Tumors and tumor-like conditions of the clivus. A comprehensive review.

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Learning objectives

The main objective is to describe the normal appearance of the clivus and some disorders that typically affect this area, focused on the characteristics on MR and CT imaging that we should be familiar with in order to make an accurate diagnosis.

Background

Due to its strategic location in the skull base and its embryologic origin, some disorders typically affect the clivus. After a quick review of the normal anatomy of the skull base, we classified these lesions into:

a) neoplastic processes arising from the clivus like chordoma, plasmacytoma, lymphoma, chondrosarcoma, meningioma and metastatic tumors.

b) tumor-like conditions such as fibrous dysplasia, Paget disease, Langerhans hystiocytes and radionecrosis.

c) paraclival lesions which often involve the clivus: pituitary macroadenoma and nasopharyngeal neoplasms.

To summarize, a comparison between the main radiologic features of each disorder and the essential characteristics in the discrimination between malignant and benign clival processes are described.

Imaging findings OR Procedure details

ANATOMY (figure 1)

The clivus is the part of the skull base situated between the foramen magnum and the dorsum sellae. It results from the fusion of the synchondrosis between the basioccipital and exoccipital bones, with growth and ossify from the 3 to the 25 year of age to form the basisphenoid and the basiocciput\(^1\).
The anterior margin of the clivus abuts the sphenoidal sinus, whereas the posterior surface is the anterior limit of the prepontine and premedullary cisterns. The inferior margin represents the posterior nasopharyngeal surface. The clivus is bounded laterally by the petrooccipital fissure, which begins near the cavernous sinus and extends inferiorly to the yugular foramen.

Normal CT appearance: Clivus is best seen in the axial and sagittal view. Compact cortical bone forms the anterior and posterior boundaries, whereas the central portion consists of cancellous bone including narrow elements. Along with the fatty metamorphosis, the clivus is filled up with fatty narrow in adults.

Normal MR appearance: In a sagittal view, the clivus resembles a triangle with the base near to the dorsum sellae and the apex pointed to the anterior margin of the foramen magnum. Compact cortical bone is depicted as a black line on T1 and T2 images. Cancellous bone signal depends on the amount and nature of the narrow elements. Normally, haematopoietic tissue predominates at a young age and looks hipointense on T1 weighted images; however, because of fatty methamorphosis, T1 weighted signal becomes more hyperintense due to the age. Most abnormalities show a T1-weighted decrease and high signal on T2-weighted images.

NEOPLASTIC PROCESSES

Chordoma (figure 2 and figure 3).

Chordomas are rare, slow-growing tumors that arise from embryonic notochordal remnants along the length of the neuraxis, from the skull base to the sacrum. Although chordoma has no a specific radiologic sign, this tumor should be considered whenever a destructive clival lesion is detected in a middle-aged person. Approximately 35% affect the skull base, and most involve the clivus. Petrous apex chordomas are possible but extremely rare. The most common age at onset is 20-40 years, and men and women are affected equally.

Although by strict criteria chordomas are histologically benign, their aggressive behavior and nearly 100% recurrence rate despite radical surgery account for the poor prognosis associated with these tumors. Histologic malignancy or distant metastases are rare, and metastases appear to be more likely with sacrococcygeal chordomas.
Radiologically, chordomas appear as soft-tissue masses with bone destruction. Chordomas are often quite large, extending into the epidural space and causing compression of the vertebrobasilar system and brainstem. CT shows areas of calcification, many of which are actually fragments of destroyed bone. At MRI, chordomas are isointense to slightly hypointense on T1-weighted MR images and hyperintense on T2-weighted images; they also may contain areas of decreased signal intensity corresponding to calcification. Cystic areas can be detected as well. Strong enhancement occurs with contrast administration in both techniques. CT and MR are equally reliable in detecting this tumor, but MR imaging is considered superior for evaluating extent of disease, especially displacement or encasement of vascular structures and degree of intracranial involvement.

Chondroid chordomas is a subset of chordomas, appear to be associated with a considerably better prognosis. There is no consensus about if there is a radiological differente between chondroid and classical chordoma.

Multiple myeloma / Plasmacytoma (figure 4)

Plasmacytoma refers to a malignant plasma cell tumor growing within soft tissue or within the skeleton. The skeletal forms usually have other occult tumors and frequently disseminate to multiple myeloma over the course of 5-10 years. Myeloma is diagnosed with blood tests (protein electrophoresis, peripheral blood smear), microscopic examination of the bone marrow (bone marrow biopsy), and radiographs.

Several studies have demonstrated improved sensitivity of multidetector CT over that of the radiographic skeletal survey for evaluation of the extent of lytic bone involvement. At CT, they appear as lytic lesions without sclerotic rims. At MR imaging, plasmacytoma is identifiable at MR imaging as areas of decreased fat and increased signal intensity within the marrow on T1-weighted images. High signal is seen on STIR and T2-weighted imaging, which are the most sensitive sequences for depicting these changes. When contrast-enhanced imaging is performed, untreated lesions demonstrate diffuse contrast enhancement. Plasmacytomas may show intratumoral flow voids and restricted diffusion with low apparent diffusion coefficients because of their high cellularity. Radiation therapy is the primary treatment for these highly radiosensitive tumors, with surgery considered the second-line therapy.

Lymphoma
Primary bone lymphoma is an uncommon malignancy that accounts for less than 5% of all primary bone tumors. It is rare in patients younger than 10 years and there is a peak prevalence among patients in the 6th to 7th decades of life. Although the femur, pelvis, humerus and tibia are the most common sites affected, vertebral and clivus involvement are not unusual.

Primary lymphoma of bone manifests with insidious and intermittent bone pain that can persist for months. Other signs and symptoms include local swelling, a palpable mass, and systemic symptoms such as weight loss and fever.

CT provides a better depiction of the lytic or blastic-sclerotic Pattern, cortical breakthrough, periosteal reaction and soft tissue masses than conventional radiographs.

On MRI, T1-weighted pulse sequences are the best for demonstrating marrow changes, as T1-weighted images reveal areas of low signal intensity within the marrow. On T2-weighted images, these areas generally appear bright. Peritumoral edema and reactive marrow change can also produce high signal intensity on T2-weighted images. However, if fibrosis is present in a lesion, it may show low signal intensity. Areas of enhancement are seen within the lesion after contrast media administration. Soft tissue Involvement around the affected bone is common and well seen on MRI.

**Chondrosarcoma**

Chondrosarcoma is a slow-growing, malignant cartilaginous tumor. It represents approximately 6% of all skull base lesions and three fourths of all cranial chondrosarcomas are located in the skull base. They can arise in cartilage, endochondral bone, or primitive mesenchymal cells in the brain, meninges, membranous bone, or soft tissue. Secondary chondrosarcoma can occur in diseased bone (fibrous dysplasia, Paget's disease, osteochondroma). Presentation depends on location, but typically it is manifested by insidious onset of single or multiple cranial neuropathies.

CT is useful in evaluating the characteristic chondrosarcoma calcified matrix. The calcification varies in appearance but can be stippled and amorphous. Other CT findings include bone erosion and destruction, an enhancing soft-tissue mass, and a sharp zone of transition to normal tissue.

MRI is generally less specific and is better suited for evaluating extent of disease. The tumor is hypointense relative to brain on T1-weighted images and hyperintense on T2-weighted images. Heterogeneous internal areas of decreased signal represent
calcifications. Enhancement is seen with paramagnetic contrast agent and may be heterogeneous for the same reason \(^2\).

**Meningioma**

Meningiomas are common benign intracranial tumors that arise from arachnoid cells on the inner surface of the dura mater. Approximately 33% affect to the skull base, specially the wings of the sphenoid bone. Clivus involvement could be seen in plaque meningiomas and intraosseous meningiomas, which are less frequent variants of this tumor.

CT findings include a hyperdense enhancing mass and an intense hyperostotic bony response, which indicates invasion of the sphenoid bone by tumor, unlike the typical reactionary hyperostosis associated with other meningiomas. It is possible to confuse this hyperostosis with such bone conditions as fibrous dysplasia; some suggested differentiating features are the patient's age, the presentation, and the presence of a soft-tissue mass with meningiomas \(^11\).

On MR, meningiomas are generally isointense or slightly hypointense relative to gray matter on T1-weighted MRI. On T2-weighted images, approximately 10% are hypointense, 50% remain isointense, and 40% become hyperintense relative to brain. Bright homogeneous contrast enhancement is generally observed \(^12\).

**Metastatic tumors** (figure 5)

Although hematogenous metastases to the skull base occur infrequently, they are more common than primary neoplasms. The most likely primary sites of such metastases are prostate, lung, breast and kidney. The tumor may have a soft-tissue component.

Most of these metastatic lesions are seen as areas of lytic bone destruction on CT, except for prostatic metastases, which are usually osteoblastic. On T1-weighted MRI, the hallmark of metastatic disease is replacement of normal bone marrow with material of decreased signal intensity. On T2-weighted images, metastases are generally hyperintense relative to adjacent normal bone marrow. With contrast material, bone and soft-tissue components usually show enhancement.
In patients with no history of underlying malignant disease, imaging alone often does not allow differentiation between primary and metastatic neoplasms. The presence of other sites of metastatic disease in the calvaria is of course helpful in the diagnosis.  

TUMOR-LIKE CONDITIONS

Fibrous dysplasia (figure 6)

Fibrous dysplasia is a skeletal bone-forming anomaly of unknown cause. As the bone grows, the softer, fibrous tissue expands, weakening the bone. Fibrous dysplasia is a benign disease but can cause the affected bone to deform and become susceptible to fracture. In the skull base it can also result in cranial nerve impingement. Fibrous dysplasia can also occur anywhere in the skull base; thus, skull involvement occurs in 27 percent of monostotic and up to 50 percent of polyostotic patients.

On CT this lesion has a typical "ground glass appearance", the bone is enlarged and neuroforamina and fissures can be narrowed or displaced, but the lesion follows in general the pre-existing normal bone shape. On MR inactive fibrous dysplasia has a low signal on T2W images and is only slightly or not enhancing on T1W images. Active lesions contain high signal cystic lesions on T2W images, contain spontaneous high signal intensity regions on unenhanced T1W images and enhance very strongly after Gd-administration.

Paget disease

Paget's disease can also affect the skull base, especially the clivus and surrounding sphenoid bone structures. The pathologic abnormality in Paget disease is excessive and abnormal remodeling of bone whose final result is a thickened, disorganized trabecular pattern of bone, referred to as a "mosaic" or "jigsaw" pattern. Three pathologic phases have been described: the lytic phase (incipient-active), in which osteoclasts activity predominate; the mixed phase (active), in which osteoblasts cause repair superimposed on the resorption; and the blastic phase (late-inactive) in which osteoblasts predominate.

CT Findings include loss of normal trabeculae in the lytic areas, cortical and disorganized trabecular thickening. Areas of sclerosis may be seen in the blastic phase of the disease. The marrow space in Paget disease often reveals fat attenuation.
The MR imaging appearance of the remainder of the marrow in Paget disease is variable and depends on the disease phase and, more important, on the histologic composition of the narrow space. Three patterns of the marrow space in Paget disease are noted on MR images:

1) In the majority of cases, the yellow marrow signal intensity is maintained regardless of pulse sequence, reflecting the fact that most disease is in the mixed phase and is relatively longstanding.

2) Sometimes, in the lytic to early mixed active phase, the marrow space has heterogeneous signal intensity with both T1- and T2-weighted sequences. On T1-weighted images, the marrow has decreased signal intensity, generally similar to that of muscle; however, it typically contains foci of intermixed, normal and maintained yellow marrow, whereas on T2-weighted MR images, the marrow has heterogeneous high signal intensity, which is accentuated with water-sensitive pulse sequences. The volume of the medullary canal can be decreased secondary to encroachment by cortical thickening.

3) The final MR imaging pattern is seen in the late blastic inactive phase, in which the marrow space has low signal intensity representing sclerosis regardless of pulse sequence.¹⁴

**Langerhans Cell Histiocytosis**

Langerhans Cell Histiocytosis (LCH) is an idiopathic neoplastic disorder. Skull base, including clivus, is one of the most affected sites.

At CT, LCH appears as a well-circumscribed destructive lesion, usually with nonsclerotic margins. Bone erosion can occur. At MR imaging, LCH lesions appear as focal soft-tissue masses surrounded by extensive ill-defined bone marrow and soft-tissue edema. Marked enhancement is seen at both, CT and MR imaging.¹⁵

**Radionecrosis** (figure 7)

Central skull base necrosis is frequently seen after radiotherapy for nasopharyngeal carcinoma, particularly in the sphenoid floor, body and clivus. CT classically shows bony cortical disruption with loss of marrow trabeculations, as well as heterogeneous increased T2-weighted signal and patchy enhancement on T1-weighted post-contrast enhanced sequences in the adjacent bone are depicted on MR images.¹⁶
Osteoradionecrosis with or without osteomyelitis can be extremely difficult to differentiate from recurrent tumor, although frank bone destruction without a soft-tissue mass is most suggestive of osteoradionecrosis. Adjacent muscles may appear edematous and show intense enhancement, which can be difficult to differentiate from recurrent tumor if bone changes are not visible on CT. When a bulky soft-tissue mass is seen in conjunction with bone destruction, a biopsy should be performed to exclude tumor recurrence.\(^{17}\)

**PARACLIVAL LESIONS**

**Invasive Nasopharyngeal Carcinoma** (figure 8)

The most common primary malignant lesion that involves the skull base is squamous cell carcinoma, usually arising in the nasopharynx.

Nasopharyngeal carcinoma is a hypodense soft-tissue mass on CT, isointense relative to skeletal muscle on T1-weighted MR images and hyperintense on T2-weighted images. It enhances in both, MR and CT. When there is invasion of the clivus, it shows erosion on the CT and normal bone marrow replacement by lower signal intensity tumor on T1-weighted sequences.

In the absence of an identifiable nasopharyngeal origin, imaging findings may be nonspecific, and other diagnoses should be considered. Metastases, lymphoma, and primary bone neoplasms are other entities that can cause destruction of the skull base and a soft-tissue mass in the nasopharynx.\(^{2}\)

**Juvenile Angiofibroma**

Juvenile angiofibroma is an uncommon, highly vascular tumor that affects adolescent boys. Clinical presentation is related to common sites of tumor extension. Nasal obstruction, epistaxis, and facial deformity are the initial signs and symptoms. At the time of presentation, extensive spread beyond the site of origin is common; however, posterior invasion into the clivus and cavernous sinuses is possible and must be sought radiologically.

CT shows a homogeneously enhancing soft-tissue mass in the nasopharynx and adjacent spaces. This neoplasm has low to intermediate signal intensity on T1-weighted MR and is variably hyperintense on T2-weighted images. On both sequences, we could see internal foci of punctate or serpiginous low signal intensity representing tumor vessels. There is a strong enhancement on CT and MR techniques. Arteriography is
often used to provide detailed information about the vascular supply to this tumor and to facilitate preoperative embolization\textsuperscript{2}.

**Invasive Pituitary Adenoma**

Most pituitary neoplasms in adults are adenomas. These lesions are generally slow growing, histologically benign, and confined to the sella or suprasellar cistern. They can extend laterally into the cavernous sinus or inferior and posteriorly into the sphenoidal sinus and skull base. Such extension can make it difficult to distinguish pituitary adenoma from other skull base lesions such as sphenoidal sinus carcinoma, chordoma, or superior extension of nasopharyngeal carcinoma.

CT typically shows an expanded sella and an enhancing soft-tissue mass that, as expected, shows bone destruction. T1-weighted MR images show an isointense to slightly hypointense mass that enhances after administration of paramagnetic contrast\textsuperscript{2}.

Although it is a very uncommon case, we should remember that during embryology the pharyngopituitary canal of Rathke is involved in the formation of the anterior lobe of the pituitary gland. When remnants of this canal remain in the area of the bone, then an intraosseous pituitary adenoma can develop\textsuperscript{18}.

**Other entities**

In this presentation we describe the most frequent processes involving the clivus; however, there is a huge range of uncommon entities of different origin (neoplastic, infectious, metabolic and unknown) able to cause a clival lesion. An extremely rare affection by ecchordosis physalifora, a benign lesion that arises from ectopic notochordal remnants, is shown on figure 10.

**KEY DIFFERENTIAL DIAGNOSIS ISSUES** \textsuperscript{19}

A clival lesion may present as an incidental imaging finding or with headache or cranial neuropathies, especially from the 6\textsuperscript{th} cranial nerve.
MR imaging is the best modality to detect and characterize a lesion in the clivus. Sagittal T1 sequence is the most important: lesion is seen as loss of bright fatty narrow.

CT is complementary to MR, but often best for primary bone lesions. It clarifies bone lesions such as Paget disease, fibrous dysplasia or bone tumor.

When the lesion invade from nasopharynx, we should think about nasopharyngeal carcinoma (juvenile angiofibroma could be possible in young patients) or lymphoma.

If the lesion arises from pituitary, think about pituitary macroadenoma.

When hyperintensity is seen on T2-weighted images, consider chordoma and chondrosarcoma.

Images for this section:

Fig. 1: Normal clivus appearance. MDCT scan with MIP reformat in the axial view (A), T2-weighted with fat suppression MRI axial view (B) and T1-weighted MRI sagittal view (C). 1: Clivus, 2: Pterygoid canal, 3: Foramen lacerum, 4: Carotid canal, 5: Pterygopalatine fossa, 6: foramen ovale, 7: Hypoglossal canal, 8: Petrosphenoidal fissure, 9. Pituitary, 10: Sphenoid sinus, 11: Prepontine cistern, 12: Nasopharyngeal mucosa, 13: lateral pterygoid muscle.
Fig. 2: Chordoma MRI. Isointensity is seen on T1-weighted images (A) with moderate enhancement after contrast administration (B). Chordoma (*) shows high signal on axial (C) and sagittal (D) T2-weighted images.
Fig. 3: Chordoma CT and MR study. CT (A) shows a soft-tissue mass with bone destruction (*). Hyperintensity is seen on T2-weighted with fat suppression MR images (B). Enhancement can be depicted when T1-weighted images before (C) and after contrast administration (D) are compared. Courtesy of Dr. Jens Fiehler. Neuroradiology department. Universitätsklinikum Hamburg-Eppendorf (Germany).
Fig. 4: Non-enhanced CT scan performed in a patient with multiple myeloma. Bone focal Hypodensity shows clival affection (*). B,C,D: MR performed in another patient, heterogeneous high signal (arrow) is seen on sagittal T2-weighted MRI (B). Contrast enhancement could be seen when native T1 (C) and after contrast T1-weighted images (D) are compared.
**Fig. 5:** Destructive lytic lesion in the clivus because of a lung cancer metastasis (*). Axial CT scan (A) shows a clival tumor with soft-tissue component. On the CT sagittal reformat (B) a completely clivus destruction can be seen, as well as another metastatic lesion in the skull (arrow). T1-weighted MRI after contrast administration (C) shows a marked enhancement. A heterogeneous hyperintense destructive lesion in the clivus is clearly seen on T2-weighted MRI (D).
Fig. 6: Fibrous dysplasia in the clivus. Typically, a ground glass appearance (arrow) is seen on the CT scan (A,B), that correspond with a hypointense core (*) on T2-weighted (C) and T1-weighted MRI (D).
Fig. 7: Clivus radionecrosis. Native T1-weighted MRI (A) demonstrates normal high signal loss and moderate enhancement is seen after contrast (B). T2-weighted images (C) show a heterogeneous hyperintensity (*).

Fig. 8: Nasopharyngeal carcinoma with invasion and destruction of the clivus (*) is seen in axial CT scan (A), sagittal reformat (B) and T1-weighthed after Gd-administration MRI (C). A marked enhancement can be seen in this last sequence. Courtesy of Dr. Jens Fiehler. Neuroradiology department. Universitätsklinikum Hamburg-Eppendorf (Germany). D: In a different patient, a subtle invasion of the clivus (arrow) can be seen on sagittal CT.
**Fig. 9:** Invasive pituitary macroadenoma (*). Sagittal CT (A), T1-weighted MRI after contrast administration (B) and T2-weighted MRI show a sellar enhancing mass with bone destruction in the upper part of the clivus.

**Fig. 10:** Although it is an uncommon entity we should not consider most of the times in the differential diagnosis of lesions in the clivus, we like to show this CT (A,B) performed in a patient with an infrequent lesion called ecchordosis physalifora. It is seen as a lytic process in the clivus (arrow) and histological study is required for its diagnosis.
Conclusion

Clival disorders encompass a range of entities whose knowledge is crucial for diagnosis. MDCT and MRI allow a correct diagnosis of most of these conditions, a reliable distinction between benign and malignant processes and, when necessary, an excellent evaluation of the tumor extent.

Personal Information

References


