Diagnostic Imaging Dilemma of a Clival Lesion and Its Clinical Management Implications

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Abstract

Keywords

- ▶ ecchordosis physaliphora
- ▶ neuroenteric cyst
- ▶ chordoma
- ▶ benign
- ▶ malignant
- ▶ gadolinium
- ▶ enhancement

Background A retroclival lesion can represent a notochordal remnant–derived mass. The differential diagnoses includes benign lesions such as ecchordosis physaliphora (EP) and neuroenteric cyst or malignant ones such as chordomas. In the case of EP and chordoma, although both types arise from remnants of fetal notochord tissues, they represent two separate entities with different radiographic and biologic behaviors.

Case Description We present a case of an incidental finding of a retroclival lesion. The magnetic resonance imaging (MRI) characteristics of the lesion match the neuroimaging profile of a benign lesion and are suggestive of an EP. There was no enhancement noted with the addition of gadolinium. Nonetheless, pathology determined the lesion to be a malignant chordoma.

Conclusion The differential diagnosis of a retroclival lesion includes benign and malignant notochordal lesions. Here we present a case of a patient with an incidental finding of a retroclival lesion. Radiographic findings were suggestive of a benign lesion, possibly EP, yet the pathology revealed a chordoma. This report suggests that despite benign imaging, chordoma cannot be excluded and the implications for treatment can be significant. It is important to achieve the correct diagnosis because the prognostic and therapeutic implications are different.

Introduction

In 1856, Lushka first described the ectopic location of notochordal tissue remnants in the posterior wall of the clivus,^{1,2} and in 1857, Virchow described the microscopic structure of these findings, and coined it *ecchondrosis physaliphora spheno-occipitalis*.^{3,4} Later work by Muller and Ribbert defined it as ecchordosis physaliphora (EP).^{5,6}

EPs are benign ectopic notochordal remnants, typically located midline of the craniospinal axis. This is in contrast to chordomas, which also demonstrate notochordal differentiation; however, they are large osteolytic destructive malignant neoplasms that typically arise extradurally in the bone. Benign notochordal cell tumors (BNCTs) are benign intraosseous lesions also of notochordal cell origin.^{7,8}

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As such, there are diverse pathologies that have identical anatomical characteristics and originate from the same embryological remnant. Thus differentiating between them is important and challenging because the implications for treatment are critical and different.

We report a case of an asymptomatic retroclival lesion, with radiographic evidence of a benign lesion with a differential that favored an EP but actually proved to be a chordoma. This case poses a challenging conundrum in diagnosis because the chordoma was masked based on imaging suggestive of a benign lesion. The pathology report revealed it to be a chordoma. The purpose of this report is to remind readers of the differential diagnosis between benign and malignant notochordal lesions, but also to make readers aware that imaging alone cannot be used to determine the difference between them.

Case Report

History

We present a 51-year-old woman with a congenital hearing loss as her only past medical history. She has been having intermittent headache for the last 2 years. Physical examination was not significant except for the headaches. There were no neurologic deficits noted nor any signs suggesting raised intracranial pressure. As such, her family physician obtained a computed tomography (CT) scan of the head that showed an incidental lesion in the clivus (►Fig. 1). Consequently, the patient was referred for a neurosurgical consultation.

Imaging Findings

For further characterization of the lesion, a contrast-enhanced magnetic resonance imaging (MRI) brain scan was obtained (►Fig. 2). It appeared isointense on a T1-weighted image and hyperintense on a T2-weighted image and

involving the dorsum sellae. There was slight protrusion into the prepontine cistern posteriorly and sphenoid sinus anteriorly. It was hypointense on fluid attenuated inversion recovery (FLAIR). Addition of gadolinium did *not* provide any enhancement. As such, the main differential was thought to be that of a benign clival lesion such as EP or a neuroenteric cyst.

The patient expressed a strong desire for definitive tissue diagnosis, and, as such, a repeat image guidance protocol head CT for possible surgical planning was obtained that demonstrated a well-defined scalloped lesion in the midline of the clivus. There was evidence of bony sclerotic margins.

►Fig. 1 shows unenhanced CT scans of the head. ►Fig. 2 shows axial MR images of the brain.

Operative Procedure

Using an expanded endoscopic endonasal approach that we described previously,⁹ and with the help of the neuronavigation system, the clival lesion was identified. The patient underwent a limited and targeted transclival approach for the lesion. At the time of surgery the lesion was believed to be a benign neuroenteric cyst, and, as such, marsupialization was achieved. The patient had an uneventful course. Surprisingly, the pathology returned as a chordoma, and the patient was returned to the operating room for a more extensive resection.

During the second procedure, a wide clivectomy and lateral extension with carotid mobilization and intradural resection was undertaken. The pituitary was also mobilized superiorly to allow access to the dorsum, allowing for improved resection margins.¹⁰ The residual lesion was found to be adherent to the arachnoid membrane of the prepontine cistern and stripped away from the brainstem perforators. The previously used nasoseptal flap was found to be somewhat short for the second phase because the resection had

Fig. 1 Unenhanced computed tomography scans of the head. (A) Axial scan obtained at mid-fourth ventricle level reveals a hypodense lesion contained within the upper margin of the clivus extending to the sphenoid sinus. (B) Coronal scan at same level shows a well-defined scalloped lesion. (C) Sagittal scan demonstrates sclerosis of the bone and protrusion of the lesion into the prepontine cistern posteriorly as well as the sphenoid sinus anteriorly.

Fig. 2 Axial magnetic resonance images of the brain. (A) Spin-echo T1-weighted image demonstrating an isointense lesion within the clivus. (B) Spin-echo T2-weighted image showing the hyperintense lesion. (C) Spin-echo T1-weighted image obtained with contrast that does not show any enhancement of the lesion.

been extended significantly; therefore the reconstruction was augmented with collagen grafts.

Postoperative Course

The patient did well with no focal neurologic deficit. However, the patient developed a cerebrospinal fluid (CSF) leak 1 week postdischarge that was managed conservatively with a lumbar drain. Unfortunately, she ultimately failed this conservative management trial. The patient has obstructive sleep apnea and is moderately obese. She had a high flow intraoperative leak with multiple cisterns, thus putting her at the

highest risk factors for postoperative CSF leak. As such, she was brought to the operating room for a transnasal endoscopic transsphenoidal repair because the previous flap was contracted and pulled away from the margins. The area was augmented with abdominal fat graft. She recovered well with no subsequent CSF leak.

Pathologic Examination

The final pathology report described the lesion as a chordoma. Sections (► **Fig. 3**) showed a neoplasm consisting of markedly vacuolated cells with copious clear or vacuolated

Fig. 3 Histopathology stains. (A) Hematoxylin and eosin stain showing tumor cells with vacuolated cytoplasm (physaliferous cells) disposed randomly and in ill-defined cords on a myxoid matrix. (B) Cytokeratin 8/18 positivity. (C) Epithelial membrane antigen positivity. (D) S100 protein positivity. (E) Large fibrous bands separating the tumor into lobules.

cytoplasm and small round central or eccentric nuclei. The cells were disposed predominantly in featureless sheets interrupted by a few fibrous bands that separated the tumor into lobules. Focally, there was discernible cord formation on a myxoid matrix, but this was rare. No definite chondroid differentiation was appreciated. No definite anaplastic features or dedifferentiation were identified. Immunohistochemically, the tumor cells showed intense staining for broad-spectrum cytokeratin as well as for epithelial membrane antigen and cytokeratin 8/18, consistent with chordoma. The cells showed diffuse cytoplasmic and focal nuclear staining for S100. The Ki-67 labeling index was low.

Discussion

The notochord is the primitive skeleton of vertebrates that forms in the third week of embryonic life. It induces neural plate and vertebral column formation, all the while providing structural support to the developing axial skeleton.¹¹ It persists in adults as the nucleus pulposus of the intervertebral disc. Nonetheless, few ectopic notochordal nests can be found outside of the intervertebral disc along the craniospinal axis, mostly either at the sacrococcygeal or dorsum sella/clival region.¹

Chordomas are rare malignant bone neoplasms primarily involving both ends of the axial skeleton that present as destructive bone lesions with a large soft tissue mass. Remnants of the primitive notochord, they represent 2 to 4% of primary bone tumors with a lower prevalence than EP.¹² They are primarily extradural and cause bony infiltration and destruction.^{13,14} The most frequent location is the sacrococcygeal region, but a third of all chordomas are located in the clival region.¹⁴ There are rare variants of intradural chordomas noted.^{1,2,15} Cranial chordomas typically present with specific symptoms such as headaches in addition to multiple cranial nerve palsies. Despite radical surgical debulking and adjuvant radiotherapy, the prognosis can often be poor.

EP is a rare benign hamartomatous lesion of gelatinous tissue. It is typically located intradurally and attached classically to the dorsal wall of the clivus via a delicate filiform pedicle.^{16,17} It is more rarely located in the sacrococcygeal region.^{2,18} If intracranial, it lies mostly within the subdural and subarachnoid space in the prepontine cistern.^{13,14} It is usually attached to the dorsal clivus by a small pedicle that may be associated with a bony defect, as suggested in this case by the imaging.

EP is usually asymptomatic due to its small size and indolent slow growth pattern. It is found incidentally in 0.4 to 2% at autopsies.^{1,2,19} There have been only a few rare cases of symptomatic EP, due to tumor expansion and compression of surrounding structures and extratumoral hemorrhage.^{16,18–23}

A recently recognized condition with an identical anatomical distribution to that of classic chordoma is BNCT. It has been shown in addition that it may also undergo malignant transformation to classic chordoma.⁸ However, it has many histopathologic differences. BNCTs have characteristic well-demarcated although unencapsulated sheets of adipocyte-like vacuolated and less vacuolated eosinophilic cells within axial bones. The affected bone trabeculae are often sclerotic but without the associated bone destruction seen in classic chordoma. The most important histologic point to distinguish BNCTs from chordomas is the lack of any intracellular myxoid matrix, and they are negative for CK18 by immunohistochemistry.⁷

With the increasing evidence that classic chordoma develop from intraosseous BNCT,^{24,25} it is important to distinguish both entities.

It is often difficult to distinguish small samples of EP and chordomas through histologic, immunohistochemistry, and ultrastructural studies, apart from the infiltrative growth of chordomas.^{1,2,26} Histologically, both EP and chordomas demonstrate cells that contain multiple clear cytoplasmic vacuoles indenting the nucleus known as physaliphorous cells¹¹ with copious extracellular pools of mucin.¹³ Positive stains include vimentin, S100, epithelial membrane antigen, and low molecular weight cytokeratin.¹¹ Chordomas may display a degree of cellular pleomorphism, syncytia formation, necrosis, and atypia that correspond to their malignant course; however, this is not always the case.¹¹ Because chordomas have a high degree of cellularity, a negative MIB-1 index stain has been proposed to be useful in the differentiation of EP and chordomas (4:1), but intradural chordomas can also demonstrate such a stain pattern.²¹ This has raised the possibility that intradural chordomas may arise from EP, which may represent a precursor lesion.^{13,21}

Several articles have described the differentiation between EP and chordomas. On MRI, EP appears as a well-circumscribed extra-axial lesion in the prepontine cistern. It demonstrates low signal intensity on T1-weighted images, high signal intensity on T2-weighted images, and does *not* show any enhancement despite the addition of gadolinium.^{16,19,27–29} This is in contrast to chordomas, which

Table 1 Summary of imaging characteristics of clival lesions

Pathology	Intradural/Extradural	Usual location	Contrast enhancement	Bone involvement
Ecchordosis physaliphora	Intradural	Midline	No	No
Chordoma	Extradural	Midline	Yes	Yes
Intradural chordoma	Intradural	Midline	Yes	No
Benign notochordal cell tumor	Extradural	Midline	No	Yes
Dermoid/Epidermoid cysts	Intradural	Cerebellopontine Angle	No	No

commonly enhance markedly with gadolinium.^{27,28} Even intradural chordomas show considerable contrast enhancement.²⁷ As such, it was suggested that if the lesion enhances, it more likely represents an extradural/intradural chordoma, whereas a lack of enhancement suggests an EP.²⁸ This pattern is ideal to facilitate the preoperative differential of a benign lesion in this case. In addition, high signal intensity on T1-weighted image and lack of enhancement may indicate a neuroenteric cyst, another benign condition.^{30,31} In regard to BNCTs, there was no enhancement on contrast-enhanced T1-weighted imaging, which reflects the histopathologic features of a scanty vascular network.³² This case demonstrates that enhancement pattern *cannot* be completely relied on, and therefore the intent of this report is to consider this finding carefully in determining the management plan.

On CT, chordomas have the typical appearance of a centrally well-circumscribed expansive softtissue arising extradurally from the intraosseous part of the clivus, thus causing local bone destruction.^{15,33} This is associated with extensive lytic bone destruction and intratumoral calcification.³⁴ This is in complete contrast with BNCTs where an important feature is a lack of bone destruction with focal sclerosis.³² Of note, there are reports where the presence of an osseous stalk on thin-section CT that connects the retroclival mass with the clival notochord remnant is the morphological hallmark of EP.^{1,16,28,33,35}

Other differential diagnoses of a lesion in that area commonly include dermoid, epidermoid, arachnoid cyst, and neuroenteric cyst. Arachnoid cysts appear as sharp marginated homogeneous unilocular masses with isointense signal on CT and MRI. Epidermoid cysts are usually less sharply defined, more heterogeneous, and more commonly seen at the cerebellopontine angle cistern. Dermoids are extra-axial masses containing fat or calcification and located in the midline.²⁸ Neuroenteric cysts of the clivus are uncommon developmental lesions that occur as a result of notochordal dysgenesis during embryonic development.³⁰ They usually occurs in the posterior fossa, occurring typically midline anterior to the brainstem or in the cerebellopontine angle.³⁶ Radiographic imaging reveals typical cystic appearance on MRI but do not enhance with contrast. These findings are summarized in **Table 1**.

Our case does present contradictory features, which makes the diagnosis in this setting challenging. The clinical presentation was that of a benign lesion, suggesting an EP or neuroenteric cyst. The radiographic findings were also suggestive of a benign incidental lesion. There was no evidence of enhancement on gadolinium-enhanced MRI, as would be expected in EP or a neuroenteric cyst.

However, in our case the patient was adamant in proceeding with surgery to ensure this was truly a benign lesion. Despite the reassuring neuroimaging, the final pathology report proved it to be a chordoma. This is, to our knowledge, the first case of an asymptomatic nonenhancing chordoma with extensive bony invasion and a benign clinical presentation masking as a benign lesion. There was a report of a giant intradural EP that presented with sudden sensorineural hearing loss; however, that case differs from ours in the presentation, size of lesion, and the intradural location.²¹

In conclusion, benign lesions such as EP and malignant ones such as clival chordoma share similarities that may be misleading and as such, may create challenges in diagnosis and therapy. Recognition of imaging features seen on both MRI and CT scans is helpful in the challenging diagnosis of a retroclival lesion. However, it is also important to do so in conjunction with intraoperative and neuropathologic findings because the therapy is very divergent.

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