Medical imaging and analysis of dedifferentiated chondrosarcoma using CT, MRI and ultrasound

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Abstract. Chondrosarcoma (CS) is a type of bone cancer that arises from the malignant transformation of chondrocytes and spreads metastatically to the surrounding bone tissue. CSs tend to grow and spread slowly, dedifferentiating into high-grade tumours; however, the cancer may grow rapidly too. What causes chondrosarcoma is not known, though it may arise from a benign tumour or bone conditions. Typically, CS tumours originate from the bones of the axial skeleton, but they may also occur in other parts of the body. CS patients usually experience aching pain around the tumour, especially at night or during physical activity, and it slowly deteriorates. Medical imaging tests play an important role in the diagnosis of CS; nevertheless, a tissue biopsy is required to confirm its diagnosis. The role of medical imaging is also vital in guiding and monitoring treatments. Surgical resection of the tumour is commonly the primary treatment for most types of CS due to its resistance to chemotherapy and radiation therapy. This work presents the case of a deceased middle-aged male subject with dedifferentiated CS of the right chest wall, including analysis of medical images involving both ionising (computed tomography) and non-ionising techniques (ultrasound and magnetic resonance imaging), in addition to treatments the subject received, along with their outcomes. Five generations of the subject’s family were investigated in detail and the subject was found the only cancer case in his family. Furthermore, the subject did not benefit from any treatments he underwent, and he died within two years from the diagnosis.

1. Introduction

Chondrosarcoma (CS) is the third most common type of primary bone cancer and its onset lies in chondrocytes [1] [2]. Chondrocytes are the only cells found in healthy cartilage and they secrete the extracellular matrix to maintain the cartilage [3] [4]. Despite the aetiology of CS being unknown, the tumour may grow out of bone conditions and benign tumours, or due to radiotherapy (RT) [5]. RT has been widely used to treat certain benign bone tumours and other bone diseases; however, RT may cause CS [1]. CSs account for about 20% of all primary malignant bone tumours, mainly affecting adults between the age of 40 and 75 years, with a slight male predominance [2]. Diagnostic procedures for CS
include medical imaging and biopsy tests. Based on their histopathology, CSs are divided into three histologic grades: grade I (low), grade II (medium), and grade III (high) [6]. Furthermore, dedifferentiated CSs are considered as grade IV [3]. Typically, dedifferentiated CS occurs in middle-aged or older subjects. Dedifferentiated CSs are rare, but extremely aggressive tumours, which make up about 11% of all CSs [4]. CSs of the chest wall tend to grow slowly and they recur locally [7]. Common treatments involve a wide surgical resection of the tumour; however, local recurrence may occur post-operatively. Chemotherapy is often ineffective and RT is used mainly as a palliative tool. The five-year survival rates among adult subjects with CS are at 90% for grade I tumours, 81% for grade II tumours, and 29% for grade III tumours [8] [6]. However, the five-year survival rate for dedifferentiated CS is between 7% to 24% [8].

2. Medical history
The case of a 54-year-old deceased male subject with CS is presented and discussed in this study. The subject was first admitted to the hospital because of chest and back pain, in addition to swelling around the area where back pain was perceived. Diagnostic tests were carried out and included both ionising (computed tomography (CT)) and non-ionising medical imaging techniques (ultrasound and magnetic resonance imaging (MRI)), besides open biopsy. Based on the findings from these tests, the subject was diagnosed with CS of paravertebral localisation and intra-thoracic and extra-thoracic regions. The subject received a combination of treatments involving surgical resection, chemotherapy and RT; nevertheless, the subject did not survive for more than two years post-diagnosis.

3. Diagnosis
In general, CSs do not make people feel weak or ill; however, most subjects with CS will eventually experience swelling and/or pain due to various activities [9]. Pain and swelling may imply active growth of a tumour when other bone problems are excluded. Therefore, CSs are usually huge masses at the time of diagnosis [3]. Medical imaging has a major role to play in the diagnosis and treatment planning of CS. Each imaging modality plays an independent role in the diagnosis, assessment of local complications, as well as preoperative evaluation and preparation. Ultrasound can assist in determining the texture of the mass and the commonly associated calcifications, i.e., accumulation of calcium salts; however, the site of the origin of CS is often not determined using ultrasound due to its reduced contrast and resolution [10] [11]. Figure 1 is the ultrasound image of the chest of the subject, presenting a well-defined large mass with a cystic component and calcifications.

![Figure 1 Right thorax ultrasound of the subject presenting a large mass.](image)

Despite the use of ionising radiation, CT is leveraged to obtain high-contrast and high-resolution images and to provide further information about the morphology of the tumour to perform a more accurate diagnosis [12]. CT can show the extent of metastasis of a tumour, in addition to its origin [11].
The bony destruction caused by CS, as well as the associated small calcifications, can also be observed via CT. CT is helpful to assess any related structural cues, such as pathological fractures associated with CS, and it can provide a confident pre-operative diagnosis. Figure 2 illustrates the three views of a CT scan of the chest of the same subject in Figure 1, with IV contrast (C+) demonstrating a large tumour in the right hemi-thorax around the lower thoracic spine.

![CT Images](image_url)

**Figure 2** Coronal (A), sagittal (B), and axial (C) views of the chest imaged via CT with IV contrast (C+) arterial phase, identifying a huge tumour (see the arrows), localisation paravertebral with intra-thoracic and extra-thoracic regions.

Open biopsy of the known cancer was performed, and the histological examination of its tissue confirmed the tumour of chondroid origin. CT is a useful imaging modality in a subject who cannot take MRI due to, for example, having a pacemaker or claustrophobia. CT with IV contrast (C+) is the gold standard structural imaging modality for the diagnosis and treatment planning of CS [13]. However, MRI can produce clearer images when compared to CT for further functional assessments [14], such as in evaluating the involvement of soft tissue. Figure 3 is the T2-weighted MRI of the thoracic spine of the same subject in Figure 1 and Figure 2, showing a large tumour (marked by arrows).
Figure 3 Coronal (A), sagittal (B), and transverse (C) T2-weighted MRI TSPINE demonstrating a huge tumour of chondroid origin (see the arrows) intra-thoracic and extra-thoracic and paravertebral at the lower thoracic spine, also highlighting how the neighbouring soft tissue was also affected.

4. Treatment Options
Typically, CS subjects undergo a combination of surgery and adjuvant therapy, such as chemotherapy and RT. A wide margin of healthy tissue is typically removed with the complete surgical resection of the tumour. However, most CSs do not respond to chemotherapy or RT. These therapies have been ineffective, except for palliative purposes.

5. Surgery
Following the open biopsy and the diagnosis after one month, the subject received surgical treatment. Tumour resection was performed by thoracotomy on the right side of the chest. Moreover, a partial resection of the chest wall and ribs 9–11 was performed, as well as mediastinal pleurectomy (part of the pleura was removed to help in preventing fluid from collecting in the affected area), and the removal of the autochthonous back muscles. The aim of the resection margin around the removed tumour was to prevent the extension of the malignant growth. The resection margin for the subject was classified RX-resection (RX means the presence of residual tumour (R) cannot be assessed).

6. Radiotherapy
Further to the RX-resection after four months, the subject received RT. The target volume was the right paravertebral region using the technique of carbon ion therapy (C12) with active raster scanning, in addition to orthogonal X-rays for image guidance. RT is curative when undergone following incomplete resection for maximal local control; however, RT is palliative when resection is not possible. The subject received surgical intervention for the second time after about one month from the first date of undergoing RT, including right re-thoracotomy, partial resection of chest wall, back muscles and processus spinosus T7/T8, as well as mediastinal and paracardial tumour resection. Tumour recurrence paracardial and
paravertebral occurred after about six months from the date of the second surgery. Nevertheless, another resection was not possible; alternatively, the subject was evaluated for re-RT or chemotherapy.

7. Chemotherapy
Chemotherapy was recommended according to the EUROpean Bone Over 40 Sarcoma Study (EURO-B.O.S.S.) protocol [15]; however, following the first cycle of cisplatin (CIS) / doxorubicin (DOX), the subject experienced acute kidney failure (AKF) as a complication. CIS is a class of platinum-based anti-cancer chemotherapy drugs, and it works by forming platinum complexes when binding to DNA, causing cross-linking of the DNA strands leading to apoptosis. Instead, DOX is a class of anti-cancer chemotherapy drug known as ‘anthracycline’ and it acts by blocking the enzyme required by cancer cells to divide and grow known as Type II topoisomerase, causing slowing, or stopping the growth of cancer cells. To avoid re-exposition of CIS, the subject received ifosfamide (IFO) / DOX according to EURO-B.O.S.S.; nonetheless, the subject experienced the same complication of AKF, in addition to exsiccosis, i.e., bodily dehydration due to insufficient intake of fluids. IFO is a class of anti-cancer chemotherapy drugs called ‘alkylating’ agents and it reduces or prevents the growth of cancer cells.

8. Progressive disease
In comparison to the time when the disease was first diagnosed, imaging tests confirmed progressive disease with growth of recurring CS of the back, in addition to constant lymph-nodal and progressed pulmonal and pleural metastases. The subject started to receive Carboplatin and Etoposide (Carbo / Etop) chemotherapy (salvage chemotherapy) according to the protocol of the Cooperative Osteosarcoma Study Group 96 (COSS-96) [16]. The term salvage chemotherapy refers to chemotherapy administered if none of the treatment strategies were effective. After the subject received the first cycle of salvage chemotherapy, he experienced complications of fever during neutropenia. Neutopenic fever is a chemotherapy side effect and it involves a temperature of or greater than 100.4°F (38.0°C). Following the second cycle of salvage chemotherapy, the subject experienced complications of fever during neutropenia, in addition to detection of streptococcus sanguinis in blood culture. The subject received the third and the fourth cycle of salvage chemotherapy. However, imaging tests confirmed constant sizes of the recurring CS in the autochthonous back muscles, as well as paracardial lymphnodal metastasis. The subject received the fifth cycle and the sixth cycle salvage chemotherapy Carboplatin and Etoposide (Carbo / Etop) with dose reduction to 66%. Imaging tests confirmed stable oncological findings with no evidence of significant cancer change within the diagnosed tumour relapse of the back.

9. Summary
The subject was first diagnosed with a CS paravertebral with intra-thoracic and extra-thoracic parts. Following resection and RT with carbon ions, there was a progressive disease with an extended tumour mass 9 cm x 3.5 cm with infiltration of the right vertebral body, right ventricular myocardial after nearly two years from the first time of diagnosis, which could not be resected. Chemotherapy was recommended according to the EURO-B.O.S.S. protocol. However, after each cycle, the subject developed AKF and he presented a progressive tumour via imaging tests; thus, it was not possible to continue with the chemotherapy. Further to the required evaluation, the subject was recommended an adjustment to the COSS-96 protocol with Carboplatin and Etoposide. The therapy was tolerated well with supportive medication and further antiemesis, except for fever in neutropenia and therapy-induced anaemia/thromboctopenia subject to transfusion. Staging analysis after the sixth cycle showed a stable disease. However, further surgery was not possible due to reaching a stable condition.

10. Conclusion
The case of a 54-year-old deceased male subject diagnosed with recurrent progressive CS was presented and discussed in this article. The subject first underwent surgical resection and received post-operative RT to the paravertebral region. The subject also received multiple lines of salvage chemotherapy. The
subject was not found suitable for surgical intervention due to extensive tumour with multiple metastatic lesions. RT was carried out as a palliative treatment and had no therapeutic benefits; the subject also showed toxicity. The subject was not suitable for any further systemic anti-cancer treatments due to poor clinical status. The subject underwent palliative care to minimise the symptoms, improve quality of life and for symptomatic management (pain, vomiting, shortness of breath and other side effects) until he died.

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