Chronic cerebrospinal fluid rhinorrhea as an initial presentation of chordoma: illustrative case

Kiana Y. Prather, BS,1 Helen H. Shi, MD,1 Kibwei A. McKinney, MD,2 and Ian F. Dunn, MD1

1Department of Neurosurgery, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma; and 2Department of Otolaryngology–Head and Neck Surgery, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma

BACKGROUND Skull base chordomas are typically extradural and present with cranial nerve deficits, headache, and visual disturbances. Clival chordoma involving the dura and presenting as a spontaneous cerebrospinal fluid (CSF) leak is extremely rare and can be mistaken for other skull base lesions. Here the authors present a case of chordoma with an unusual presentation.

OBSERVATIONS A 43-year-old female who presented with clear nasal drainage was diagnosed with CSF rhinorrhea secondary to a clival defect previously thought to be ecchordosis physaliphora. The patient subsequently developed bacterial meningitis and underwent endoscopic, endonasal, transcervical gross-total resection of the lesion with repair of the dural defect. Pathology revealed brachyury-positive chordoma. She received adjuvant proton beam radiotherapy and has remained stable for 2 years.

LESSONS Spontaneous CSF rhinorrhea can occur as a rare primary presentation of clival chordoma, requiring careful radiological interpretation and a high index of suspicion for diagnosis. Chordoma cannot be reliably differentiated from benign notochordal lesions based on imaging alone; thus, intraoperative exploration and immunohistochemistry play key roles. Clival lesions presenting with CSF rhinorrhea should undergo prompt resection to facilitate diagnosis and prevent complications. Future studies on connections between chordoma and benign notochordal lesions may help to establish management guidelines.

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KEYWORDS cerebrospinal fluid; chordoma; CSF rhinorrhea; ecchordosis physaliphora

Chordoma is a primary bone malignancy arising from remnants of the embryonic notochord. It is a rare tumor that accounts for up to 3% of all bone cancer and has a predilection for skull base (35%) and sacral (50%) locations.1 The majority of primary chordomas are located extradurally, although they can extend intradurally, which is more often seen in recurrent than in primary tumors.2 The most common presenting signs and symptoms of skull base chordoma are cranial nerve palsy (51%), headache (17%), and visual disturbances (17%).3 Cranial cerebrospinal fluid (CSF) leakage occurs when CSF escapes the subarachnoid spaces of the anterior or middle skull base into the surrounding sinonasal (rhinorrhea) or middle ear cavities (otorrhea) through a dural defect. Most CSF leaks are secondary to trauma (80%), followed by iatrogenic causes (18%) and various other etiologies.4 A CSF leak as a result of primary chordoma is exceedingly rare and has only been reported in the literature in a few case studies.5–9 In this case report, we describe the unusual presentation of CSF rhinorrhea as the initial sign of a primary clival chordoma and discuss the pearls and pitfalls of the diagnosis and management of such cases.

Illustrative Case

History and Presentation
A 43-year-old female presented with an 8-month history of clear, watery nasal drainage that was worse in the morning, with acute exacerbation over a few days and new-onset dysgeusia. Her past medical history was significant for a right facial nerve injury with hemifacial spasm, for which she received routine Botox injections (Allergan). A computed tomography (CT) scan of the brain demonstrated fluid in the

ABBREVIATIONS CSF = cerebrospinal fluid; CT = computed tomography; EP = ecchordosis physaliphora; MRI = magnetic resonance imaging.

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sphenoid sinus, thinning of the sphenoid sinus walls, and a focal osseous defect of the posterior clivus (Fig. 1), with an associated lesion previously suspected to be echordosis physaliphora (EP). Magnetic resonance imaging (MRI) of the brain further demonstrated a multiloculated, T1-hypointense, T2-hyperintense, nonenhancing lesion of the posterior aspect of the right sphenoid sinus, measuring approximately 1 cm in diameter (Fig. 2). This was slightly larger than its radiographic appearance 1 year prior when she was evaluated elsewhere. She was diagnosed with CSF rhinorrhea secondary to the sphenoid defect and was scheduled for outpatient surgical repair.

The patient returned to the emergency department 3 days later with a fever, headache, and photophobia concerning for meningitis in the setting of CSF leak. A lumbar puncture was performed, with findings that were consistent with bacterial meningitis (elevated protein, white blood cells, and neutrophils with low glucose), and the patient was treated with empirical antibiotics.

Operative Management

The patient subsequently underwent endoscopic, endonasal, transclival resection of the clival mass and repair of the cranial base defect in a 2-surgeon, 3-handed approach with neurosurgery and otolaryngology. Intraoperatively, we performed a posterior septectomy and a wide spheno-ethmoidectomy to provide an expanded view of the sphenoid cavity followed by exposure of the clivus, revealing the presence of a small arachnoid granulation extruding through the bone of the upper clivus, with an associated low-flow CSF leak. Further exploration of the leak site demonstrated abnormal calcifications and sequestered bone fragments, concerning for chordoma. An aggressive resection of the abnormal bone was subsequently performed with circumferential drilling around the defect to remove the sellar floor back the level of the dorsum sellae. Gross-total resection of the grossly abnormal bone was performed, with a large dural opening into the prepontine cistern and a high-flow leak. Intradural and extradural abdominal fat grafts were placed, followed by extradural Durepair (Medtronic), a right-sided nasoseptal flap, and fibrin glue. The tumor specimen was sent for permanent pathological analysis.

Pathology

The classically described histological appearance of a clival chordoma was noted, including the presence of vacuolated physaliphorous ("bubble-like") cytoplasm. There was no evidence of high-grade features. The tumor cells stained positive for cytokeratin 8/18, pancytokeratin, and brachyury, with a Ki-67 labeling index of 4.3%, confirming a chordoma diagnosis.
to their coexistence on a spectrum.16 In the present case, the clival such as EP has been an ongoing discussion, with evidence pointing logically stable and free of symptoms for 2 years postoperatively. Surveillance imaging at 6-month intervals and has remained radio-

UMBER BEAM RADIATION without complications. The patient was followed the clival chordoma (Fig. 3). She also completed adjuvant external pro-

a month postoperatively, demonstrating complete resection of the clival lesion without pathologi-

FIG. 3. One-month postoperative sagittal T1-weighted MRI with contrast showing complete resection of the clival lesion without pathological enhancement.

Outcome
The patient’s CSF rhinorrhea resolved following surgery, and she was safely discharged on postoperative day 5. MRI of the brain was obtained 1 month postoperatively, demonstrating complete resection of the clival chordoma (Fig. 3). Also completed adjuvant external pro-

ton beam radiation without complications. The patient was followed with surveillance imaging at 6-month intervals and has remained radiologically stable and free of symptoms for 2 years postoperatively.

Discussion
Observations
Ecchordosis Physaliphora Versus Chordoma
EP is a benign, extraosseous hamartomatous lesion originating from ectopic notochord remnants. Similar to chordoma, EP typically occurs in the clival and sacral regions and shares similar histopathological features. Cranial EP is most commonly located intradurally in the prepontine cistern and is usually asymptomatic, although rare cases of symptomatic extradural EP have been reported.15–12 As such, differentiating chordoma from EP can be challenging. On MRI, both lesions are T1-hypointense and T2-hyperintense, but, unlike EP, chordoma typically demonstrates contrast enhancement.13 Unfortunately, this is not a reliable diagnostic feature, as demonstrated by this case. On immunohistochemistry, chordoma and EP typically both stain positive for S100, pan-cytokeratin, and brachyury due to their notochord origin; however, a key difference is that the Ki-67 labeling index is lower in EP (typically <1%) compared with chordoma (>2%).14 A Ki-67 labeling index greater than 5% is associated with a more aggressive clinical course and poorer prognosis.15

Distinguishing between chordoma and benign notochordal lesions such as EP has been an ongoing discussion, with evidence pointing to their coexistence on a spectrum.16 In the present case, the clival lesion had a radiological appearance that was more suggestive of an EP and no necrotic or mitotic features on histology; however, chordoma was diagnosed based on a high Ki-67 labeling index (4.3%). This combination of findings, along with the unique clinical presentation, underscores the possibility that this lesion resulted from malignant transformation of a pre-existing EP. Although the mechanism underlying chordoma transformation is unclear, ongoing studies of the molecular markers and biochemical pathways of this disease may shed light on its pathogenesis in the future. In an EP classification system proposed by Lagman et al.,14 based on symptoms and radiological findings, lesions with bony invasion or contrast enhancement are considered to indicate malignant transformation from EP to chordoma, and resection is recommended for any symptomatic lesion.

Causes of CSF Leak in Chordoma
As a primary bone malignancy, chordoma with intradural involvement can occur. The precise mechanism of CSF leak caused by a skull base chordoma involves a dural defect from direct extension of an extradural chordoma or, as some have speculated, as a result of dural rupture due to the compressive effect of the tumor.17 Rare cases of primary intradural, extraosseous chordomas have also been reported in the literature.18,19 The clival lesion in this case may represent an extradural chordoma with intradural extension, or an EP with malignant transformation and subsequent clival invasion.

Pearls and Pitfalls
CSF rhinorrhea requires careful interpretation of CT and MRI scans to localize the defect. Chordoma should be included in the differential diagnoses for patients with CSF rhinorrhea secondary to a clival lesion, which warrants careful surgical exploration and complete resection. Intraoperative observation aids in confirming the diagnosis and determining the extent of resection, although the index of suspicion for chordoma should already be high in such cases.

Correct and prompt diagnosis of chordoma is of paramount importance, as chordoma carries a substantial risk of recurrence and requires aggressive management. We propose that symptomatic clival lesions with radiological features of EP (i.e., nonenhancing, <2 cm) and evidence of bony invasion should be resected in the same manner as a chordoma. Postoperative management should be based on a combination of factors, including clinical and immunohistochemical findings, bearing in mind that the lesion may fall on a spectrum from benign to malignant. Pathological confirmation of chordoma calls for adjuvant radiotherapy.

The endoscopic, endonasal, transclival approach has become the favored surgical approach for resection of small to moderate-sized chordomas and repair of associated dural defects.20 It allows for direct access to the clival region with adequate visualization. Care must be taken to ensure maximal resection while preserving vital structures such as the internal carotid arteries, the basilar artery, and cranial nerves nearby. Given that the dural defect in this case was substantial, abdominal fat grafts, a dural allograft, and a nasoseptal flap were used to achieve a watertight closure and avoid the need for revision.

Lessons
Although rare, spontaneous CSF rhinorrhea can occur as the primary presentation of clival chordoma. CSF leak requires careful imaging interpretation to facilitate diagnosis and treatment planning,
since delayed management increases risk of meningitis and other complications. Spontaneous CSF rhinorrhea through a clival defect warrants a high index of suspicion for chordoma; if intraoperative observations reveal concerning features, a complete resection should be pursued. Chordoma cannot be reliably differentiated from benign notochordal lesions based on imaging; thus, immunohistochemistry plays a key role. Given the presence of intradural chordoma and extradural EP in the literature, chordoma and EP may exist on a continuous spectrum, although further studies are required to investigate this hypothesis and establish the management guidelines for lesions with intermediate features.

References