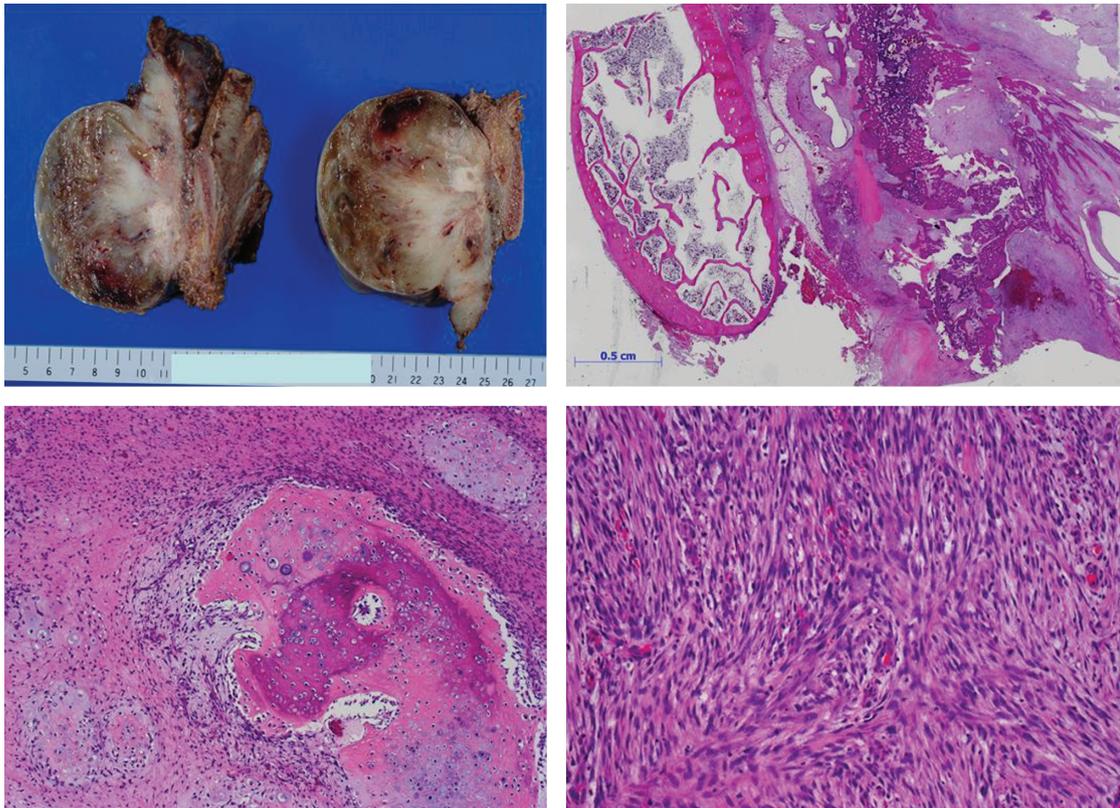


Fig. 3 (a) Macroscopic findings; There were no relationships between the ribs and the tumor. (b–d) Pathological findings of H.E. staining; (b) There were no relationships between the ribs and the tumor. (loupe image) (c) There were isolated areas with the cells differentiating into cartilage and bone. (×4) (d) Highly atypical spindle cells arranged in an interlacing pattern. (×20).

using cisplatin (CDDP) and adriamycin (ADR) based on the systemic chemotherapy protocol for osteosarcoma in young adults. A new lesion was observed 9 months postoperatively, and additional two courses of systemic chemotherapy were performed, but the tumor

became enlarged. So second and third line systemic chemotherapy were performed, no therapeutic effects were observed, the tumor were extensively invaded to the right lung he died due to respiratory failure about 2 yrs after the operation.

Discussion

Causes of pleural calcification can be benign or malignant.^{1,2)} Benign processes include previous trauma, pleural infection, pneumothorax, calcifying fibrous pseudotumor of the pleura, and pleural plaque from asbestos exposure.³⁾ The malignant processes include pleural metastasis from osteosarcoma, chondrosarcoma, adenocarcinoma, parosteal osteosarcoma, and calcification or ossification in a pleural mesothelioma.³⁾

Differential diagnosis between osteosarcoma of pleura and mesothelioma with heterologous elements may be difficult. Identification of epithelial components and labeling for cytokeratins in spindle cells may help for the diagnosis of malignant mesothelioma.^{4,5)} If the anatomical distribution conforms to that of mesothelioma, a diagnosis of heterologous mesothelioma should be made in preference to a diagnosis of primary pleural osteosarcoma.⁵⁾ The patient in this report had a large localized mass in the right thorax. Histologically, there was no component of epithelioid mesothelioma, and cytokeratins were negative in spindle cells or heterologous elements. From these findings we diagnosed this case as extraskeletal osteosarcoma of the pleura, because there was no evidence which supports the diagnosis of malignant mesothelioma.

Extraskeletal osteosarcoma is rare, accounting for 1%–2% of all soft tissue sarcomas and 4% of all osteosarcomas.¹⁾ While primary osteosarcoma of the bone occurs mainly in adolescents and young adults, extraskeletal osteosarcoma occurs predominantly in women and men over 30 yrs old.^{2,3)} The most common sites for extraskeletal osteosarcoma are upper and lower extremities, thigh, and retroperitoneum. It very rarely occurs in the pleura.¹⁾ Relationships have been reported between the incidence of tumor and previous trauma and between the incidence of tumor and a history of radiotherapy.³⁾ Such relationships were not evident in the case of the present report. As in our case, plain radiography can show calcifications in approximately half of the extraskeletal osteosarcoma cases. The following are conditions for diagnosis of extraskeletal osteosarcoma. (1) Skeletal origin can be ruled out by radiographic or intraoperative findings. (2) Sarcoma tissue produces malignant osteoid or malignant bone tissue. (3) Malignant mesenchymal tumor can be ruled out.^{2–8)} Osteosarcoma is a malignant tumor arising from soft tissue and characterized by a uniform sarcomatoid

pattern and osteoid production. A tumor is diagnosed as osteosarcoma if it has the aforementioned findings in one area and even if it shows other histological characteristics in the majority of the other areas. Differential diagnosis includes calcifying malignant tumors such as malignant fibrous histiocytoma (MFH), liposarcoma, fibrosarcoma, and malignant teratoma.

There have been 8 reports of primary extraskeletal osteosarcoma of the pleura,^{9–17)} including the case of the present report. All eight cases were men over 60 yrs old. Involvement of asbestos exposure was indicated in our case and one other case.¹⁴⁾ In the neoplasm arising from the pleura, primary extraskeletal osteosarcoma of the pleura should be considered, and the differential diagnosis is malignant pleural mesothelioma with osseous and cartilaginous differentiation.

Extraskeletal osteosarcoma can be asymptomatic or symptomatic. Symptoms include those arising from enlarging tumor and pain. The first-choice treatment is surgical resection. Although there are reported cases treated by radiotherapy or systemic chemotherapy, these treatments are not well established. Prognosis is poor and the five-year survival rate is less than 40%.⁷⁾ In extraskeletal osteosarcoma, an important factor determining the prognosis is considered to be a tumor size of 5 cm or less. In our case, the tumor size was over 5 cm. Thus, postoperative systemic chemotherapy was performed.

Conclusion

Primary extraskeletal osteosarcoma of the pleura is very rare, but we should be considered it if we find pleural calcifications.

Disclosure Statement

We have no personal conflict of interest or outside support for this research. This research is a part of the research and development and dissemination projects related to the 13 fields of occupational injuries and illnesses of the Japan Labour Health and Welfare Organization.

References

- 1) Rosenberg AE, Heim S. Extraskeletal osteosarcoma. In: Fletcher CDM, Unni KK, Mertens F eds.; World

- Health Organizing Classification of Tumours. Pathology and Genetics of Tumours of Soft Tissue and Bone. Lyon: IARC Press, 2002; pp 182-3.
- 2) Lidang JM, Schmacher B, Myhre JO, et al. Extraskelatal osteosarcomas: a clinicopathologic study of 25 cases. *Am J Surg Pathol* 1998; **22**: 588-94.
 - 3) Chung EB, Enzinger FM. Extraskelatal osteosarcoma. *Cancer* 1987; **60**: 1132-42.
 - 4) Yousem SA, Hochholzer L. Malignant mesotheliomas with osseous and cartilaginous differentiation. *Arch Pathol Lab Med* 1987; **111**: 62-6.
 - 5) Klebe S, Mahar A, Henderson DW, et al. Malignant mesothelioma with heterologous elements: clinicopathological correlation of 27 cases and literature review. *Mod Pathol* 2008; **21**: 1084-94.
 - 6) Bane BL, Evans HL, Ro JY, et al. Extraskelatal osteosarcoma. A clinicopathologic review of 26 cases. *Cancer* 1990; **65**: 2762-70.
 - 7) Sordillo PP, Hajdu SI, Magill GB, et al. Extrasosseous osteogenic sarcoma. A review of 48 patients. *Cancer* 1983; **51**: 727-34.
 - 8) Kransdorf MJ, Meis JM. Extraskelatal osseous and cartilaginous tumors of the extremities. *Radiographics* 1993; **13**: 853-84.
 - 9) Kasagi Y, Yamazaki K, Nakashima A, et al. Chondroblastic osteosarcoma arising from the pleura: report of a case. *Surg Today* 2009; **39**: 1064-7.
 - 10) Tokue H, Tsushima Y, Endo K. Computed tomography findings of the progress of calcification in extraskelatal osteosarcoma without calcification derived from the pleura. *Gen Thorac Cardiovasc Surg* 2011; **59**: 447-50.
 - 11) Wang W, Quan CB, Li N, et al. Diagnosis of pleural cavity extraskelatal osteosarcoma: a case report and literature review. *Zhonghua Jie He He Hu Xi Za Zhi* 2010; **33**: 202-5. (in Chinese)
 - 12) Matono R, Maruyama R, Ide S, et al. Extraskelatal osteosarcoma of the pleura: a case report. *Gen Thorac Cardiovasc Surg* 2008; **56**: 180-2.
 - 13) Chandak P, Hunt I, Rawlins R, et al. Bone or pleura? Primary pleural osteosarcoma. *J Thorac Cardiovasc Surg* 2007; **133**: 587-8.
 - 14) Sabloff B, Munden RF, Melhem AI, et al. Radiologic-pathologic conferences of the University of Texas M. D. Anderson Cancer Center: Extraskelatal osteosarcoma of the pleura. *AJR Am J Roentgenol* 2003; **180**: 972.
 - 15) Meeus I, Galdermans D, Roland J, et al. Spectacular bone scintigraphy and transverse SPECT images in primary osteosarcoma of the pleura. *Clin Nucl Med* 1994; **19**: 738-40.
 - 16) Connolly JP, McGuyer CA, Sageman WS, et al. Intrathoracic osteosarcoma diagnosed by CT scan and pleural biopsy. *Chest* 1991; **100**: 265-7.
 - 17) Cohn L, Hall AD. Extrasosseous osteogenic sarcoma of the pleura. *Ann Thorac Surg* 1968; **5**: 545-9.