Intradural Invasion of Chordoma: Two Case Reports

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ABSTRACT

Chordomas are rare tumors of the central nervous system and primarily occur in the extradural space. We report two patients with intracranial chordomas located in the region of the clivus that invaded the prepontine cisterns. The patients, 45 and 62 years old, had histories of cranial neuropathies and headache, respectively. Petrosal approaches were performed in both with radical resection of the tumors. Anatomopathological studies confirmed the diagnosis of chordoma. The symptoms of both patients resolved, and they have had no recurrence after 18 months of follow-up. Intradural chordomas or extradural chordomas that invade the intradural space are difficult to differentiate from ecchordoses physaliphorae, a non-neoplastic entity with similar radiological features. MBI-1 studies were therefore performed to confirm the diagnosis of chordoma. The differential diagnosis for these two entities, the different modalities of treatment, and prognosis are reviewed.

KEYWORDS: Chordoma, intradural invasion, ecchordosis physaliphora, pre-sigmoid approach, skull base tumor

Chordomas are midline tumors of the central nervous system (CNS), which arise from remnants of the primitive notochord. These heterotopic notochordal cells rests are usually situated extradurally within the bones of the axial skeleton.¹⁻⁹ They are rare and mainly occur in the sacrococcygeal area (50%) and in the basisphenoidal region (30 to 40%). Most of the remainder are related to vertebral bodies. Their incidence among primary in-

tracranial brain tumors is 0.5%.¹⁰ This tumor is thought to be extradural and typically is associated with an extradural extension and bone destruction.^{11,12} If left to grow for long periods, however, it may invade the dura and extend intradurally as well as extradurally. Dural integrity may be preserved, despite the huge size of the tumor and its intradural extension as visualized on magnetic resonance imaging (MRI). Therefore, primary intra-

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dural extraosseous growth of a chordoma is very rare. The clinical outcomes and rate of recurrence of chordoma are poorly understood.

An important differential diagnosis for chordomas with an extension into the subdural space is ecchordosis physaliphora, a nonregressive and non-neoplastic lesion and a possible heterogenic remnant of the notochord without intrinsic growth potential.¹³⁻¹⁵ Despite their divergent biological behavior and histopathological features, the differential diagnosis of these two entities can be challenging. The MIB-1 index is a proliferation indicator that is important to measure and determine the proliferation potential of glial tumors.^{16,17}

We report two patients with large chordomas located in the petroclival region and associated with intradural extensions that were resected via the petrosal approach and review the differential diagnosis, treatment, and prognosis associated with these lesions.

ILLUSTRATIVE CASES

Case 1

In September 1999, a 62-year-old man was referred to the department of neurosurgery of Wayne State University for the evaluation of dizziness and headaches. His neurological examination revealed axial ataxia associated with rotary nystagmus in the lateral gaze and upward gaze of eyes. Computerized tomography revealed questionable destruction of the clivus bone with obliteration of the lower portion of the sphenoid sinus on the right. T1-weighted MRI demonstrated a hypointense lesion in the middle portion of the clivus on the right and a lesion extending into the prepontine cistern compressing the pons and the medulla. The T1-weighted gadolinium MRI showed homogenous and intense enhancement of the lesion and its extension (Fig. 1). The putative diagnosis was chordoma.

Figure 1 Preoperative T1-weighted sagittal magnetic resonance image shows the intradural extension of the tumor into the prepontine cistern (Case 1).

The patient underwent two surgical procedures. The first, on October 4, 1999, was a right-sided craniotomy and a transpetrosal approach. The mastoid process and petrosal ridge were removed, and a complete mastoidectomy was achieved. The sigmoid sinus was unroofed entirely. An occipitoparietal frontotemporal craniotomy was completed with a middle fossa approach consisting of a zygomatic osteotomy, extradural exploration of the trigeminal ganglia, and resection of the petrous apex. Next, the dura was incised along the floor of the middle fossa and the superior petrosal sinus was transected. The temporal lobe, tentorium, and transverse sinus were elevated. The tentorium was incised so that the fourth cranial nerve remained attached to the edge of the tentorium. The fifth cranial nerve was traced into Meckel's cave. The tumor, which was soft, was identified.

The tumor was slowly mobilized away from the brainstem and debulked internally using a combination of dissection and suction. As the tumor was debulked, two perforators arising from the basilar artery were carefully dissected and preserved. The remaining portion of the tumor near the brainstem was removed, preserving pial integrity. After the tumor was radically resected from the brainstem, the portion of the tumor expanding

Figure 2 Postoperative T1-weighted sagittal magnetic resonance image shows the extent of tumor resection. (Case 1).

toward the clivus was radically resected. At the end of the resection, the entire length of the basilar artery with its perforators; the anterior inferior cerebellar artery; the superior cerebellar artery; and the third, fourth, and sixth cranial nerves were identified.

After surgery the patient complained of double vision, which was caused by right abducent nerve palsy. Cerebellar signs, such as ataxic gait and speech disturbance, resolved. Postoperative MRI showed a possible residual mass in the middle portion of the clivus with a possible extension toward the mucosal surface of the sphenoidal sinus and bone invasion on the right (Fig. 2). Given these findings, the patient underwent a trans-sphenoidal trans-septal approach on November 18, 1999. Pathological analysis of the tissue revealed the absence of tumor cells and the presence of an inflammatory process and reactive tissue. No evidence of chordoma was found.

The patient underwent no postoperative chemotherapy or radiation therapy. During his follow-up, which lasted 15 months, no tumor regrowth was recognized on MRI, which was performed twice yearly.

The final histological diagnosis was chordoma (Fig. 3). Examination of the proliferation potential of the tumor, accomplished by using

Figure 3 Representative photomicrograph from first surgical specimen showing chordoma composed of cords of vacuolated cells (arrows) in a loose myxoid matrix. No atypical features are noted (hematoxylin and eosin, 20 × original magnification).

MIB-1 antibody against Ki-67 antigen, showed a low proliferation index.

Case 2

A 45-year-old man was referred to the department of neurosurgery of Hospital Alemão Oswaldo Cruz, São Paulo, Brazil, for evaluation of dizziness and temporary sixth cranial nerve palsy on the left side. His neurological examination revealed no deficits. CT showed no destruction of the clival portion of the occipital bone. T1-weighted MRI showed a hypointense lesion in the clivus on the left. A clear intradural portion of the lesion extended dorsally into the prepontine cistern, compressing the pons and medulla (Fig. 4). The putative diagnosis was chordoma.

In August 1999, the patient underwent a left-sided craniotomy for a presigmoid approach. The tumor was resected uneventfully in a procedure much like that described for Case 1.

The patient's immediate postoperative course was uneventful. After the fifth day, he developed partial complex seizures, which were controlled by antiseizure medication. Postoperative MRI showed a small lesion that suggested a contusion in the

Figure 4 Preoperative T1-weighted sagittal magnetic resonance image shows the enhanced lesion in the clival region with extension into the intradural space of the prepontine cistern. (Case 2).

posterior portion of the temporal lobe, probably caused by excessive retraction of the brain parenchyma, but no residual mass could be identified (Fig. 5).

After surgery, no chemotherapy or radiation therapy was administered. During the patient's postoperative follow-up, which lasted 21 months, no tumor regrowth was recognized on MRI, which was performed twice yearly.

Figure 5 Postoperative T1-weighted sagittal magnetic resonance image shows the extent of resection (Case 2).

As in the first patient, histological examination revealed a chordoma and the MIB-1 testing revealed a low proliferation index.

DISCUSSION

Nineteen cases of intradural chordomas or chordomas with early dural space invasion have been reported in the literature (Table 1).¹⁸⁻³³ The mean age of these patients was 43.1 years. Ten patients were male and eight were female (no gender information was given for one patient). The location of the lesions included the prepontine region in 10 patients; the suprasellar region in two patients; the spinal region in three patients; and the intrasellar region, foramen magnum, and tentorium cerebelli in one case each. The pontine-cerebellar angle was related in one case. In one study⁴ the distribution of chordomas was reported as 65% sacrococcygeal, 11% spheno-occipital, and 22% vertebral. In another study, the distribution was 54% sacrococcygeal, 25% spheno-occipital, and 20% vertebral.¹ Therefore, the intracranial region, especially the preontial region, appears to be the most common site for intradural extraosseous chordomas.

The differences between ecchordosis physaliphora and chordomas are discussed in detail elsewhere.^{15,26,28,33} In 1857 Virchow first described the microscopic appearance of ecchordosis physaliphora and also coined the pathologic term. The origin of ecchordosis from the notochord was subsequently postulated by Muller and demonstrated conclusively by Ribbert. Later studies confirmed the histological and ultrastructural similarity between fetal notochord, chordoma, and ecchordosis physaliphora.

Unlike their neoplastic counterpart (chordomas), ecchordoses are usually asymptomatic and only found incidentally at autopsy. However, four cases of symptomatic ecchordosis physaliphora have

Table 1 Clinical Summary of 19 Published Cases of Predominantly Intradural Chordomas

Authors & Year	Age (yrs) Sex	Tumor Location	Symptoms & Signs	Follow-up
Dahlin & McCarty, 1952 ¹	ND	Prepontine	Asymptomatic	ND
Bartolini, 1974 ¹⁸	57, M	Prepontine	Headache, dysarthria, cranial nerve palsies	ND
Mathews & Wilson, 1974 ²⁵	41, M	Intrasellar	Acromegaly, bitemporal hemianopsia	4 weeks
Vaquero et al., 1983 ²⁹	39, F	Suprasellar	Headache, changes in emotional state	ND
Mapstone et al., 1983 ²⁴	26, M	Prepontine	Cranial nerve palsies, hemiparesis	ND
Ramiro et al., 1986 ²⁷	33, F	Thoracic spine	Paraparesis, T6 sensory level	12 months
Yuhi et al., 1986 ³³	28, M	Prepontine	Headache, cranial nerve palsies	18 months
Katayama et al., 1991 ²²	30, F	Foramen magnum	Coma, paraparesis	11 months
Warnick et al., 1991 ³²	58, M	Tentorium cerebelli	Lethargy, dysarthria, nystagmus	ND
Hardie, 1992 ²¹	28, F	Prepontine	Headache, diplopia	ND
Tashiro et al., 1994 ²⁸	56, F	Prepontine	Tetraparesis, cranial nerve palsies	ND
Wanibuchi et al., 1994 ³¹	54, M	Suprasellar	Hemianopsia	5 months
Vaz et al., 1995 ³⁰	37, F	C5-T2	Paresthesia, abnormal tendon reflex	18 months
Nishigaya et al., 1998 ²⁶	56, M	Prepontine	Headache, cerebellar signs	5 years
Gelabert-Gonzalez et al., 1999 ²⁰	65, M	Cervical spine	Paraparesis	ND
Korinith et al., 1999 ²³	48, F	Prepontine	Headache	ND
Danilewicz et al., 2000 ¹⁹	19, F	Prepontine	Cranial nerve palsies	12 years
Present study	45, M	Prepontine	Cranial nerve palsies	21 months
	62, M	Prepontine, intrasellar	Headache, nystagmus	15 months

ND, not described.

been reported, of which two were located intradurally.^{34,35} Their size ranged from a few millimeters to 2 cm in diameter. They are known to be nonregressive and are probably heterogenic remnants of the notochord without intrinsic growth potential.

Due to their notochordal origin, ecchordosis physaliphorae are usually located in the clival portion of the occipital bone. The bulk of the lesion often occupies the subarachnoid space of the prepontine cistern. In most cases an attachment to the clivus is present and may be associated with a dural and bony defect in the clivus with extension of the physaliphorous cells into the clivus. Ecchordosis physaliphorae seldom cause symptoms during life.

In a rare case, it can cause a cerebrospinal fluid fistula associated with a clival lesion.³⁴

The differential diagnosis of ecchordosis physaliphora and chordoma based on radiological and histological features is difficult, even for experienced professionals. Some texts confuse the terms chordoma and ecchordosis physaliphora with intradural chordomas.^{15,22,28,31} Despite the different manifestations of the notochord in adults, histological and ultrastructural examinations of fetal notochord, ecchordosis physaliphora, and chordoma reveal striking similarities.³⁶ All three are composed of physaliphorous cells with abundant intracytoplasmic vacuoles and extracellular pools of

mucin. Their electron microscopic features include unique rough endoplasmic reticulum-mitochondrial complexes, intracytoplasmic invaginations, numerous intracytoplasmic vacuoles, and plasma membranes with pinocytotic vesicles and cell junctions. Fetal notochord and chordoma are also similar immunohistochemically, staining positively for cytokeratin, vimentin, and S100.

The monoclonal antibody Ki-67 detects a proliferation-associated nuclear antigen not present in cells in the resting (G0) phase of the cell cycle. Recently, the monoclonal antibody MIB-1 has become the main factor measured to determine the proliferation potential of several kinds of tumors in the CNS, mainly glial tumors. MIB-1 is equivalent to Ki-67, which is used in frozen sections and reacts with a nuclear protein that is expressed through the cell cycle. It has been used in cases of breast cancer and meningioma to estimate prognosis. The MIB-1 proliferating cell index may be useful in the histological differential diagnosis between ecchordoses physaliphorae and intradural chordoma. First, because of its non-neoplastic features, the MIB-1 index is usually zero. In chordomas, however, the results of this test are usually low but not zero. Both of our patients had a low MIB-1 index, indicating a neoplastic lesion with a low growth rate.

Chondrosarcomas are another important differential diagnosis for chordomas with early dural invasion. Chondrosarcomas are invasive tumors with a predilection for the skull base, especially the sphenoid bone and clival basiocciput. Immunohistochemistry (e.g., EMA, vimentin) must be performed when chondrosarcoma is a possible diagnosis.

Most patients with skull base chordomas have been treated with a combination of surgery and radiotherapy although the efficacy of radiotherapy remains controversial.^{37,38} Yasargil⁹ reported a series of 39 cases of chordomas treated postoperatively with fractionated radiotherapy with no improvement in survival. Stereotactic radiosurgery is valuable and effective as a primary or adjuvant

treatment for selected patients with chordomas and has clear advantages over fractionated irradiation.³⁹ Long-term follow-up of these patients is necessary to confirm the effectiveness of this therapeutic modality.

Our patients are still being followed with periodic neurological examinations and MRI studies but have shown no signs of recurrence. If a recurrence is found, the patients will probably undergo a new surgical approach followed by radiosurgery if a complete resection cannot be achieved.

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