Dedifferentiated chordoma
A REPORT OF FOUR CASES ARISING ‘DE NOVO’


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Dedifferentiated chordoma is a rare and aggressive variant of the conventional tumour in which an area undergoes transformation to a high-grade lesion, typically fibrous histiocytoma, fibrosarcoma, and rarely, osteosarcoma or rhabdomyosarcoma. The dedifferentiated component dictates overall survival, with smaller areas of dedifferentiation carrying a more favourable prognosis. Although it is more commonly diagnosed in recurrences and following radiotherapy, there have been a few reports of spontaneous primary excision, and discuss the associated clinical and radiological features.

Patients and Methods
We performed a retrospective review of 29 patients with histologically-verified sacrococcygeal chordoma who had been referred to our orthopaedic oncology unit between 1997 and 2007. These cases were identified using the histopathology database of the department. Of the 29 patients, four had a dedifferentiated chordoma, which was diagnosed ‘de novo’ following primary excision. There were no cases of dedifferentiation arising in recurrences or after radiation treatment. We obtained data from the case notes, hospital databases, imaging studies and clinic reviews.

Results
Case 1. In 2000, a 57-year-old man presented with a history of acute-on-chronic urinary retention for four weeks and of lower back pain and rectal tenesmus for six months. Rectal examination revealed a large mass overlying the sacrum.

A radiograph of the lower sacrum showed erosion and destruction, with areas of patchy sclerosis (Fig. 1). MRI revealed a large tumour arising from the S3 segment and extending anteriorly to fill the whole width of the pelvis, with a large posterolateral extension into the left buttock. A pre-operative needle biopsy revealed moderately pleomorphic spindle cells in a collagenous matrix. Vimentin was uniformly positive, and S100 was positive in scattered tumour cells. These findings were suggestive of a primary spindle-cell tumour.

The patient underwent a partial sacrectomy combined with an abdominoperineal resec-


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Histopathological examination revealed a lobulated, necrotic tumour consistent with the diagnosis of chordoma, with multiple areas of high-grade dedifferentiation (Fig. 2). The margins of excision were incomplete. The patient was treated with single agent, doxorubicin, but within ten weeks developed extensive local recurrence in the scar and in the pelvis, in addition to mediastinal and pulmonary metastases. He died seven months after initial presentation.

**Case 2.** In 2002, a 61-year-old man presented with a six-month history of a progressively enlarging mass in his lower back. It did not cause pain, but he was aware of it when sitting for long periods or when driving. Clinical examination revealed a large soft-tissue lump over the sacrum and coccyx in the midline, firm in consistency and fixed to the underlying tissues. MRI showed a large mass, 14 cm in diameter, arising from the coccyx and displacing the rectum anteriorly, with both anterior and posterior extrasosseous components. On MRI the T2-weighted images showed two different areas within the lesion in terms of signal characteristics, a hyperintense component and a reduced signal component (Fig. 3). He underwent partial sacrectomy, and histopathological examination confirmed the diagnosis of chordoma containing a small area of high-grade spindle-cell dedifferentiation. The margins of excision were incomplete. After operation radiotherapy was instituted, with fractions of 55 Gy over six weeks. After this, he was in remission for three years. In 2005 he developed an enlarging mass in the ninth left rib. A needle biopsy confirmed that this was a metastasis but did not show areas of dedifferentiation. The rib was completely excised. Histopathological examination showed a high-grade spindle cell component, which the needle biopsy had failed to detect. As the surgical margins were clear, no further treatment was deemed necessary. In early 2007 he began to experience shooting pains in his lower back. Clinical examination revealed an ataxic gait, brisk reflexes and bilateral extensor plantar responses. There was patchy sensory loss and reduced power in both limbs. MRI showed a 5 cm soft-tissue mass arising from T9 and compressing the thoracic cord (Fig. 4). An urgent surgical decompression with complete excision of the mass was successfully performed, with instrumented stabilisation from T7 to T11. Histology showed a metastatic dedifferentiated chordoma with clear margins of excision. He remains well 63 months after the initial treatment, and no further treatment is planned.
Case 3. A 57-year-old man was referred in 2003 with severe coccygeal pain, worse at night, with difficulty in defecation. He had been diagnosed with prostatic carcinoma two years earlier and this was responding to simple hormone treatment. His prostatic specific antigen level had fallen from 2800 ng/ml to 0.3 ng/ml. Rectal examination revealed a significant mass displacing the rectum anteriorly. MRI showed a large mass extending distally from the level of the S2-3 disc to involve the majority of the distal sacrum. It was associated with a huge extraosseous component with well-defined margins. The tumour had two small satellite lesions in contact with the main mass. An abdominoperineal resection and subtotal sacrectomy were performed and histological analysis confirmed that the lesion was a chordoma. There was extensive necrosis within the tumour, and a significant number of focal high-grade dedifferentiated areas where the cells were spindle-shaped with pleomorphic hyperchromatic nuclei, in keeping with a high-grade spindle-cell sarcoma (Fig. 5). The margins of excision were clear. The posterior wound broke down partially, leaving a small sinus that healed uneventfully. This delayed the commencement of radiotherapy. The patient died of lung metastases nine months after operation.

Case 4. In 2006, an 81-year-old woman presented with a history of pain in the buttock for seven months without any bowel or urinary symptoms. Examination revealed a large, smooth, firm mass lying in the midline behind the rectum and extending to the tip of the coccyx. MRI revealed a spherical, lobulated mass, 9 cm in diameter, arising from the S3 level and displacing the rectum anteriorly. The T2-weighted images demonstrated two different components within the lesion, one with a hyperintense signal and the other with a low signal intensity (Fig. 6). Further imaging did not detect any secondary lesions. A partial sacrectomy was performed. Histological examination revealed a biphasic tumour displaying two patterns. One component had the appearance of a classic chordoma, whereas the other showed high-grade cellular spindle-cell dedifferentiation. The margins of excision were incomplete. After operation, radiotherapy was instituted in the form of 25 fractions of 50 Gy over five weeks. The patient is alive and free from tumour one year later.

Discussion

Dedifferentiation within a chordoma heralds an ominous prognosis with an aggressive clinical course culminating in metastases and rapid demise. The metastases commonly contain the dedifferentiated component.\(^4,21\) The clinical features of patients presenting with conventional chordoma are similar to those of the four cases in this series. Dedifferentiated tumours arising \textit{de novo} are rare.\(^19,22\) Sarcomatous change following radiation has been observed more frequently, but a causal relationship is difficult to prove.\(^9,11-13,17,23\) Although the prognosis is almost universally dismal, this may not always hold true. One patient reported by Meis et al\(^19\) was found to have only a small focus of dedifferentiation with the appearances of osteosarcoma. This patient survived for 76 months, eventually succumbing to metastatic disease. Of note was that the metastases did not contain the dedifferentiated elements. Case 2 in our series, who also had only a small focus of dedifferentiation showing a malignant fibrous histiocytoma, is alive 63 months after initial treatment. In contrast, cases 1 and 3 had multiple significant foci of sarcomatous changes and both died of their disease after...
seven and nine months, respectively. This suggests that the size of the dedifferentiated component is a significant predictor of survival. MRI features suggesting sarcomatous change within conventional chordoma have not been previously reported. Typically, conventional lesions are hyperintense on the T2-weighted images, with intraliteral septation a common feature. Pre-operative T2-weighted MR images in three of our cases clearly identified areas of low-signal intensity, indicating dedifferentiation, in a predominantly hyperintense, conventional component. Pre-operative identification of sarcomatous change has potential advantages, including increasing the accuracy of the definitive diagnosis, which enables earlier institution of adjuvant treatment, such as chemotherapy. The identification of areas of dedifferentiation with respect to chordro-sarcoma using MRI has been described, with obvious implications for preferential targeting of pre-operative biopsies. It has also been shown that infiltration of tumour into the surrounding musculature, namely the glutei and piriformis, is an important predictor of local recurrence, and more aggressive resection has been advocated. Thus, accurate assessment of the sacrococcygeal region by MRI is vital when planning surgery in these cases.

Cases 2 and 4 in this series received conventional photon radiotherapy following primary excision, which was marginal in both patients. It was given with the aim of achieving better local control, thereby improving survival. The local control of chordomas irradiated with doses of up to 40 Gy to 60 Gy of conventional photon beams at five years range between 20% and 40%. A few authors have advocated the use of hadrons, such as high-dose protons or charged particles carbon or helium, either alone or in combination with photons to improve the radiobiological effect, mainly in lesions at the base of the skull. The physical and ballistic properties of hadrons allow the delivery of higher doses to the target volume, while sparing organs at risk. The rates of local control at five years range between 50% and 60%. However, there are few published prospective studies to demonstrate the superiority of proton beam therapy in managing sacral chordoma.

Imatinib mesylate, which is a tyrosine kinase inhibitor targeting platelet-derived growth factor receptor-β, has been shown to have an anti-tumour effect. In this study, clinical and radiological improvement was seen in six patients with advanced chordoma treated with 800 mg daily of imatinib for one year.

Primary dedifferentiated chordoma is an extremely rare and distinct entity with a more aggressive clinical course than conventional chordoma. Careful assessment of the MRI studies, especially the T2-weighted images, should always be carried out to identify any areas of low signal intensity, which might indicate the presence of dedifferentiation and should be the preferred site of biopsy. Further studies are required to evaluate the role of radio- and chemotherapy in this disease.

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References


Fig. 6
A T2-weighted MR image in case 4. Hyperintense (arrowheads) conventional and low signal (arrow) dedifferentiated areas are present within the tumour mass.


