

Malignant Fibrous Histiocytoma in Chordoma

—Immunohistochemical evidence of transformation from chordoma to malignant fibrous histiocytoma—

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Sarcomatous transformation in chordoma (dedifferentiated chordoma) is a very rare condition and has been emphasized as a distinct entity because of its more aggressive clinical course. Here we describe a case of dedifferentiated chordoma (chordoma associated with malignant fibrous histiocytoma) arising from the sacrococcygeal region of a 55-year-old woman. The results of immunohistochemical stain in the chordoma area were strong positive for cytokeratin, epithelial membrane antigen and S-100 protein. The spindle and giant cells in the transitional areas of chordoma and malignant fibrous histiocytoma were positive for cytokeratin and epithelial membrane antigen in addition to vimentin and alpha-1-antichymotrypsin. The spindle and giant cells in the central area of malignant fibrous histiocytoma were negative for cytokeratin and epithelial membrane antigen, but positive for vimentin and alpha-1-antichymotrypsin. This supports the pathogenesis of sarcomatous transformation from chordoma.

Key Words: Chordoma, transformation, dedifferentiated chordoma, cytokeratin

Chordoma is a relatively uncommon tumor, comprising 3~4% of all primary malignant bone tumors and is believed to arise from the remnants of notochordal tissue (Chambers and Schwinn, 1979). Rarely chordoma is associated with sarcomatous change, either in the primary tumor or the recurred tumor. Since Debernardi's first report in 1913 (Debernardi, 1913), 19 more cases of chordoma associated with sarcoma have been reported (Davison and Weil, 1928; Fox *et al.* 1968; Knechtges, 1970; Chambers and Schwinn, 1979; Makek and Leu, 1982; Halpern *et al.* 1984; Miettinen *et al.* 1984; Belza and Urich, 1986; Meis *et al.* 1987;

Mierrinen *et al.* 1987). But the pathogenesis of this lesion still remains unclear. We herein report a case of dedifferentiated chordoma (chordoma associated with malignant fibrous histiocytoma, MFH) with an emphasis on histology and immunohistochemical evidence of transformation.

CASE REPORT

A 55-year-old woman was admitted to our hospital because of pain on the left lower extremity, which has aggravated recently. She had a 5-year long history of pain of gradual onset on the sacrococcygeal region radiating to the left lower extremity. She had a past history of pulmonary tuberculosis, 15 years ago, and otherwise were unremarkable. Physical examination revealed tenderness on the

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sacrococcygeal region with hyperesthesia and dysfunction of anal and urethral sphincter. The pelvic computed tomography and magnetic resonance image revealed a mass of soft tissue density in the pelvic cavity which obliterated the L5 vertebral body and sacrum (Fig. 1). The mass contained some specks of calcified densities, which seem to be pieces of destroyed bone. The patient underwent excision of the mass with subtotal removal of the L5 vertebral body and sacrum. On gross examination the resected tumor revealed a $6.5 \times 5.5 \times 4$ cm sized lobulated, rubbery to soft mass with a shaggy irregular contour and some fragments of adherent muscle. The sectioned surface of the tumor was variegated; some areas being opaque, white and firm and others being myxoid, gray or brown with focal dark red hemorrhagic area.



Fig. 1. The pelvic computed tomography revealed a 6.5×5 cm sized mass with irregular margin and various internal densities in the pelvic cavity involving L5 vertebral body and sacrum.

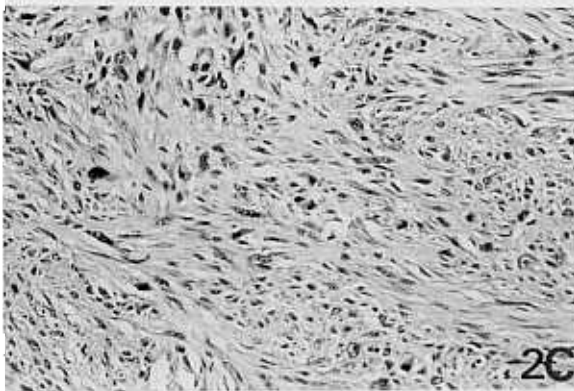
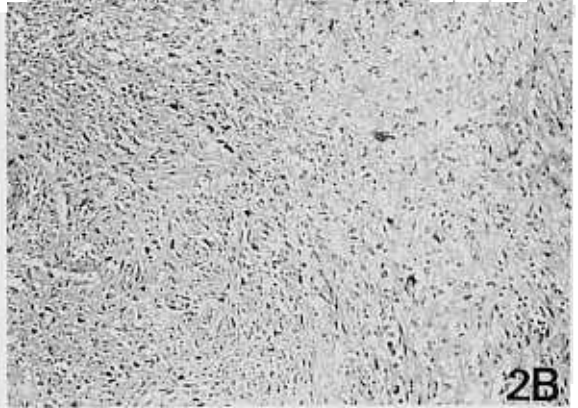
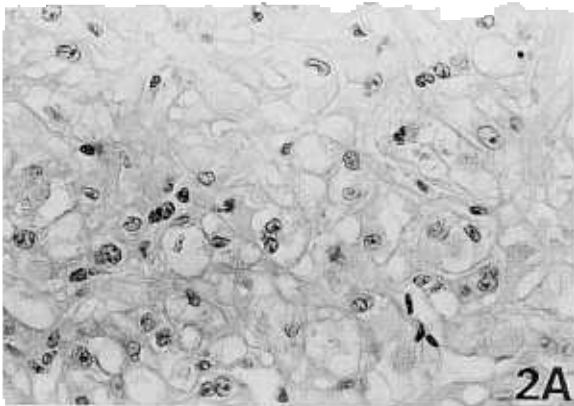


Fig. 2A. Conventional chordoma with strands of epithelial cells (physaliferous cells) surrounded by mucinous stroma (H & E, $\times 400$).

Fig. 2B. Areas of transition with spindle and giant cells between chordoma and MFH (H & E, $\times 100$).

Fig. 2C. Highly cellular pleomorphic spindle and giant cells with storiform pattern of MFH (H & E, $\times 200$).

Histologic findings

The tumor consisted of mainly two different components. One area had the characteristic appearance of conventional chordoma with clusters or cords of medium to large, plump cells with abundant lightly basophilic to clear cytoplasm containing small and large vacuoles (physaliferous cells) against a myxoid stromal background (Fig. 2A). The epithelial component of the conventional chordoma was stained with periodic acid Schiff (PAS), while the amorphous stromal components stained with alcian blue. Some areas representing conventional chordoma were infiltrated and partially surrounded by spindle cells which formed many interlacing bundles (Fig. 2B). Most of these cells were elongated with various amounts of eosinophilic cytoplasm, spindle shaped nuclei and poorly defined cell boundaries. Several irregularly shaped, triangular or rectangular giant cells which had multiple or large nuclei and abundant cytoplasm, were scattered throughout the spindle cell area. The mitotic count was over 20 per 10 high power fields. This area was classified as a malignant fibrous histiocytoma (Fig. 2C).

Immunohistochemical findings

Most of the epithelial components of classical chordoma were strong positive for cytokeratin (Fig. 3A), epithelial membrane antigen (EMA) and S-100 protein. Some of them were weakly positive for alpha-1-antichymo-trypsin (α_1 -ACT). Adjacent spindle and giant cells in the transitional zones of classical chordoma and MFH revealed strong cytokeratin (Fig. 3B) and EMA positivity. In the central area of MFH, the spindle cells and multinucleated giant cells were negative for cytokeratin and EMA, but positive for vimentin and α_1 -ACT. Spindle cells are revealed to have focal positivity for S-100 protein. Some giant cells were also stained lysozyme. The results of immunohistochemical stain were summarized in table

DISCUSSION

The coexistence of the sarcomatous lesion with conventional chordoma has been reported previously by several authors (Chambers and

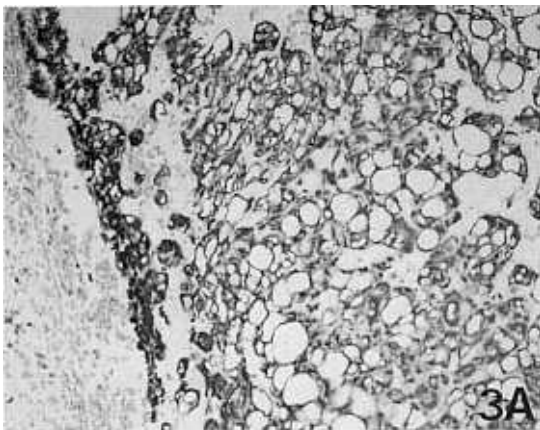


Fig. 3A. Most of the epithelial cells of conventional chordoma are revealed to have diffuse strong positivity for cytokeratin (Immunoperoxidase, $\times 200$).

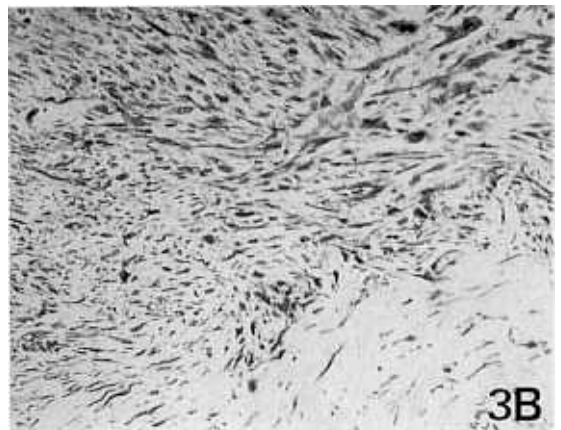


Fig. 3B. In the transitional zones of chordoma and MFH, spindle and giant cells are also stained for cytokeratin (Immunoperoxidase, $\times 200$).

Table 1. Results of immunohistochemical stain of dedifferentiated chordoma

| Antibody | Chordoma | Malignant Fibrous Histiocytoma | |
|-----------------|----------|--------------------------------|--------------|
| | | transitional area | central area |
| Cytokeratin | + | + | - |
| EMA | + | ± | - |
| Vimentin | - | + | + |
| α_1 -ACT | + | + | + |
| Lysozyme | - | + | + |
| S-100 | + | - | + |

EMA: Epithelial membrane antigen

 α_1 -ACT: Alpha-1-antichymotrypsin

Schwinn, 1979; Belza and Urich, 1986; Meis *et al.* 1987). There are 3 theories on the pathogenesis of coexistence of sarcoma with chordoma: (a) collision of two distinct, independent tumors, (b) transformation of a chordoma to a sarcoma due to a dedifferentiation process, and (c) transformation via radiation induction.

This case, as well as previously reported sarcomas in chordoma without irradiation history (Debernardi, 1913; Knechtges, 1970), indicates that radiation induction cannot explain all cases. Irradiation seems to enhance or accelerate that change. The evidence of collision tumor cannot be found. The transformation theory from chordoma to sarcoma appears well supported by histological and immunohistochemical evidence of a gradual change from chordoma to MFH. Especially, the spindle and giant cells in transitional zones of classical chordoma and MFH that revealed epithelial differentiation properties such as cytokeratin and EMA positive cells, clearly suggest sarcomatous transformation from chordoma (Belza and Urich, 1986; Meis *et al.* 1987; Mierrinen *et al.* 1987; Nanda *et al.* 1991). Some of the reported cases revealed disappearance of cytokeratin positive cells in sarcomatous lesion confirmed by rebiopsy. This finding supports the transformation theory as well (Belza and Urich, 1986). In this case, focal areas of S-100 protein positive cells in the MFH were regarded as the focal remnants of chordoma. The term "dedifferentiation" was introduced by Dahlin and Beabout in the

dedifferentiated chondrosarcoma to describe a distinct clinicopathologic entity wherein a low grade chondrosarcoma was juxtaposed to a histologically different high grade sarcoma, in a purely descriptive and morphological sense (Dahlin and Beabout, 1971). Other authors have used "dedifferentiation" referring to different things or spectrum of tumor grades (Willis, 1958; Snover *et al.* 1982). Meis *et al.* used the "dedifferentiated chordoma" according to Dahlin's original definition (Meis *et al.* 1987). We adopted the term in favor of that view.

Sarcomatous transformation was reported as being associated with an accelerated or more fulminant clinical course as previously reported dedifferentiated chondrosarcoma or liposarcoma (Meis *et al.* 1987; Miettinen *et al.* 1984; Mierrinen *et al.* 1987; Nanda *et al.* 1991). But it is difficult to predict or differentiate the clinical behavior according to the type of sarcoma, because few cases of sarcomatous transformation in chordomas have been reported. This poor prognosis and the lack of other effective treatment modalities suggest that initial aggressive surgical intervention combined with oncological therapy is necessary to treat this lesion. In addition, differential diagnosis of this lesion from the conventional chordoma is very important.

The histogenesis of "dedifferentiation" has remained controversial and unresolved. But it should be emphasized that "dedifferentiated chordoma" means a chordoma expressing

histologically different high grade sarcoma with a fulminant clinical course.

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