Case Report
Dedifferentiated chondrosarcoma of the rib with a malignant mesenchymomatous component: An autopsy case report

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A rare variant of dedifferentiated chondrosarcoma with malignant mesenchymomatous component in a 57-year-old male is reported. The patient presented with a posterior mediastinal mass arising from the left eighth and ninth ribs showing well differentiated, low-grade chondrosarcoma. Five years later, local recurrence occurred and an excised specimen also showed the same histological features as the primary tumor. Another 6 years later, the tumor recurred and metastasized to the multiple organs, the patient dying 4 months later. Autopsy revealed that the recurrent and metastatic tumors showed malignant mesenchymomatous 'dedifferentiation' of chondrosarcoma composed of rhabdomyosarcoma, angiosarcoma, chondrosarcoma, osteosarcoma, and leiomyosarcoma, in addition to fibrosarcomatous areas. Although the less differentiated component of dedifferentiated chondrosarcoma usually shows the histological features of malignant fibrous histiocytoma and fibrosarcoma, multilineage differentiation can occur in that component. The phenomenon of 'dedifferentiation' in chondrosarcoma and the relationship to and distinction from malignant mesenchymoma of soft tissue and bone are discussed.

Key words: bone, dedifferentiated chondrosarcoma, malignant mesenchymoma, multilineage differentiation

The phenomenon of dedifferentiation of chondrosarcoma (CS) was first reported by O'Neal and Ackerman in one case of their series of 40 cases of CS.1 Jaffe also described in his textbook the same phenomenon of anaplastic fibrosarcomatous dedifferentiation of CS.2 Dahlin and Beabout reported in detail 33 cases of dedifferentiated chondrosarcoma (DCS) out of 370 cases of chondrosarcoma.3 Dedifferentiated chondrosarcoma is a highly malignant tumor which is histologically characterized by low-grade chondrosarcoma with a juxtaposed 'dedifferentiated' non-cartilaginous sarcomatous component, usually showing histological features of fibrosarcoma (FS), malignant fibrous histiocytoma (MFH), or osteosarcoma (OS).3,4 On rare occasions, rhabdomyosarcoma (RMS),4,5,6 angiosarcoma (AS),7 and giant cell tumor-like MFH8-13 were reported as 'dedifferentiated' sarcomatous components.

To our knowledge DCS with a malignant mesenchymomatous component has not been described in the English literature. We report such a case of DCS and discuss the pluripotential ability of 'dedifferentiated' sarcoma.

CLINICAL SUMMARY

A 57-year-old male who had no contributory family and past histories, suffered a traffic accident resulting in a right fourth rib fracture. At that time, a mediastinal tumor was pointed out in the chest roentgenogram. At the operation, the tumor was located in the left paravertebral region and arose from the left eighth or ninth rib. Marginal excision of the tumor was carried out. Five years later, local recurrence of the tumor was disclosed. The two separate tumors in the para-aortic region with involvement of the left fifth and tenth ribs were surgically excised, respectively. Six years after the second operation, another local recurrence of the two tumors was revealed. One tumor was located in the paravertebral region of the upper thoracic spine with involvement of the left fifth and tenth ribs, and the other was in the paravertebral region at the tenth thoracic spine level. Excision of the former tumor was performed, however, the latter tumor could not be excised. After the operation, paraplegia appeared, thus a laminectomy from the eighth thoracic to the first lumbar spine was performed. One month later, multiple pulmonary metastases were detected and the patient died due to progressive respiratory failure. Although the total clinical course was 12 years, the clinical course after the second recurrence was very rapid and was only 4 months.
PATHOLOGICAL FINDINGS

Autopsy examination showed edema of the lungs and slight hypertrophy of the left ventricle of the heart. Extramedullary hematopoiesis was found in the liver, spleen, and kidneys. Compression necrosis of the spinal cord with pencil-shaped softening at the level of the eighth to tenth thoracic spinal cord was seen.

The first recurrent tumors

The two paravertebral tumors at the left sixth and tenth ribs, each measuring 6 × 4 × 3 cm and 2 × 1 × 0.6 cm in size, respectively, showed histology similar to that of the primary tumor (low-grade (grade 1) chondrosarcoma).

The second recurrent tumor

The tumor, measuring 12 × 10 × 6 cm in size, involved the apex of the left lung, and showed an elastic firm, yellowish-white, fleshy sarcomatous appearance. There was no area showing chondroid appearance. Histologically, diffuse proliferation of poorly differentiated spindle and pleomorphic tumor cells without chondroid matrix was observed. Tumor cells with abundant, elongated or round, eosinophilic cytoplasm suggesting rhabdomyoblastic differentiation were occasionally found.

The primary tumor

The excised tumor, measuring 13 × 6 × 6 cm in size, was well circumscribed and lobulated showing chondroid appearance. Histologically, the tumor consisted of well differentiated hyaline cartilage with occasional atypical and binucleate chondrocytes (Fig. 1). An histopathological diagnosis of low-grade (grade 1) chondrosarcoma was made.

Figure 1. The primary tumor showing well-differentiated hyaline cartilage consistent with low-grade chondrosarcoma.

Figure 2. The second recurrent tumor consists of fibrosarcomatous spindle cells with herring-bone pattern.
The recurrent and metastatic tumors at autopsy

Autopsy was performed 2 h and 8 min after death. The tumor had recurred locally in the left paravertebral region at the level of the tenth thoracic spine. Metastatic tumors were found in the lungs (multiple), liver (several), left kidney (several), almost the entire length of vertebral bodies, left adrenal, and sigmoid colon. Lymph node involvement of the right pulmonary hilar, para-aortic, and right venous angular nodes was also found. Metastatic tumors showed variable histological appearances. The basic pattern of the tumors was fibrosarcoma-like spindle cell sarcoma (Fig. 2) and spindle and pleomorphic sarcoma with rhabdomyoblastic differentiation (Fig. 3). In addition to these patterns, the tumor was composed of irregular vascular channels with papillary growth of atypical endothelial cells consistent with AS, which was observed in the vertebral metastasis (Fig. 4). Intermediate grade (grade 2) chondrosarcomatous component was also noted in the vertebral and para-aortic lymph node metastases (Fig. 4a,b). In the metastatic nodule of the sigmoid colon, neoplastic osteoid formation, that is, osteosarcomatous component, was seen (Fig. 5). In the recurrent and vertebral metastatic tumor, a few small foci of spindle cell sarcoma with interlacing fascicle pattern, suggesting leiomyosarcomatous component, were noted (Fig. 6). These histological varieties of the tumors are summarized in Table 1.

Figure 3  Rhabdomyosarcomatous component of the tumor. (a) Rounded and elongated rhabdomyoblasts with abundant eosinophilic cytoplasm. (b) Elongated rhabdomyoblast with distinct cross striation (PTAH stain). The tumor cells are positive for (c) desmin, (d) HHF-35, and (e) myoglobin.
Immunohistochemical findings

An immunohistochemical study was performed using formalin-fixed, paraffin-embedded materials by the avidin-biotin-peroxidase complex method. The monoclonal or polyclonal primary antibodies used in the present study were as follows: vimentin (DAKO, Carpinteria, CA, USA), desmin (DAKO), cytokeratin (KL-1; Immunotech, Marseille, France), muscle specific actin (HHF-35; Enzo Biochem, New York, NY, USA), \( \alpha \)-smooth muscle actin (1A4; DAKO), myoglobin (DAKO).
Multilineage dedifferentiation of chondrosarcoma

Factor VIII related antigen (DAKO), S-100 protein (DAKO). The immunohistochemical results are summarized in Table 2. In the primary and first recurrent tumors showing the features of low-grade chondrosarcoma, the chondrocytic tumor cells were positive for vimentin and S-100 protein. In the second recurrent tumor and metastatic tumors, rhabdomyosarcomatous component was positive for desmin, vimentin, myoglobin, HHF-35, and occasionally 1A4 (Fig. 3c-e).

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Chondrosarcomatous component was positive for vimentin and S-100 protein (Fig. 4b), whereas angiosarcomatous component was positive for vimentin and factor VIII related antigen (Fig. 4d). Positive reaction for vimentin, HHF-35, 1A4, and KL-1 was found in leiomyosarcomatous component (Fig. 6b,c), but this component was negative for desmin and myoglobin. Fibrosarcomatous and osteosarcomatous components were positive only for vimentin.

DISCUSSION

Non-cartilaginous and high-grade sarcomatous component, that is, ‘dedifferentiated’ component of DCS has been reported to be FS, OS, or MFH in most cases. On rare occasions, ‘dedifferentiated’ component showed histological features of RMS, AS, or giant cell type MFH mimicking giant cell tumor. To date, malignant mesenchymomatous ‘dedifferentiation’ of CS, like the case presented in this study, has not been described.

In surgically excised specimens, low-grade CS was observed in the primary and first recurrent tumors, while only rhabdomyosarcomatous component was found in the second recurrent tumor. Other sarcomatous components could be revealed by careful examination of the autopsy specimens.

Table 2 Summary of immunohistochemical results of dedifferentiated chondrosarcoma with malignant mesenchymomatous component

<table>
<thead>
<tr>
<th></th>
<th>CS</th>
<th>FS</th>
<th>RMS</th>
<th>AS</th>
<th>OS</th>
<th>LMS</th>
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<tr>
<td>Vimentin</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>Desmin</td>
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<td>+</td>
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<td>Keratin (KL-1)</td>
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<td>MSA (HHF-35)</td>
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<tr>
<td>SMA (1A4)</td>
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<td>-</td>
<td>+</td>
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<td>Myoglobin</td>
<td>-</td>
<td>+</td>
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<td>-</td>
<td>-</td>
<td>+</td>
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</table>

CS, chondrosarcoma; FS, fibrosarcoma; RMS, rhabdomyosarcoma; AS, angiosarcoma; OS, osteosarcoma; LMS, leiomyosarcoma; MSA, muscle specific actin; α-SMA, α-smooth muscle actin; Factor VIII RA, factor VIII related antigen.

Table 1 Summary of the histological varieties of the tumors

<table>
<thead>
<tr>
<th>Surgical specimens</th>
<th>Primary</th>
<th>First recurrent</th>
<th>Second recurrent</th>
<th>Locally recurrent</th>
<th>Autopsy specimens</th>
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<tbody>
<tr>
<td>CS</td>
<td>+</td>
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<td>RMS</td>
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<td>OS</td>
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<td>LMS</td>
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</table>

CS, chondrosarcoma; FS, fibrosarcoma; RMS, rhabdomyosarcoma; AS, angiosarcoma; OS, osteosarcoma; LMS, leiomyosarcoma; S, colon, sigmoid colon.
Malignant fibrous histiocytoma is the most common histological feature as a ‘dedifferentiated’ component of DCS, and MFH is a final common pathway in soft tissue tumor progression. p53 overexpression and mutation has been described in grade 3 CS and in non-cartilaginous sarcomatous component of DCS, but not in low-grade CS. This fact may represent one of the phenomena of tumor progression of CS.

The present case, ‘dedifferentiated’ components have been not only FS, which is another primitive form of mesenchymal tumor, but also other types of sarcoma including RMS, AS, CS, OS, and leiomyosarcoma (LMS). This phenomenon could be explained by the differentiation regulatory genes may ‘switch on’ in the process of tumor progression. In the other sarcomatous components, similar genetic events probably occur and induce divergent differentiation in ‘dedifferentiated’ sarcomatous components during the process of tumor progression. However, these events are far less frequent, and MFH and FS are the most common phenotypes of ‘dedifferentiated’ sarcomatous component.

The combination of two or more unrelated malignant mesenchymal tumors with distinct differentiation, in addition to the fibrosarcomatous element in the present case, may fulfill the criteria of malignant mesenchymoma. Malignant mesenchymoma of soft tissue is usually less aggressive than the tumor
expected by its histology. In contrast, the present case showed a very aggressive clinical course and the patient survived only 4 months after 'dedifferentiation' occurred. This does not fit into the usual behavior of malignant mesenchymoma of soft tissue. Newman and Fletcher excluded a case from their series of malignant mesenchymoma of soft tissue, because it was DCS with rhabdomyosarcomatous component arising within the lumbosacral spine and forming a large mass in the retroperitoneum. The patient died only 4 months after presentation with lung and brain metastases.

Malignant mesenchymoma of bone is a rare neoplasm and most of the cases reported show a combination of liposarcoma and OS. A similar case of ours has been described as malignant mesenchymoma of acetabulum that was composed of RMS, CS, and OS in a 69-year-old man. This is possibly another case of DCS with malignant mesenchymomatous component. Although multilineage differentiation found in both malignant mesenchymoma of bone and DCS with malignant mesenchymomatous component may be a similar phenomenon, these two seem to be different entities. It is suggested that malignant mesenchymoma is a peculiar variant of OS or OS related tumor, because malignant mesenchymoma of bone affects the metaphysis of long bones in adolescents and young adults. In contrast, DCS with malignant mesenchymomatous component affects older patients just like conventional DCS, and other clinicopathological findings described in the present study also fit the requirements for a highly aggressive variant of OS.

REFERENCES