

Original Article

Primary mediastinal chondrosarcoma: a case report and review of literature

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Abstract: Objective: The goal of this study was to investigate the diagnosis, treatment, and prognosis of mediastinal primary chondrosarcoma. Methods: One case of primary mediastinal chondrosarcoma which was misdiagnosed as mediastinal teratoma preoperation by Gansu Provincial Hospital underwent postoperative pathological examination. The diagnosis, treatment, and prognosis of primary mediastinal chondrosarcoma were explored in combination with literature review. Conclusion: Mediastinal primary chondrosarcoma is a rare extraosseous chondrosarcoma. It is difficult to diagnose and requires a combination of pathological findings. Complete resection is an effective method to improve prognosis.

Keywords: Primary mediastinal chondrosarcoma, complete resection, prognosis

Introduction

Chondrosarcoma is a malignant tumor derived from the primitive mesenchymal tissue with the potential for chondrogenesis. It is composed of highly undifferentiated small cells and hyalinized cartilage of different degrees of differentiation. It is one of the rare malignant tumors and has potential of bidirectional differentiation. It can occur in any part of the body's internal cartilage, divided into primary soft tissue chondrosarcoma and primary chondrosarcoma of bone. Extraskeletal chondrosarcoma is a rare, aggressive neoplasm which occurs in the soft tissue and is classified as myxoid and mesenchymal based on histologic criteria. Extraskeletal chondrosarcomas were first reported in 1959 [1], and in recent years, they have been reported in substantial organs and other soft tissues, such as breast [2], kidney [3], vein [4], peripheral nervous system [5], ankle [6] etc. Rozeman [7] reported that there were several histological subtypes, including conventional (85%), dedifferentiated (10%), mesenchymal (2%), and clear cell (1%). Two rare subtypes, extraskeletal mesenchymal, and extraskeletal myxoid chondrosarcoma, do not have typical features of

chondrosarcoma. Extraskeletal mesenchymal chondrosarcoma carry mixed features of Ewing sarcoma and chondrosarcoma, while extraskeletal myxoid chondrosarcoma is a soft tissue sarcoma. The mesenchymal subtype has a poor prognosis [8]. Mediastinal neoplasms include primary and metastatic tumors, thymomas account for approximately 50% of primary tumors, while 20% are lymphomas, parathyroid, or thyroid tumors, germ cell neoplasms, and neurogenic tumors. The occurrence of primary mediastinal chondrosarcoma in the anterior superior mediastinum is extremely rare. Here, a case of primary mediastinal chondrosarcoma is reported that was located in the anterior superior mediastinum. This report reviews the diagnosis, treatment, and prognosis of primary mediastinal chondrosarcoma by reviewing the literature, so as to improve understanding of the disease.

Case report

A 66 year-old female patient was referred to our hospital (Gansu Provincial Hospital, China), with "discontinuous chest and back pain for six months". Chest enhanced CT showed that there

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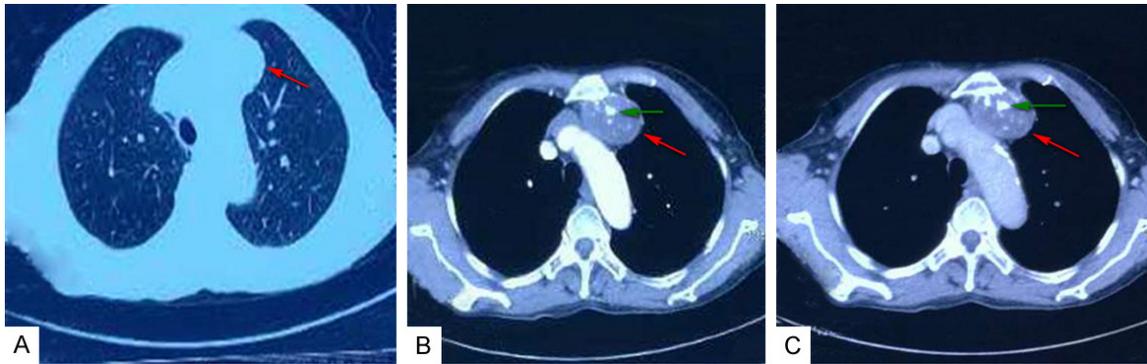


Figure 1. Chest enhanced CT: A-C: There was an elliptical cystic mass in the superior mediastinum, the size was about 5.6*3.8 cm, the boundary was clear (Red arrow indicated). B and C: There were multiple spotted high density calcifications (Green arrow indicated) in it, and the edge was uniform enhancement.

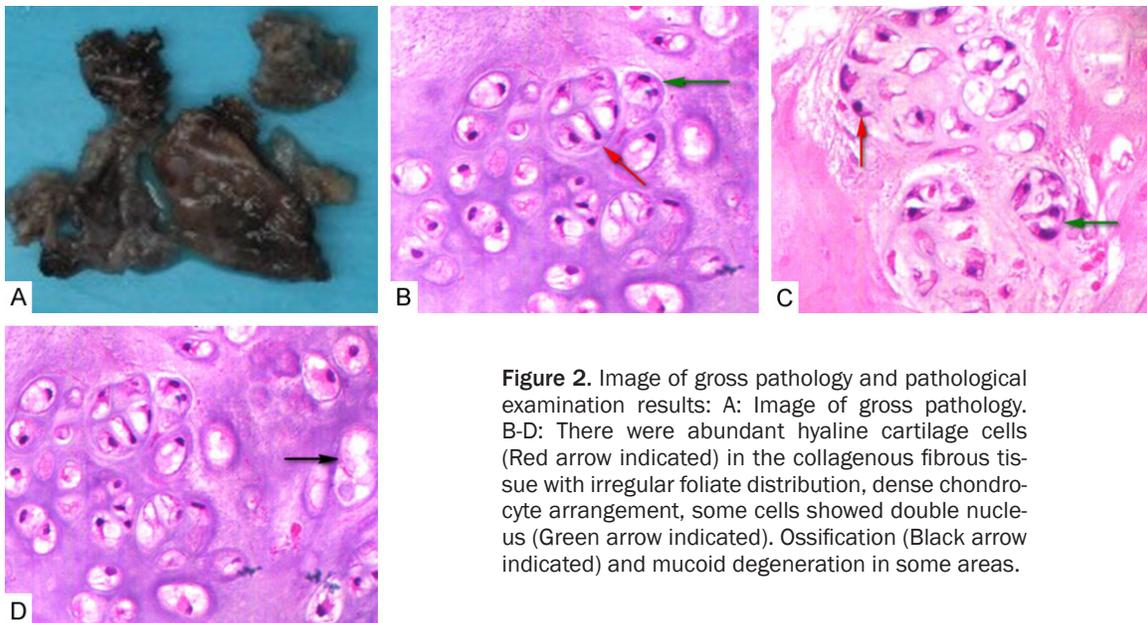


Figure 2. Image of gross pathology and pathological examination results: A: Image of gross pathology. B-D: There were abundant hyaline cartilage cells (Red arrow indicated) in the collagenous fibrous tissue with irregular foliate distribution, dense chondrocyte arrangement, some cells showed double nucleus (Green arrow indicated). Ossification (Black arrow indicated) and mucoid degeneration in some areas.

was an elliptical cystic mass in the superior mediastinum, the size was about 5.6*3.8 centimeters, the boundary was clear, and the edge showed uniform enhancement in contrast enhanced scan (**Figure 1**). No enlarged lymph nodes were found in the mediastinum. No abnormality was found among tumor markers. Anterior mediastinal teratoma was diagnosed before operation, and mediastinal mass excision was performed under the aid of video-assisted thoracoscopic robot, and the tumor was completely removed. The results of postoperative pathological examination showed chondrosarcoma (**Figure 2**). The patient recovered well and accepted radiotherapy after operation. There was no recurrence or metastasis until the end of the follow-up.

Discussion

Chondrosarcoma is a common malignant bone tumor that originates in cartilage or connective tissue of cartilage. The incidence rate is second only to osteosarcoma, accounting for 16.1% of malignant bone tumors. It occurs mostly in long bones, cartilaginous tissues and soft tissues in the limbs. Chondrosarcoma occurs in soft tissues is an extra, rare bone chondrosarcoma, which is not related to bone and periosteum. Extraskelatal chondrosarcoma originates from the embryonic tendon attachment at the residual cartilage, but a few are developed from soft tissue or visceral epithelial tissue metaplasia. About 12.5% of the patients had a history of trauma, 5% of the patients have a history of

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local radiation therapy. It can also be evolved by soft tissue lesions such as ossifying myositis and malignant fibrous histiocytoma [9]. The incidence of extraskeletal chondrosarcomas was only 1% of the soft tissue sarcoma and 4% of osteosarcoma [10]. Unlike primary osteosarcoma, extraskeletal chondrosarcomas is more common in people over 40 years, with a peak incidence of 60-70 years, males slightly more than women [11]. The most common location is the hip, lower limbs, shoulder, upper limb, chest wall and other soft tissue. There were less than 500 cases had reported all over the world, occurred in the mediastinum was extremely rare, and most of them were case report or literature review. Due to the special anatomic structure of the mediastinum, primary mediastinal chondrosarcoma lacks of characteristic clinical symptoms, and the main manifestation is painless mass which growth slowly. In our case, the patient has no history of chest trauma and exposure to radioactive material, so it was considered evolved from soft tissue lesions or embryonic remnant tissue. Pain in the chest is the mainly symptom for the patient, which may be associated with the compression of the nerves.

In the new classification of bone tumors in 2013, chondrosarcoma classified into conventional chondrosarcoma, clear cell chondrosarcoma, mesenchymal chondrosarcoma, dedifferentiated chondrosarcoma, and periosteal chondrosarcoma according to histopathological characteristics by the World Health Organization, periosteal chondrosarcoma is classified as a subtype of common chondrosarcoma. According to the degree of malignancy and cell differentiation, it was divided into rank I-III [11], grade I indicates a high degree of differentiation of cells, low malignancy, and reduced invasiveness. Grade III shows that cells have a low degree of differentiation and strong invasiveness; Grade II is between them. The extraskeletal chondrosarcomas has a clear boundary commonly and most of them have a complete envelop. The section plain is white, shiny, with uneven texture, and visible focal irregular cartilage calcification and ossification zone. A biphasic differentiation that composed of undifferentiated primitive mesenchymal cells and scattered small island like highly differentiated hyaline chondrocytes can be seen under microscope [12]. Undifferentiated mesenchymal tu-

mor cells were small round or fusiform, relatively uniform in size, hyperchromatic nuclei, unclear nucleoli, less cytoplasm, tumor cells closely arranged, the heteromorphosis is not obvious, and the mitosis is rare, the interstitium is rich in blood vessels. Mesenchymal cells transform into chondrocytes gradually. There are no chondrocytes around the hyaline cartilage lesions, and the size and shape of the chondrocytes are different. The boundary between the cartilaginous and undifferentiated areas is clear, and the proportion is indeterminate. Calcification and ossification can occur in the cartilaginous focus [8, 9].

Primary mediastinal chondrosarcoma lacks characteristic findings on chest radiography and ultrasound examination. CT shows soft tissue mass with uneven density and extensive calcification in mediastinum, enhanced scan shows obvious enhancement of edge and internal performance is flocculated or striped strengthening, which is typical CT imaging manifestation of mesenchymal chondrosarcoma and have high diagnostic value. MRI expresses as equal or low signal in T1WI and mixed signal in T2WI, enhanced scan displays inhomogeneous enhancement, and the calcification area was also enhanced, which might be also a rich blood flow in the calcification area [4]. Due to the rich blood flow characteristics of the tumor, the "pepper surface sign" can be seen in T2WI, which is one of the important imaging modalities that indicates chondrosarcoma. CT can accurately predict the growth pattern of mediastinal chondrosarcoma and the distribution of neoplastic cartilage and cartilage calcification, and can judge the blood supply and central necrosis of tumor by enhanced scanning further more. MRI has better tissue resolution and contrast than CT, and can multidimensional imaging in order to observe the relationship between tumor and adjacent tissue better. CT and MRI examination can accurately display the internal typical structure of mediastinal chondrosarcoma and the relationship with adjacent tissues. If the imaging is typical, chondrosarcoma can be considered before operation, but it must be confirmed by pathology. In this case, CT showed clear elliptical cystic mass and enhanced edge with multiple punctate high density calcifications. These valuable imaging data are important for the diagnosis of mediastinal chondrosarcoma. However, unfortunately

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it was misdiagnosed as teratoma preoperation because extraskelatal chondrosarcomas are rare in clinical practice, which is a lesson to be learned.

The characteristic of primary mediastinal chondrosarcoma is lack typical clinical manifestations, the mainly symptom is compression of surrounding organs or chest pain. The imaging findings are cystic solid soft tissue mass and multiple irregular calcifications. The diagnosis of extraskelatal chondrosarcomas depend on pathological examination, which need to found the biphasic differentiation that composed of undifferentiated primitive mesenchymal cells and scattered small island like highly differentiated hyaline chondrocytes [12]. The vimentin protein was positive in different degrees, CK was negative, NSE and CD99 were positive in small cell area, and S-100 positive in cartilage region, Sox9 can also be used as an important immuno-histochemical marker [13].

Primary mediastinal chondrosarcoma is rare disease and is misdiagnosed easily, which needs to be identified with the following diseases: Mediastinal teratoma: most commonly seen in anterior, middle mediastinum, uneven density, calcification, and malformation of bones, teeth and fat. Thymoma: usually located in the anterior and middle mediastinum. About 15% of the patients have myasthenia gravis. The masses are round or round like, the boundary is clear, with capsule, uniform density, enhanced scan indicates homogeneous enhancement. Neurogenic tumors: most of them are in children. Most of them are located in the posterior mediastinal paraspinal sulcus. The tumors are round like, with smooth edges and uniform density. They can suppress the adjacent bone and cause local bone resorption. Typical lesions are dumbbell shaped when they are located inside and outside the spinal canal.

There is currently no consensus on the treatment of extraskelatal chondrosarcomas. However, as a member of the mesenchymal tumor family, the sensitivity to chemotherapy is poor. Surgical resection of the tumor completely and achieving the margin negative (R0) is considered the gold standard for surgical treatment [2-6]. In view of the special anatomical structure of mediastinum, for the tumors that are adhered to main vessels tightly or wrap around important vessels, it is necessary to use vascu-

lar surgical techniques to reconstruct the important vessels.

Radiotherapy has been recommended in a multidisciplinary internal meeting [2]. After studying 107 cases of interstitial chondrosarcoma, Xu et al [14] suggested that radiotherapy for patients with positive margins or unresectable can be used as a remedy measure to reduce the recurrence. Proton therapy was used for treating chondrosarcoma, the results showed that high dose proton therapy could help to improve the survival rate [15]. Most scholars believe chemotherapy is not effective for chondrosarcoma, but Mitchell [16] thought that supplemented chemotherapy (doxorubicin and cisplatin) in a few cases can increase the patient's survival after radical resection. Aksoy [17] reported that temozolomide on intracranial mesenchymal chondrosarcoma treatment is effective, and can promote the effect of radiotherapy. However, there are few studies on chemoradiotherapy for chondrosarcoma at home and abroad, there is no consensus on whether chemotherapy can prevent tumor recurrence and increase the survival rate. Targeted therapy is a research hotspot in cancer treatment. Although targeted therapy of chondrosarcoma is still in basic research and clinical trials, miRNA-497, miR-181A, adiponectin and other targets have achieved encouraging results [18-20]. In order to treat tumors that fail to achieve complete resection and prevent recurrence, radiotherapy, chemotherapy, molecular targeted therapy, and biological therapy can be used to improve the prognosis.

Mediastinal chondrosarcoma is highly malignant with rapid progress, the recurrence rate being high as 70.6% and the transfer rate of 23.4% [5]. It is easy to recur *in situ* and transfer to the lungs, lymph nodes and bones through blood, and the prognosis is poor. Nakashima [21] reported that the 5-year survival rate was 54.6% and the 10-year survival rate was 27.3%. The study of children and adolescents by Dantonello [22] showed that the total survival rate of 10 years was 67%.

Conclusion

Primary mediastinal chondrosarcoma is a rare and highly malignant extraskelatal chondrosarcoma. It is easy to misdiagnose and prognosis is poor. The pathological features of the tumor

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and the typical imaging findings are of great value for the diagnosis. The key to improve prognosis is to completely remove tumors and ensure negative margins. Further research should be focused on its pathogenesis and diagnostic methods.

Disclosure of conflict of interest

None.

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