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Case Report

Intracranial chordoma presenting as acute hemorrhage in a child: Case report and literature review

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Abstract

Background: Chordomas are rare, slow-growing malignant neoplasms derived from remnants of the embryological notochord. Pediatric cases comprise only 5% of all chordomas, but more than half of the reported pediatric chordomas are intracranial. For patients of all ages, intracranial chordomas typically present with symptoms such as headaches and progressive neurological deficits occurring over several weeks to many years as they compress or invade local structures. There are only reports of these tumors presenting acutely with intracranial hemorrhage in adult patients.

Case Description: A 10-year-old boy presented with acute onset of headache, emesis, and diplopia. Head computed tomography and magnetic resonance imaging of brain were suspicious for a hemorrhagic mass located in the left petroclival region, compressing the ventral pons. The mass was surgically resected and demonstrated acute intratumoral hemorrhage. Pathologic examination was consistent with chordoma.

Conclusion: There are few previous reports of petroclival chordomas causing acute intracranial hemorrhage. To the authors' knowledge, this is the first case of a petroclival chordoma presenting as acute intracranial hemorrhage in a pediatric patient. Although uncommon, it is important to consider chordoma when evaluating a patient of any age presenting with a hemorrhagic lesion of the clivus.

Key Words: Chordoma, children, intracranial hemorrhage

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INTRODUCTION

Chordomas are rare, slow-growing malignant neoplasms derived from remnants of the embryological notochord.[4] These tumors are often locally invasive[9,21] and can occur anywhere along the craniovertebral axis.[32] They most commonly present during the fourth decade of life[4] and are most often found in the sacrococcygeal region, followed by intracranial and elsewhere along the vertebral column.[18,23]

Pediatric cases comprise only 5% of all chordomas, but more than half of the reported pediatric chordomas are intracranial.[17,18] For patients of all ages, intracranial chordomas typically present with symptoms such as headaches and progressive neurological deficits occurring over several weeks to many years[5] as they compress or invade local structures.[9,21,24] There are rare reports of these tumors presenting acutely with intracranial hemorrhage in adult patients.[8]

We present the case of a 10-year-old boy with a previously undiagnosed petroclival chordoma who experienced sudden-onset cranial nerve deficits from an intratumoral hemorrhage. To our knowledge this is the first case reported in the literature of a chordoma presenting with acute hemorrhage in a pediatric patient.

CASE REPORT

A 10-year-old boy presented to his primary care provider one day after the onset of fever, headache, emesis, diplopia, and left ptosis. Ophthalmologic evaluation confirmed a pupil-sparing partial third nerve palsy and a left sixth nerve palsy [Figure 1]. Head computed tomography (CT) demonstrated a hemorrhagic intracranial mass. A head CT angiogram demonstrated a lytic defect of the clivus and widening of the left petrous apex without calcification of the expansile mass. The mass displaced the basilar and left carotid arteries [Figure 2]. A magnetic resonance imaging (MRI) of the brain demonstrated a lobular mass arising from the central skull base, asymmetric to the left side. The mass measured 45 × 25 × 28 mm and demonstrated heterogeneous T2-weighted signal with layering suggestive of recent hemorrhage [Figures 3 and 4]. The presence of blooming on a gradient echo sequence was also suggestive of hemorrhage [Figure 3b]. The differential diagnosis of the mass included a chordoma with atypical internal hemorrhage, chondrosarcoma, or metastatic lesion.

Surgical exploration and subtotal resection were performed via an extended middle fossa approach. The tumor consisted of gelatinous material and hemorrhage of different ages. The bone surrounding the resection cavity had a "moth-eaten" appearance with tumor invasion.

On pathologic examination, the tumor was moderately cellular and displayed a vague lobular appearance. The tumor cells were arranged in small groups or cords and had relatively uniform nuclei and moderately abundant eosinophilic cytoplasm. This showed a variable degree of vacuolization (*physaliphorous cells*) [Figure 5a and b].

The cellular component of the lesion was associated with a rich myxoid-like matrix, multiple areas of hemorrhage, and occasional fibrous septae. Focally, there were areas of calcification. Mitoses and necrosis were not observed. Immunohistochemically, the tumor cells were strongly positive for cytokeratin [Figure 5c] and S-100 protein. Epithelial membrane antigen was also positive in a membranous pattern [Figure 5d]. These features are consistent with a pathological diagnosis of chordoma.

At 2-month follow-up, the patient had resolution of the partial left third nerve palsy and improvement of his left sixth nerve palsy [Figure 6]. A coinciding MRI confirmed subtotal resection and demonstrated residual mass effect on the ventral pons. The patient was taken back to the operating room for endoscopic endonasal transclival resection of the remaining mass for gross total resection verified by intraoperative MRI. The patient did develop a lumbar cerebrospinal fluid (CSF) leak secondary to a lumbar drain placed preoperatively, but recovered well from this. The patient has been followed by radiation oncology since his initial presentation and will now proceed with proton beam therapy.

DISCUSSION

Including this case, a literature search revealed only 15 cases of intracranial chordomas presenting with hemorrhage.[1,3,5,8-10,14,15,20,22,27,28,30,31] No previously reported patients were children. Three patients who were described as cases of hemorrhagic intracranial chordoma

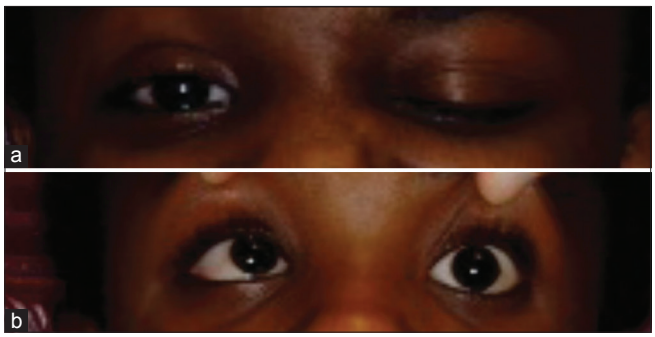

Figure 1: Preoperative examination of the patient. (a) Significant ptosis of left eye at rest. (b) Patient in leftward gaze demonstrating complete abduction deficit of left eye

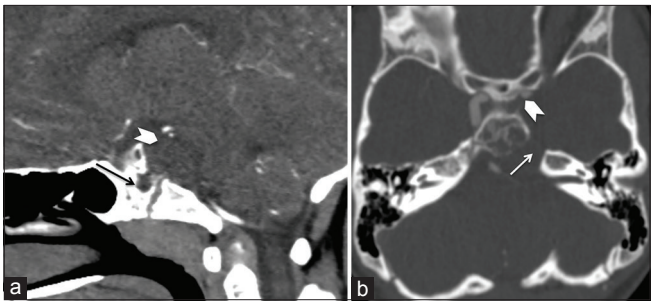

Figure 2: Initial presentation CT angiography. (a) Sagittal image demonstrating a lytic defect in the clivus (black arrow) and associated soft tissue mass (arrowhead) extending into the prepontine cistern. (b) Axial image demonstrating involvement of the left petroclival synchondrosis (arrow) and compression and anterior displacement of the left cavernous carotid artery (arrowhead). No internal calcified or ossified matrix is demonstrated within the mass

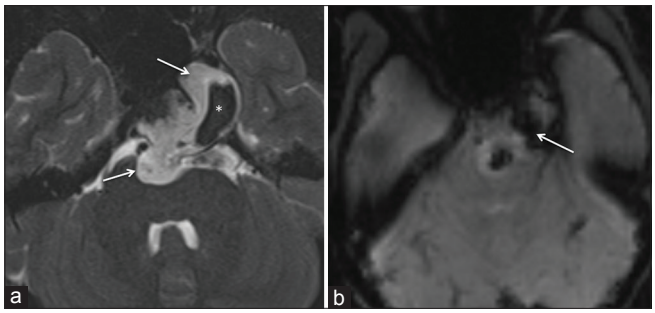

Figure 3: Initial presentation MRI. (a) Axial T2-weighted image demonstrating a lobular mass (arrows) arising from the clivus asymmetric to the left side with primarily T2-weighted hyperintense signal except for a region of T2-weighted signal hypointensity (asterisk). The mass extends into the prepontine cistern and deforms the brainstem, extends into the left cavernous sinus and left Meckel's cave with mass effect on the medial left temporal lobe. (b) Axial T2 gradient echo image demonstrating an area of susceptibility corresponding to the previously noted area of T2-weighted hypointensity (arrow) consistent with internal blood products

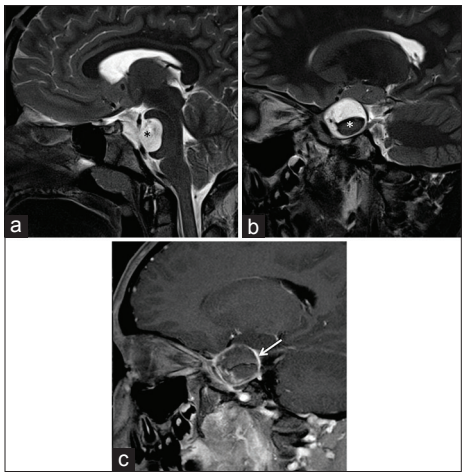

Figure 4: Initial presentation MRI. (a) Sagittal T2-weighted image demonstrating the T2 hyperintense mass (asterisk) arising from the clivus and compressing the pons. (b) Sagittal T2-weighted image demonstrating internal layering T2 hypointensity consistent with hemorrhage (asterisk). (c) Sagittal T1-weighted postcontrast image demonstrating peripheral enhancement of the mass (arrow)

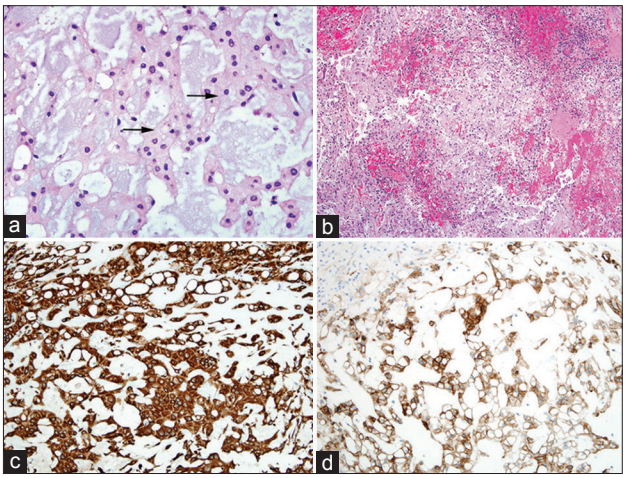

Figure 5: Surgical pathology. (a) Groups and cords of epitheliod cells embedded in a myxoid stroma with characteristic physaliphorous cells (arrows). H&E ×400. (b) Chordoma with large areas of hemorrhage. H&E ×100. (c) Tumor cells showing diffuse cytoplasmic positivity for cytokeratin with antibodies against AE1/AE3. H&E counterstain ×200. (d) Positive membranous staining with antibodies against epithelial membrane antigen. H&E counterstain ×200

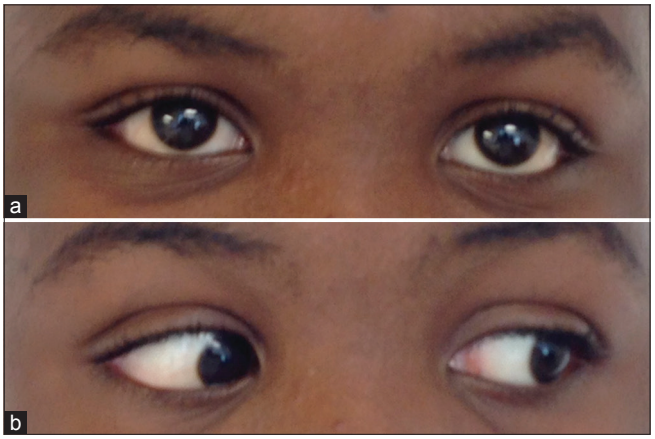

Figure 6: Examination at 2-month postoperative outpatient follow-up demonstrating resolution of left ptosis (a) and left sixth nerve palsy (b)

in the literature were excluded from our analysis; one was more accurately diagnosed as ecchordosis physaliphora,[28] another experienced a known recurrence that worsened because of a subacute hemorrhage in the setting of imatinib therapy,[20] and a third presented with hemorrhage after trauma.[31] This left 12 cases of intracranial chordoma initially presenting with acute spontaneous hemorrhage (6 males and 6 females, including our patient). Excluding our patient, the average age of all patients presenting with spontaneous hemorrhage was 43.9 years. The youngest patient previously reported in the literature was a 29-year-old male. A summary of the presenting symptoms and outcome for each patient with a true spontaneous hemorrhage is shown in Tables 1 and 2. These data show that our patient presented with three of the four most commonly reported symptoms of hemorrhagic intracranial chordoma.

A review by Borba *et al.*[4] reported that the most common presenting symptoms of intracranial chordomas in patients aged between 5 and 20 years were abducens nerve palsy (55%) and diplopia or nystagmus (55%), followed by headache (42%), palatal weakness (20%), accessory or hypoglossal nerve palsy (20%), ataxia (20%), and nasopharyngeal mass (20%). Pamir *et al.*[25] reviewed 26 patients with intracranial chordoma aged between 5 and 82 years and found that the most common presenting symptoms were cranial nerve palsies (69%) and headache (69%). The most common cranial nerve deficit in their review was the sixth nerve (14 of 18 cases).

Table 1: Summary of hemorrhagic chordoma cases reported in the literature

Author, year	Age, sex	Symptoms	Tumor Location	Diagnostic measures	Operation (s)	Outcome
Aki *et al.*, 1981[1]	48, M	Chronic diplopia and hemiparesis; acute headache and loss of consciousness	Ventral pons	Autopsy	None	Death
Bartolini, 1974[3]	57, M	Headache, vertigo, CN palsies	ND	Autopsy	None	Death
Franquemont *et al.*, 1989[5]	49, F	Headache, dysarthria, hemiparesis	Clivus, right petrous temporal bone	Autopsy	None	Death
Kim *et al.*, 2012[8]	55, F	Headache, emesis, pan-hypopituitarism	Dorsum sellae	Imaging, surgical pathology	Trans-sphenoidal, GTR	Alive with neuro deficits
Kitai *et al.*, 2005[9]	32, M	Headache, epistaxis	Clivus, sphenoid sinus	Imaging, surgical pathology	Endonasal trans-sphenoidal, GTR	Alive without neuro deficits
Koga *et al.*, 1988[10]	38, F	Headache, emesis, dysarthria, nystagmus	Clivus, sphenoid sinus	Autopsy	None	Death
Lee *et al.*, 1998[14]	70, F	Confusion, emesis	Dorsum sellae, sphenoid sinus, third ventricle	Imaging, surgical pathology	Endonasal trans-sphenoidal, frontal craniotomy, GTR	ND
Levi *et al.*, 1991[15]	29, M	Hemiparesis, hemi-hypesthesia	Clivus, midbrain/ pons invasion	Imaging, surgical pathology	Suboccipital, STR	Alive with stable neuro deficits
Nakau *et al.*, 2003[22]	66, M	Headache, emesis, stupor	Clivus, petrous temporal bone	Imaging, surgical pathology	Supra- and infra-tentorial exploration, GTR	Alive without neuro deficits
Simonsen, 1963[27]	38, F	Halitosis, bad taste in mouth	Clivus	Autopsy	None	Death
Uda *et al.*, 2006[30]	35, F	Headache, hemi-hyperalgesia	Clivus, prepontine cistern	Imaging, surgical pathology	Trans-condylar, STR; evacuation of hemorrhage	Alive with neuro deficits
(Current case)	10, M	Headache, emesis, CN palsies	Clivus, petrous apex, cavernous sinus	Imaging, surgical pathology	Extended middle fossa STR, endoscopic endonasal for GTR	Alive without neuro deficits

Abbreviations: CN: Cranial nerve; GTR: Gross total resection; STR: Subtotal resection; ND: Not defined

Table 2: Presenting symptoms of all reported cases of hemorrhagic chordoma

Symptom	Number of patients (%)
Headache	9 (75)
Decreased level of consciousness	6 (50)
Nausea, emesis	6 (50)
Cranial nerve palsy	5 (41.7)
Other motor defect	4 (33.3)
Somatosensory defect	4 (33.3)
Epistaxis	1 (8.3)
Pan-hypopituitarism	1 (8.3)
Chronic symptoms	1 (8.3)

Similarly, our patient presented with headache, diplopia, and a unilateral sixth nerve palsy on examination. However, these symptoms began suddenly 1 week before presentation to our institution, in contrast with the typical course of intracranial chordoma symptoms, which can span from months to years.[5]

The differential diagnosis for lesions presenting in this location include chordoma, chondrosarcoma or other soft tissue sarcoma, aneurysmal bone cyst, schwannoma, and metastatic disease.[29] Schwannomas typically show significant enhancement with gadolinium administration, whereas chordomas have a more variable uptake. Aneurysmal bone cysts typically demonstrate a thin rim of calcification, bony trabeculae within the cyst, and fluid-filled levels on MRI.[19] Most skull metastases are circumscribed, intraosseous tumors located in the calvarium with the dura usually intact. Chordoma and chondrosarcoma both appear hypo- to isointense on T1-weighted imaging and hyperintense on T2-weighted imaging, and both frequently show heterogeneous enhancement with gadolinium administration. Several authors have noted that chondrosarcomas tend to have a more lateral location with medial extension, whereas chordomas originate in the midline and extend laterally.[2,7] There have been no more than five reports of intracranial chondrosarcomas presenting with acute hemorrhage, and these tumors represent approximately 0.15% of all intracranial tumors.[6,16] By comparison, chordomas are estimated to comprise 0.2–1% of all intracranial tumors with 15 total cases of reported hemorrhage.[9,12]

Due to the similar incidence and imaging findings of chordoma and chondrosarcoma, pathologic examination is necessary to definitively differentiate the two.[2] Histologically, the presence of epithelial markers such as pancytokeratin and epithelial membrane antigen are consistent with chordoma, whereas staining for these markers is negative in chondrosarcoma.[26]

The incidence of intracranial intratumoral hemorrhage for all tumor types has been reported to be as high as 14.6%.[11] A review of 188 cases of intracranial intratumoral hemorrhage in patients of all ages by Yuguang *et al*.[33] found that metastases accounted for 38.3% of hemorrhages, gliomas accounted for 35.1%, meningiomas 14.2%, pituitary adenomas 9%, schwannomas 1.6%, lymphomas 1.1%, chordomas 0.5%, and melanomas 0.5%. Medulloblastoma was the most common hemorrhagic tumor in the pediatric population. In the 58 cases occurring at their own institution, the most common presenting symptoms were headache, dizziness, and nausea or emesis. A case series of 113 pediatric patients with newly diagnosed intracranial tumors found intracranial hemorrhage to be the initial presentation for 10% of these patients.[13] There was no mention of hemorrhagic chordoma in a pediatric patient.

The etiology of spontaneous hemorrhage in intracranial chordoma has not been thoroughly elucidated.[8] Previous studies have suggested that the thin-walled or poorly formed vessels present in many tumors may become distorted by growth and rupture easily, resulting in hemorrhage.[33] Endothelial proliferation within tumoral vessels may also obliterate the vessel lumen, resulting in necrosis and hemorrhage within the tumor due to lack of vessel support by the necrotic tumor structure.[22] Other authors have noted that all chordomas associated with intracranial hemorrhage have had an intraaxial component,[9] and in these patients, hemorrhage may be due to erosion of the dura and meningeal vessels.[8] In our patient, imaging and exploration demonstrated only intratumoral hemorrhage. This implies that the tumor may not have significantly invaded the dural vasculature and instead hemorrhaged because of intratumoral necrosis secondary to vascular insufficiency. This mechanism is similar to that of pituitary apoplexy and has been postulated in previous reports.[14]

CONCLUSION

This is the first case report of a chordoma in a pediatric patient presenting with spontaneous intracranial hemorrhage resulting in acute neurological deficits. More common presentations include cranial nerve palsies, headaches, and ataxia developing over months to years. Although uncommon, it is important to consider chordoma when evaluating a patient of any age presenting with a hemorrhagic lesion of the clivus.

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