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Case Reports

Metastatic saccrococcygeal chordoma

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ABSTRACT

We report a 46-year-old man who presented with a 2 week history of worsening headaches and acute onset left sided hemiplegia. He had undergone a surgical resection of a sacral chordoma 13 years prior, followed by adjuvant radiotherapy and chemotherapy. MRI revealed multiple enhancing lesions in the brain, and the two largest were resected. The histopathology was consistent with chordoma. Sacrococcygeal chordomas are locally invasive notochord-related sarcomas. They rarely metastasize to the brain, and only eight patients have been reported. While currently available adjuvant radiotherapy and systemic chemotherapeutic regimens can be implemented in the management of these rare patients, they have shown limited success. The newer strategies that are reported here have also been disappointing.

1. Introduction

Sacrococcygeal chordomas are slow growing tumors with a propensity for local extension and recurrence. Successful treatment is limited by the difficulty of a gross total resection (GTR), and there is a 50% local recurrence rate after surgery [1–3]. Although adjuvant radiotherapy has been used to decrease local recurrence, chordomas are traditionally considered to be radioresistant and doses greater than 60–65 Gy are necessary [4]. Proton beam radiation permits the administration of higher radiation doses in sensitive areas and is now the gold standard modality for treatment of cranial base chordomas [4].

Systemic therapeutic options are an area of active research and recent studies have shown the receptor tyrosine kinase (RTK) inhibitor imatinib (Novartis AG, Basel, Switzerland) to stabilize or decrease the size of some locally advanced chordomas [3]. This effect is likely mediated through the inhibition of the platelet-derived growth factor receptor beta (PDGFRβ), which is commonly overexpressed in chordomas [5]. A recent prospective study showed disease stabilization in 72% and tumor shrinkage in 16% of patients [3].

Metastasis to the brain appears to be rare, and there are only eight case reports of this in the literature [1,3,6–11]. We report a 46-year-old man who presented with diffusely metastatic chordoma, originating from the sacrococcygeal region. A surgical resection and other subsequent treatments could not contain the spread of this tumor.

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2. Case report

A 46-year-old man initially presented in October 2001 with an 8 month history of slowly progressing urinary incontinence and worsening back pain. The imaging at that time demonstrated a multilobulated tumor of the sacral area (Fig. 1A, B). A tumor debulking was attempted in October 2001, but the extensive neurovascular involvement precluded a GTR. Therefore, he underwent adjuvant radiotherapy (70 Gy/35 fractions via intensity modulated radiation therapy) from 2001–2002.

Postoperatively, his back pain improved significantly but the urinary incontinence persisted. The residual tumor was initially found to be stable, however, local progression was found during the annual monitoring in 2009. Due to the significant morbidity of a potential resection, the patient chose to proceed with medical therapy with imatinib instead of repeat surgery. This treatment stabilized the local growth but a pulmonary metastasis was noted on imaging in December 2012.

The patient was enrolled in an open label Phase 1 dose finding clinical trial with a new FAK inhibitor (BI 1300.2 trial), but he experienced no clinical effect on his disease. Due to the inexorable progression of his disease, systemic medical therapy was deemed ineffective and was discontinued after five cycles in November 2013.

In February 2014, the patient acutely developed left sided hemiplegia (0/5 strength in arm and leg) after a 2 week history of worsening headaches and nausea. Brain MRI studies confirmed multiple brain lesions in the right hemisphere (Fig. 1C, D). The two largest tumors were in the right premotor and parietooccipital regions.

The patient underwent resection of the two lesions with the greatest mass effect. The histopathological assessment confirmed

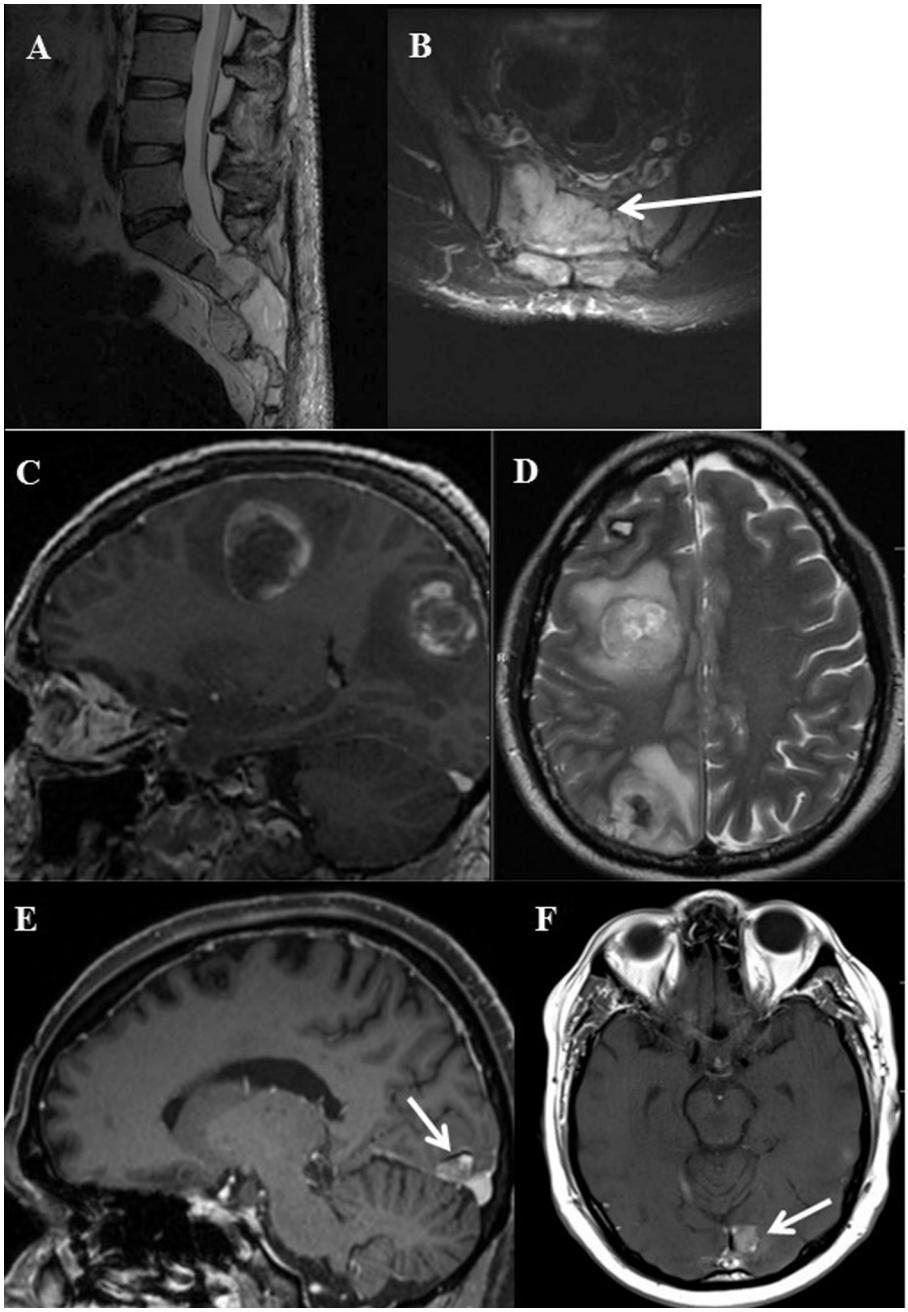

Fig. 1. (A) Sagittal T2-weighted MRI of the lumbosacral region showing a large sacrococcygeal chordoma. (B) Axial T2-weighted MRI of the sacrum. The arrow indicates the destroyed sacrum (December 2001). (C) Preoperative sagittal T1-weighted contrast-enhanced MRI of the brain showing multiple lesions in keeping with metastatic spread of chordoma. (D) Preoperative axial T2-weighted brain MRI showing the same foci. There is no enhancement with contrast (February 2014). (E) Sagittal and (F) axial T1-weighted contrast-enhanced MRI. These images indicate a new partially enhancing lesion in the left occipital lobe (arrows; July 2014).

that the tumors where metastatic chordomas. Hemotoxylin and eosin staining showed lobules of physaliferous cells separated by fibrous septa and extensive myxoid stroma (Fig. 2A). Moreover, the cells expressed S100 protein focally and the epithelial membrane antigen diffusely (Fig. 2B–D).

The repeat MRI of the brain in July 2014 demonstrated multiple new lesions bilaterally and his clinical course continued to decline (Fig. 1E, F). The patient passed away in December 2014.

3. Discussion

Chordomas are sarcomatous lesions which account for almost 5% of malignant bone tumors [12]. The most important prognostic factor in developing metastases is the feasibility of GTR. In fact, patients who need adjuvant radiotherapy, ostensibly due to incomplete resection, have a higher reported rate of metastasis. Kamel et al. suggest that a partial resection exposes residual tumor to the bloodstream, subsequently predisposing a metastasis [1].

Despite their propensity for widespread metastasis, sacrococcygeal tumors rarely spread to the brain. Table 1 shows a brief summary of reported patients with metastases. The overall prognosis of patients with chordomas remains fairly poor. The current treatment paradigm for sacrococcygeal tumors is wide surgical resection and postoperative external beam radiation therapy [13]. Unfortunately, the aggressive local extension of the disease leads to an inexorable decline in the functional capacity of most patients.