Primary extraskeletal chondroblastic osteosarcoma of the pericardium: a case report and literature review

Qianqian Wang1,2†, Xiaojie Wang3,4†, Qing Zhu2, Xinghua Gu5, Peng Gao3, Yuguo Chen1,2*, Xiaojuan Wu3*, and Chuanbao Li1,2*

1Department of Emergency Medicine and Chest Pain Center, Qilu Hospital, Shandong University, No.107 Cultural West Road, Jinan, Shandong 250012, China; 2The Key Laboratory of Cardiovascular Remodeling and Function Research, Chinese Ministry of Education and Chinese Ministry of Public Health, Qilu Hospital, Shandong University, No.107 Cultural West Road, Jinan, Shandong 250012, China; 3Department of Pathology, Qilu Hospital, Shandong University, Jinan, No.107 Cultural West Road, Shandong 250012, China; 4Department of Pathology, Weifang Heart Hospital, No.79 Phoenix Avenue, Weifang, Shandong 261206, China; and 5Department of Cardiac Surgery, Qilu Hospital, Shandong University, No.107 Cultural West Road, Jinan, Shandong 250012, China

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Background
Primary extraskeletal chondroblastic osteosarcoma has very poor prognosis, especially in the elderly. The pericardium is an extremely rare site for this tumour.

Case summary
A 67-year-old man presented with a large pericardial effusion and an intrapericardial mass. His past medical history of pulmonary tuberculosis led us to initially suspect tuberculous pericarditis. Primary extraskeletal chondroblastic osteosarcoma arising from the pericardium was diagnosed by the pathologist after surgery. The patient suffered severe intraoperative blood loss and surgical trauma. He went into shock and died a few hours after surgery.

Discussion
Extraskeletal chondroblastic osteosarcoma is a very rare tumour with a grim prognosis. Clinical manifestations frequently are not specific and can be explained by associated pathology. In this report, we describe an unusual case of primary extraskeletal chondroblastic osteosarcoma located in the pericardium and present a review of the literature.

Keywords
Pericardial tumour • Immunohistochemistry • Osteosarcoma • Tuberculosis • Case report

Learning points
• Extraskeletal chondroblastic osteosarcoma in the pericardium is very rare and has a grim prognosis. Preoperative diagnosis is difficult. Histopathology is essential for definitive diagnosis.
• Resection of the pericardial tumour appears to be the best option for treatment. Adjuvant chemotherapy or radiotherapy may help in some cases.

Introduction
Extraskeletal osteosarcomas are rare malignancies that account for about 1% of all soft tissue sarcomas. Only a few large series of these tumours have been reported. These tumours are usually located in the lower and upper extremities, the thigh, or the buttocks (45–62%). Because of its rarity and the absence of a specific biomarker, extraskeletal osteosarcoma is easily mistaken for myositis ossificans.

* Corresponding authors. Tel: 18560083097, Email: bao2460@126.com (C.L.); Tel: 8653182169325, Email: chen919085@sdu.edu.cn (Y.C.); Tel: 18560081172, Email: xiaojuanwu0709@126.com (X.W.)
† The first two authors contributed equally to this work.
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or a benign tumour. The heart and pericardium are unusual sites for primary tumours, the prevalence rate in autopsy studies being only 0.001–0.3%; metastatic tumours are far more common. Here, we report what we believe is the first case of extraskeletal chondroblastic osteosarcoma arising from the pericardium.

**Timeline**

| Date          | Event                                                                 |
|---------------|----------------------------------------------------------------------|
| 21 August 2018| The patient was admitted to a county hospital with complaints of dyspnoea. Echocardiographic examination revealed a large pericardial effusion. Computed tomography (CT) showed a large pericardial effusion and soft tissue masses in the pericardial sac. Pericardiocentesis was performed. |
| 31 August 2018| The patient was referred to our hospital for further management. Repeated echocardiographic showed a large pericardial effusion and a tumour attached to the visceral pericardium. Pericardiocentesis yielded 300 mL of bloody fluid. |
| 4 September 2018| Whole-body 18F-fluorodeoxyglucose positron emission tomography (PET)/CT scan showed heterogeneous accumulation of tracer in the pericardial mass with calcified pericardial masses. |
| 4-16 September 2018| Dyspnoea increased and pericardial fluid had rapidly reaccumulated. |
| 16 September 2018| The patient was posted for surgery, and the mass was removed. Unfortunately, he died a few hours after completion of surgery. |

**Case presentation**

A 67-year-old male patient was admitted to a county hospital for shortness of breath for 10 days. On admission, his temperature was 36.5°C; pulse rate was 112 b.p.m.; respiratory rate was 23 breaths/min; and blood pressure was 96/62 mm Hg. He had no symptoms of chest pain, weight loss, cough, or night sweats. He had history of long-term occupational exposure to asbestos and was diagnosed as pulmonary tuberculosis 20 years ago. And, he had no other past medical history. Echocardiographic examination revealed a large pericardial effusion. Computed tomographic (CT) scan of the chest (Figure 1C and D) showed a large pericardial effusion and a soft tissue mass in the pericardial sac, lung inflammation and calcification, bilateral pleural thickening with scattered calcifications, and a large left pleural effusion. Pericardiocentesis was performed. However, his dyspnoea continued to worsen, and he was therefore referred to our hospital for further management.

At our hospital, he had no symptoms of chest pain. On examination, his temperature was 36.0°C; pulse rate was 104 b.p.m.; respiratory rate was 20 breaths/min; and blood pressure was 102/72 mm Hg. Pulsus paradoxus and distended jugular veins were observed. Breath sounds over the left lung base posteriorly were decreased, and scattered wet and dry rales were heard. He had severe pitting oedema in both legs. On oxygen-enriched mixture, the partial pressure of oxygen was 81 mmHg, the partial pressure of carbon dioxide was 45 mmHg, and the pH was 7.45. Electrocardiogram revealed sinus tachycardia, with normal intervals and decreased voltage in the limb leads. Echocardiography was repeated; it showed a large pericardial effusion and an oval, 60 mm × 85 mm × 49 mm, isoechoic tumour attached to the visceral pericardium, near the right heart (Figure 1A and B). The effusion appeared to be slightly fibrinous. Fluid depth was 28 mm at the apex and 29 mm at the left ventricular lateral wall. Diastolic right ventricular collapse was observed. Left ventricular wall thickness and motion were normal. The left ventricular ejection fraction was 53%. Pericardiocentesis yielded 300 mL of bloody fluid. Adenosine deaminase level in aspirated fluid was 28 U/L and lactate dehydrogenase (LDH) level was 3414 U/L. Cytological examination for malignant cells was negative. Tests for tuberculosis infection—T-SPOT and acid-fast staining of three early morning sputum samples—were negative. Table 1 shows the results of all laboratory tests.

| Date          | Event                                                                 |
|---------------|----------------------------------------------------------------------|
| 2018          | Whole-body 18F-fluorodeoxyglucose positron emission tomography (PET)/CT scan showed heterogeneous accumulation of tracer in the pericardial mass with scattered areas of calcification. There was non-specific FDG uptake in a few non-enlarged mediastinal nodes and low uptake in bilateral thickened pleura (Figure 2). The patient was treated with diuretics, potassium supplements, and antibiotic, but his condition deteriorated rapidly over the following 2 weeks. He developed fever. Sputum culture indicated fungal infection. The dyspnoea continued to increase and the pericardial fluid rapidly reaccumulated. We therefore decided to operate (Figure 3). At surgery, the mass was found to arise from the pericardium; it had grown to partially encase the main pulmonary artery and the left atrial appendage. The tightly adherent mass had to be dissected free from surrounding structures. During the procedure, the patient suffered multiple lacerations of the lung surface and had bleeding into the trachea. He went into shock and died a few hours after completion of surgery. |
| 2018          | The excised mass was sent for pathological examination. Microscopically, the mass was mainly composed of chondroblastic cells, with scattered foci of osteoblastic or fibroblastic cells (Figure 4). Chondroid islands consisting of plasmacytoid chondrocytes or chondroblastic cells were seen embedded in the light blue chondroid matrix. In areas expressing the malignant cells, there was abundant osteoid deposition and focal mineralization, with irregular lace-like bone formation. All atypical cells had high-grade nuclei. Plenty of normal and abnormal mitotic figures were present. On immunohistochemistry, the atypical cells were positive for SATB2, CDK4, P16, S100, SMA, and EMA, but negative for CK, CK5/6, CD31, CD34, and desmin. The proliferative index of Ki-67 was approximately 60% (Figure 5). The final diagnosis was extraskeletal chondroblastic osteosarcoma. |

**Discussion**

Our patient, a 67-year-old man with past history of asbestos exposure and tuberculosis, presented with a large pericardial effusion and a mass in the pericardial sac. His past history and the presence of an
intrapericardial mass, with no other tumour demonstrated at any other site with $^{18}$F-FDG PET/CT, suggested two possible diagnoses: intrapericardial tumour or active tuberculous pericarditis.

We were initially misled by the history of exposure to asbestos and the previous diagnosis of tuberculosis. Acute cardiac tamponade can occur with tuberculous pericardial effusion, although it is rare. However, the absence of common tuberculosis-related symptoms such as fever, weight loss, cough, and night sweats, and the negative results of T-SPOT, antinuclear antibodies, and sputum smears led us to consider the possibility of cancer.

The excised mass was mainly composed of malignant chondral component embedded in a chondroid matrix, a picture typical of extraskeletal chondroblastic osteosarcoma. Furthermore, there were foci of malignant osteoid deposition in the blue-staining cartilaginous component, which represents the classic osteosarcoma pattern; however, there was little lace-like bone formation. The immunophenotype of extraskeletal osteosarcoma is non-specific, with S-100 protein, SMA, vimentin, and CDK4 being commonly expressed. Our patient was also positive for SATB2, which is a specific biomarker of osteoblastic differentiation in both benign and malignant tumours.

Due to the rarity of extraskeletal osteosarcoma, diagnosis and management can be challenging. Clinical findings, laboratory tests, and imaging are often not sufficient for diagnosis. In our patient, pericardial fluid cytology was also of no help. Soft tissue osteosarcoma presents a variety of histological patterns and, especially when osteoid formation is limited, the diagnosis can be easily missed.

The exact aetiology of extraskeletal osteosarcoma is not clear. In our patient, occupational exposure to asbestos may have resulted in metaplastic changes in the mesothelium.

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**Figure 1** Transthoracic echocardiography shows (A) a 60 mm × 85 mm × 49 mm intrapericardial mass (white arrow, outer border demarcated by four white +) adhering closely to the pericardial sac, near the right heart; (B) a large pericardial effusion is also seen (white arrow). Chest computed tomographic scan shows (C) lung inflammation and calcification (white arrow), bilateral pleural thickening and multifocal calcification, and a left pleural effusion, and (D) a large pericardial effusion, along with a soft tissue mass in pericardium (white arrow).
Our review of literature led to some conclusions. First, malignant tumour should be suspected when a large pericardial mass is found in association with a rapidly reaccumulating haemorrhagic pericardial effusion. Second, the most common abnormality in pericardial fluid is elevated alkaline phosphatase and LDH levels. Third, whole-body PET/CT scan can improve staging and treatment monitoring. Fourth, cardiac magnetic resonance imaging (MRI) provides excellent soft tissue resolution and has good tissue specificity.11 It can accurately display the shape, size and location of a cardiac tumour, and clearly demonstrate the relationship between the tumour and the heart, pericardium, and mediastinum. We considered performing cardiac MRI for our patient initially, but decided against it because his condition was such that he would not have been able to lie still for the examination.

Treatment of primary cardiac sarcoma with cardiac transplantation has been reported in the literature, but this is controversial. Lee et al.7 reported a patient with extraskeletal osteosarcoma who was successfully managed with marginal excision and postoperative radiotherapy as primary treatment; the patient was alive and free of disease at 8.8 years after treatment. A recent case report described a patient with primary cardiac chondrosarcoma who was treated with radiotherapy followed by surgery.12 The efficacy of preoperative radiotherapy, adjuvant chemotherapy, and postoperative external beam irradiation remains uncertain due to the rarity of this tumour and the lack of large randomized clinical trials.13 The survival of patients with cardiac chondrosarcomas is measured in weeks or months.14 Surgery is the first-choice therapy, but complete resection may be difficult, as in our patient. Long-term survival after excision has not been ascertained. Although radical resection can decrease recurrence rate, it has no impact on distant metastases. Recurrence after resection is a feature of extraskeletal osteosarcomas and usually occurs in more than half of the patients.8,15

## Conclusion

Extraskeletal chondroblastic osteosarcoma is a very rare tumour with a grim prognosis. Preoperative diagnosis is difficult. Histopathology is essential for definitive diagnosis. Resection of the

### Table 1 Results of laboratory tests

| Variables                          | Reference range, adults | At admission | On Day 9 |
|------------------------------------|-------------------------|-------------|----------|
| Haemoglobin (g/L)                  | 130–175                 | 148         | 123      |
| White cell count (per mm$^3$)      | 3500–9500               | 11 090      | 11 020   |
| Platelet count (per mm$^3$)        | 125 000–350 000         | 229 000     | 185 000  |
| Serum sodium (mmol/L)              | 137–145                 | 139         | 132      |
| Serum potassium (mmol/L)           | 3.6–5.0                 | 3.47        | 3.7      |
| Serum chloride (mmol/L)            | 98–107                  | 100         | 96       |
| Blood urea nitrogen (mmol/L)       | 3.2–7.1                 | 8.61        | 7.0      |
| Serum creatinine (µmol/L)          | 58–133                  | 75          | 63       |
| Blood glucose (mmol/L)             | 3.90–6.10               | 4.7         | 6.35     |
| Serum adenosine dehydrogenase (U/L) | 4–18                  | 15          | 25       |
| Serum ischaemia-modified albumin (U/L) | 0–85                  | 81.4        | 107.3    |
| Serum calcium (mmol/L)             | 2.00–2.60               | 2.19        | 1.93     |
| Serum phosphorus (mmol/L)          | 0.6–1.60                | 1.01        | 0.77     |
| Serum magnesium (mg/dL)            | 0.65–1.10               | 0.93        | 0.76     |
| Serum alkaline phosphatase (U/L)   | 45–125                  | 150         | 147      |
| Serum lactate dehydrogenase (U/L)  | 120–230                 | 518         | 565      |
| Serum aspartate aminotransferase (U/L) | 15–40                  | 22          | 28       |
| Serum alanine aminotransferase (U/L) | 9–50                   | 51          | 35       |
| Serum high-sensitivity troponin I (ng/L) | <30                  | 6.83        | 13.24    |
| Serum creatine kinase (U/L)        | 38–174                  | 35          | 65       |
| Serum creatine kinase MB isoenzyme (ng/mL) | 0.3–4.0               | 1.3         | 2.20     |
| Erythrocyte sedimentation rate (mm/h) | 0–15                   | 38          |          |
| N-terminal pro-B-type natriuretic peptide (pg/mL) | 0–300               | 119.2       | 854.8    |

| Arterial blood gas                  |                          |             |          |
|------------------------------------|-------------------------|-------------|----------|
| Fraction of inspired oxygen        |                          |             |          |
| pH                                 | 7.35–7.45               | 7.52        |          |
| Partial pressure of carbon dioxide (mmHg) | 35–42                | 37         |          |
| Partial pressure of oxygen (mmHg)  | 80–100                  | 155         |          |

aBlood chemical finding of the patient.
bReference values are affected by many variables, including the patient population and the laboratory methods used. The reference ranges used at Qilu Hospital are for adults who are not pregnant and who do not have medical conditions that could affect the results. The ranges cited here may therefore not be appropriate for all patients.
cBlood chemical finding of the patient on Day 9.
Primary extraskeletal chondroblastic osteosarcoma of the pericardium

Figure 2 (A) Whole-body fluorodeoxyglucose positron emission tomography/computed tomography scan reveals linear tracer uptake (arrow) and hypermetabolic branching foci in the chest. (B) Chest computed tomography shows a mass within the pericardium. (C) The fusion positron emission tomography/computed tomography image shows high and heterogeneous fluorodeoxyglucose uptake in the mass (SUVmax, 11.1) and mild-to-moderate metabolic activity in the right upper and middle lobes (SUVmax, 4.7). The calcified and thickened pleura show low fluorodeoxyglucose avidity bilaterally (SUVmax 2.4).

Figure 3 The excised specimen. (A) The margin is irregular, and the cut surface has a myxoid appearance, with focal haemorrhages at the periphery. (B) The irregularly shaped grayish-brown mass measures about 120 mm × 65 mm × 50 mm; on the right side of the picture a part of the pericardium can be seen. (C) Under high magnification the cut-section shows rich mucus content, with focal haemorrhages at the periphery.
mass appears to be the best option for treatment. Adjuvant chemotherapy or radiotherapy may help in some cases.

**Lead author biography**

Chuanbao Li has been working in Qilu Hospital of Shandong University since 2007, mainly engaged in resuscitation and diagnosis/treatment of cardiovascular emergencies, specialized in acute coronary syndrome interventional treatment, and completed more than 300 cases of PCI per year.

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**Supplementary material**

Supplementary material is available at *European Heart Journal - Case Reports* online.

**Slide sets:** A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

**Consent:** The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

**Conflict of interest:** none declared.

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**Figure 4** The haematoxylin and eosin stained sections show (A) the lobulated cartilaginous component (×40). (B) Under high magnification (×200), the chondroblastic differentiation osteosarcoma cells can be seen embedded in the chondroid matrix, with osteoid tissue on the left. (C) Lace-like bone can be seen (arrow) merging into the neoplastic cartilage (×200). (D) There are fibrosarcoma-like areas with focal necrosis (×40). (E) Fibrosarcoma-like region with abnormal mitosis (arrow; ×400). (F) The tumour arises from the pericardial surface; the arrow indicates normal mesothelial cells (×40).
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Figure 5 Immunohistochemical staining (×100). The tumour cells are strongly positive for P16 (A) and CDK4 (B). (C) The Ki-67 index is high in the tumour. Immunoperoxidase stain for s-100 is positive (D), indicating the presence of chondroblastic components; EMA positivity (E) indicates the presence of osteoblastic components, and SMA positivity (F) the presence of fibroblastic components. The neoplastic component is negative for CK (G) and MC (mesothelial cell) (H). In contrast, the superficial mesothelial cells are positive for both biomarkers (I). The tumour cells show a diffuse and strong nuclear reaction with SATB2.