Primary malignant bone neoplasm: a case report of dedifferentiated chondrosarcoma in the rib and review of the literature

Jin-Rong Lin¹, Wei-Min Zhang¹, Zhuo-Cai Wang²

¹ Oncology Department, Guangzhou General Hospital of PLA, Guangzhou, Guangdong 510010, P. R. China; ² Pathological Department, Guangzhou General Hospital of PLA, Guangzhou, Guangdong 510010, P. R. China

[Abstract] Dedifferentiated chondrosarcoma (DDCS) is a rare but highly malignant primary bone neoplasm, which is resistant to radiotherapy and chemotherapy. There remains uncertainty as to the best treatment of this disease and how to improve its prognosis. In this paper we reported a case of DDCS and reviewed the related literatures in order to provide references to throw a light on the histogenesis, diagnosis and therapy of this disease.

Key words: Chondrosarcoma, diagnosis, chemotherapy, dedifferentiated chondrosarcoma

Dedifferentiated chondrosarcoma (DDCS), a primary bone tumor, is a relatively rare subtype of chondrosarcoma. Besides well-differentiated chondrosarcomas or borderline cartilage lesions, it also contains one or more malignant tumor components such as fibrosarcoma, malignant fibrous histiocytoma, osteosarcoma, leiomyosarcoma, undifferentiated sarcoma and/or rhabdomyosarcoma [1,2], accounting for 1% to 2% of primary bone tumors [3] and 10% to 11% of chondrosarcomas [4]. Most of the patients with this disease aged from 40 to 60 years. One patient with dedifferentiated chondrosarcoma developing in left 7th rib was admitted to Guangzhou General Hospital of PLA on May 9, 2006 and the data of this case was reported as follows.

A 39-year-old man was admitted to the hospital because of fever, precordial discomfort, and cardiopalmus. The patient began to run a fever since February 2006, with temperature fluctuated between 38°C and 39°C, accompanying by precordial discomfort and cardiopalmus. After cardiac ultrasound examination in a hospital in Australia, the patient was diagnosed with cardiac space-occupying lesion. After treatment with antibiotic, the fever was brought down, but the chest pain and palpitations got progressively worse. Cardiac ultrasound performed in the hospital outpatient department on May 8, 2006 showed space-occupying lesions in the right atrium. Positron emission tomography-computed tomography (PET-CT) examination performed in Nanfang Hospital, Guangzhou on May 9, 2006 showed high-signal lesions in the left 7th rib and many flocculent and small patchy shadows in both lungs (Figure 1A); it also showed high-signal lesions next to right atrium and obvious pericardial thickening (Figure 1B). The weight loss was about 4.5 kg. Exploratory thoracotomy performed on May 15, 2007 showed that a mass of 1.0 cm x 1.0 cm was on the outer surface of the rib at the intersection between the left 7th rib and the middle axillary line and the mass was closely connected with the rib. Indurations whose textures were tenacious with diameters between 0.4–0.8 cm were scattered in left lung. Resection of the lesions in the left 7th rib and wedge resection of partial lesions in left lung were performed for biopsy. Treatment with high-dose MTX (methorexate) plus AP (pirurubin hydrochloride as well as cisplatin) chemotherapy, leucovorin rescue and urine alkalinization began from June 5, 2006, once every 21 days up to 6 cycles. Five days after the first cycle of chemotherapy, chest pain and palpitation gradually disappeared. After 2 cycles of chemotherapy, repeated CT examination suggested that the number of tumors in lungs was significantly reduced and tumor volume decreased obviously (Figure 1C); the tumor in the right atrium was significantly reduced (Figure 1D) and the patient was partial response.
(PR). After 6 cycles of chemotherapy, repeated CT examination suggested that the tumors in lungs almost disappeared (Figure 1E) and the patient was PR, almost complete response; tumors in the right atrium continued to shrink significantly (Figure 1F).

Figure 1  Positron emission tomography-computed tomography (PET-CT) or CT results of lungs and pericardium prior to chemotherapy (A, B), after 2 cycles of chemotherapy (C, D) and 6 cycles of chemotherapy (E, F). Significant reduction of the tumor volume was observed.

**Postoperative pathology**

Spindle cells and epithelioid cells accompanying with rich blood sinusoids in lung tissues arranged in nest were observed under microscopy. In the 7th rib, allotopic chondroid tissue and ribbon-like bone trabecula were observed, and anaplasia was seen in osteoblast and chondrocytes. Lung tumors infiltrated to the pulmonary alveolus. The pathologic diagnosis of the lung lesions was angioendothelioma metastasis of dedifferentiated chondrosarcoma (Figure 2A); the malignant tumor in the left 7th rib was dedifferentiated chondrosarcoma (Figure 2B).

Figure 2  Pathological pattern of vascular endothelioma in the left lung (A, HE x400) and dedifferentiated chondrosarcoma in the seventh left rib (B, HE x200). The images were taken from the surgery samples of the patient before chemotherapy.
Immunohistochemistry

The immunohistochemistry results were as follows: CD31 (+), CD34 (+), F8 (+), CD68 scattered (+), FN (+), CK (−), Syn (−), HHF-35 (−), MC (−), Cr (−), CD117 (±), Myo D1 (−), SMA (−), PTEN (+), Topo II (+), and S-100 protein in cartilage cells (+) (Figure 3 A−G).

Follow-up

Chest distress and breathlessness recurred on January 12, 2007 and CT result referred to tumor progression. The patient refused further chemotherapy. Therefore, the patient was given supportive and symptomatic treatment. The disease got worse gradually. On March 21, 2007, the patient had a sudden chest distress and dyspnea followed by apnea and cardiac arrest, then he died. The survival time was 10.4 months.

Discussion

Tumorigenesis and diagnosis

Chondrosarcoma is a low-grade malignant bone tumor while dedifferentiated chondrosarcoma, as a subtype of chondrosarcoma, is a highly malignant bone tumor. Dedifferentiated chondrosarcoma is most commonly found in the proximal femur, humerus, tibia, pelvis, and scapula and rarely in other parts. It was really rare that it was developed in the left 7th rib, as in this case. Dedifferentiated chondrosarcoma, also known as spindle cell chondrosarcoma, was first proposed and named by Dahlin et al. [5], who also described the clinical and pathological features of this disease in 1971. So far, 343 cases have been reported in the world, of them 184 are male and 159 are female, ranging in ages from 9 to 92.9 years (median, 58.7 years). In 1988, Lee et al. [6] firstly reported 21 cases of dedifferentiated chondrosarcoma in our country. In 2004, Xie et al. [7] reported 13 cases of dedifferentiated chondrosarcoma confirmed by pathology after surgery. Other reports are sporadic. Pathology in this case suggested that it contained a variety of tumor tissues such as allotopic cartilage-like tissue and ribbon-like trabecular bone, osteoblasts and cartilage cells with anaplasia,
dedifferentiated chondrosarcoma of angioendothelioma metastasis in the lung, and so on, which were in accord with diagnosis standard of dedifferentiated chondrosarcoma.

In the diagnosis of dedifferentiated chondrosarcoma, Xie et al. thought that there were destructions of bone and cortical bone, high incidence of periosteal reaction, and large soft tissue masses in addition to the performance of typical chondrosarcoma by image. If the disease is highly suspected clinically, more specimens should be obtained in various lesions to improve the diagnosis. The lesions were on the ribs in this case. The primary tumor is not big. Therefore there were no obvious characteristic changes shown in CT scans. Pericardial mass was the outstanding performance in clinical. All of these lead to a preoperative misdiagnosis, suggesting that we should think of the possibility of this disease when meeting similar cases in the future. PET-CT can find small lesions, which is of certain significance to determine tumor metastasis and a guide to therapy. However, it still not be applied universally because of its high cost.

Histological origin of dedifferentiated chondrosarcoma remains controversial, which is predicted to be associated with abnormalities of gene controlling differentiation of chondrocytes and osteocytes. Dahlin et al. thought that dedifferentiated chondrosarcoma was a highly malignant mesenchymal tumor which was transformed from well-differentiated cartilaginous tumor. Is dedifferentiated chondrosarcoma monoclonal or polyclonal origin? One theory insisted that dedifferentiated chondrosarcoma and chondroid-like components derived from the same pluripotent stem cells, which can differentiate into well-differentiated sarcoma. Snanerkin et al. thought that dedifferentiated chondrosarcoma may be a form of collision tumor, the differentiate components of which originated from reactive fibrous tissue in the necrotic region around cartilage. The process was similar to that of bone infarction and chronic osteomyelitis developing into fibrosarcoma. Another theory thought that these two kinds of clones have their own independent origin, some of which differentiate into poorly differentiated chondrosarcoma cells while others cannot. It is currently found that these two kinds of tumor differentiations have the same enetic alterations, which indicated that these two clones originated from the same precursor cells but differentiated into two kinds of tumors followed by a lot of genetic changes. It suggested that these two clones were independent. After several rounds of recurrence after surgery, some chondrosarcoma become dedifferentiated chondrosarcoma, which was known as secondary dedifferentiated chondrosarcoma. Using gene chip technology, Wang et al. found that there were significant differences in gene expression between dedifferentiated chondrosarcoma and ordinary chondrosarcoma, which were associated with TGF signaling pathway, Wnt signaling pathway, IHH/PTHrP axis, mechanism of apoptosis, and so on. It is useful for identification of dedifferentiated chondrosarcoma from ordinary chondrosarcoma at the molecular level and is a good foundation for further diagnosis and treatment of this disease at the molecular level.

Treatment

Early diagnosis and timely treatment are the key to improving the therapeutic effect and prolong the survival of the patients. Surgery remains to be the only treatment to cure dedifferentiated chondrosarcoma. Distant metastasis is the chief reason for treatment failure and death of dedifferentiated chondrosarcoma, therefore developing effective adjuvant therapy regimens to control distant metastasis is the main mean for improving the therapeutic efficacy and extending survival. Radical surgery is the first-line choice and a clean surgical margin is the basic principle. The local recurrence rate was over 50% and it decreased after radical surgery. Surgery is divided into radical surgery, wide resection, margin resection, limb salvage and reconstruction, amputation, tumor curettage, and so on. Mitchell et al. thought that accurate preoperative diagnosis was important for choosing appropriated operation and it was the most important factor affecting survival rate. Because dedifferentiated chondrosarcoma contains one or more malignant tumor components, two or more different tumors should be taken into account, leading to difficulty in treatment. Despite the continuous development and progress in diagnostic techniques and auxiliary treatment, there is still no good treatment for dedifferentiated chondrosarcoma at present and the prognoses of the patients remain poor. The patient had reached an advanced stage at his first visit in this case. Close adhesion between tumor and surrounding tissue led to a failure to completely remove the tumor. As a result, only biopsy can be performed and high-dose chemotherapy was given after surgery. In general, the chondrosarcoma is not sensitive to chemotherapy. Whether chemotherapy is effective for the patients with dedifferentiated chondrosarcoma is still controversial. Most scholars believe that chemotherapy had limited effects on dedifferentiated sarcoma. Dickey et al. reported 42 cases of dedifferentiated chondrosarcoma. A total of 39 patients underwent surgical resection, of which 15 (38.4%) underwent surgery alone, 22 (56.4%) underwent surgery plus chemotherapy, 1 (2.6%) underwent surgery plus radiotherapy, and 1 (2.6%) underwent surgery plus chemotherapy and radiotherapy; 27 patients were treated with new adjuvant therapy, of which 23 underwent chemotherapy alone, 2 underwent radiotherapy alone, and 2 underwent...
radiotherapy and chemotherapy. The results suggested that new adjuvant therapy could not extend survival. Five-year survival rates of the patients treated with surgery alone and adjuvant chemotherapy were 11.8% and 4%, and the median survival time was 6.4 months and 8.4 months (P = 0.69), respectively.

Since the disease is rare, there still no large, random population-based clinical data to determine which regimen of chemotherapy or radiotherapy can prolong survival of the patients with the disease. High dose of MTX plus AP chemotherapy were adopted in this case. It has a good prognosis, almost CR, suggesting that high-dose of MTX plus AP regimen can serve as an alternative chemotherapy. However, there is only one case in this report. Case studies should be further expanded. Tumor progressed 3 months after chemotherapy in this case, but the patient refused further treatment. Finally, the patient died of systemic failure caused by tumor progression, suggesting that further research still be required for more effective chemotherapy. The disease is not sensitive to radiotherapy, but if it was not completely resected by surgery; for residual lesions after operation, local radiotherapy still should be considered.

**Survival and prognosis**

The survival time of this case was 10.4 months, similar to that reported in the literature. It was reported that the median survival time of this disease was 7.5 months and 2-year survival was less than 20%. Doganavargil et al. reported that the 5-year disease-free survival was less than 10%. Disease-free survival rate was associated with postoperative adjuvant chemotherapy, surgical margin, tumor size, stage at diagnosis, histological subtype (dedifferentiated components), and limb salvage or amputation. Johnson et al. thought that dedifferentiated chondrosarcoma was much easier to metastasize and the prognosis was worse because of its osteosarcoma components or malignant fibrous histiocytoma-like components when compared to typical chondrosarcoma.

**References**


