

Clival Chordoma, Arising in Pre-existing Benign Notochordal Cell Tumor, Case Report

Maryam Almurshed^{1, *}, Lamia Alsarraf²

¹Department of Pathology, Al Sabah Hospital, Kuwait

²Department of Radiology, Ibn-Sina Hospital, Kuwait

Email address:

Maryam.almurshed@gmail.com (Maryam Almurshed)

*Corresponding author

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Abstract: Lesions of notochordal origin are unusual surgical cases that have a broad spectrum of differentiation, from remnants to benign tumors -namely “benign notochordal cell tumor BNCT”- to malignant chordoma. These lesions arise within the vertebral bodies at the ends of axial skeleton, clivus and lumbar areas. Chordoma, is a malignant destructive lesion extending from bone to surrounding soft tissue. It is hypothesized to arise from its rare benign counterpart, BNCT as evidenced by their co-existence in rare case reports, in lumbar area, an even more rare in clival region. These benign forms are even scarce to see in surgical pathology specimen and carry a histological resemblance in morphology to malignant chordoma if not recognized. Here, we report a case of chordoma arising from a benign notochordal cell tumor (BNCT), which was discovered in a 35 years old male who presented with diplopia, diagnosed as 6th nerve palsy. MRI imaging showed an expansile clival lesion with sclerotic borders invading the cavernous sinus and encasing the carotid. Histopathology showed features of chordoma within BNCT. This case highlights the rarity of the entity especially in the clival region, the wide differential diagnosis of clear cell tumor arising in the clival region and the importance of radio-pathological correlation.

Keywords: Chordoma, Benign Notochordal Cell Tumor, Morphology, Clival Mass

1. Introduction

Notochordal-related tumors are rare entities that are usually asymptomatic. These tumors are mostly diagnosed incidentally [1, 12]. The disease spectrum include benign lesions, as ecchordosis physaliphora vertebralis and benign notochordal cell tumor BNCT, and malignant chordoma [18]. As the spectrum carries an impact on patient management and follow up, recognizing and differentiating benign from malignant entities is essential [12, 14, 17]. Until recently, malignant chordoma are getting recognized to arise from notochordal remnants as documented in published case reports within the last 10 years, mostly in sacral location [1, 3, 4, 7, 8]. This initiated an insight to the aetiology of malignant chordoma. Moreover, as the histological discriminating changes are subtle, assistance of the radiologic findings is necessary [10, 11]. Here, we document a case of clival chordoma arising in a precursor benign notochordal

cell tumor, highlighting the essential histo-radiological correlation for the diagnosis. Only few case reports and short series are present in literature about these entities, especially in clival region [2]. Most of the reported cases are of sacral location.

2. Case Presentation

A 35-year-old man was referred for neurosurgery with an expansile clival mass. There was a short progressive history of diplopia diagnosed as 6th nerve palsy. Past medical history and family history reveled no tumors. Non-enhanced axial CT scan image shows a large lytic expansile midline mass (red arrow) centered on the clivus and dorsum sella with foci of calcification (Figure 1A). Sagittal T2 flair image shows that the lesion, measuring 3.6x3.6x3.4 cm (APxCCxT), is inseparable from the posterior aspect of the pituitary gland. There were erosive bony changes with the mass noted to be projecting into the sphenoid sinus (Figure 1B). Sagittal

Gadolinium contrast-enhanced T1 image shows faint heterogenous enhancement. It is effacing the prepontine cistern and the basilar artery (red arrow) is directly in contact with the dorsal aspect of the mass (Figure 1C). Endonasal endoscopic excision was performed.

3. Histopathology

The specimen was received in the histopathology lab fixed in 10% buffered formalin, labeled as “clival mass”. It consists of multiple grey-brown soft tissue fragments measuring 3.0 x 1.0 x 0.5 cm. Microscopic examination of the H&E stained slides revealed a highly cellular neoplasm with vague lobulation, arranged in sheets and composed of polyhedral cells. The tumoral cells vary in morphology and size. The majority of cells show multivacuolated clear cytoplasm with nuclear indentation. Others show a uni-vacuolated cytoplasm with eosinophilia and filled with a colloid like inclusions (Figure 1D). Prominent nucleoli and nuclear pleomorphism and atypia are also noted. The tumor seems to erode the bone trabeculae with evidence of bone remodeling. Scattered entrapped bluish chondromyxoid matrix is present within the tumor (Figure 1E). Mitosis is rare. No necrosis is seen. The tumor extends to underneath the respiratory mucosa. The tumor also includes areas of hemorrhage, and shows hemosiderin deposition. Fibrous septa are not present. No tumoral cord formation noted. Immunohistochemical examination reveals strong positivity for pancytokeratin CK AE1/AE3 (Figure 1F) and epithelial membrane antigen EMA markers (Figure 1G). In addition, S100 and vimentin are positive, while CD10 and HMB45 stains are negative.

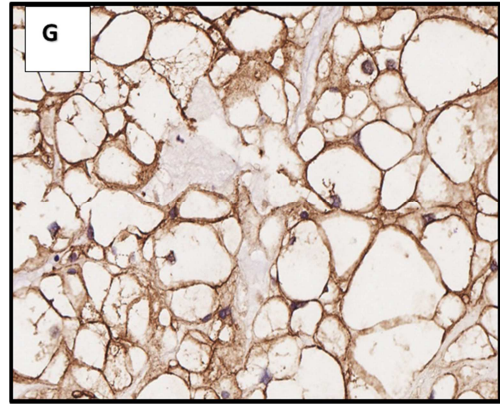


Figure 1. A. C. T head axial view shows a large lytic expansile mass centered on the clivus and dorsum sella with foci of calcification. B. MRI, T2 FLAIR highlights the heterogenous mass that is inseparable from the posterior aspect of the pituitary gland with erosive bony changes toward the sphenoid sinus. C. MRI, T1 with contrast show heterogenous mass enhancement that is seen effacing the prepontine cistern and the basilar artery. D-E. High power view show sheets of mono-vacuolated tumor cells with eosinophilic inclusions. Focal matrix noted in figure E. F. G. The tumor is diffusely positive for CK (F) and EMA (G) immunostains.

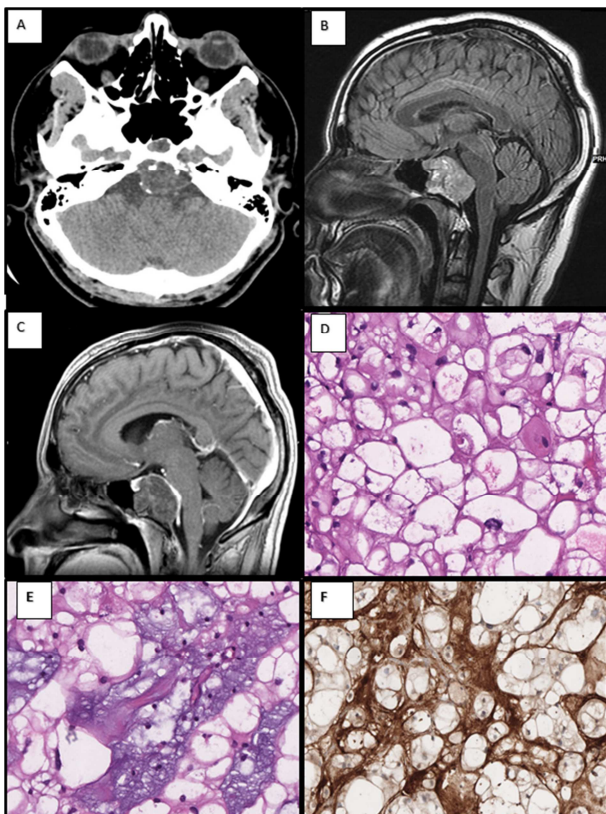
4. Diagnosis

Chordoma, arising in pre-existing benign notochordal cell tumor.

5. Discussion

Benign notochordal cell tumor is an unusual lesion that is documented as mainly asymptomatic mass diagnosed incidentally in 20% of autopsy series [18]. It is usually small in size, however, some vertebral located cases reported mild non-specific back pain if large in size [4]. Usually diagnosed by radiology for spine done for other diagnostic reasons. It is hypothesized that it is a benign lesion, with rare case reports indicating concurrent presence of chordoma, raising possibility of progression given that they both share common anatomic locations [9]. Given the limited size of histopathology biopsies, the gross imaging picture of radiology is an essential representative of the whole tumor. Histo-radiological correlation is a mandatory for the diagnosis and in correlating with the site of biopsy [6, 11].

BNCT is usually noted as a well demarcated mass located in the intervertebral body; mainly in the skull base-clival location- and sacrococcygeal regions. It usually involves single vertebral body, and rarely involves two noncontiguous vertebral bodies [4]. It is usually a single mass, however, rare case reports documented multiple synchronous lesions [19]. It is around 4 cm in size. Radiologically assessment of the lesion by Roentgenography is usually normal or show osteolytic defects [6]. Fracture or some sclerosis was reported. Computerized Tomography can demonstrate vertebral body sclerosis or otherwise no apparent abnormality. Magnetic resonance imaging studies demonstrate lesions confined to the vertebral body, with low signal intensity signal on T1, and high signal intensity on T2, with no evidence of bone destruction or soft tissue



involvement. Compared with chordoma, that is usually irregular mass, measuring up to 25cm, that shows additional features of contrast enhancement on MRI, bone destruction and soft issue infiltration [11].

Histologically, BNCT would grow as nests or sheets of cells with microcyst formation. Among the sheet, colloid-like material can be present. These sheets can permeate the existing bone trabeculae. In the other hand, chordoma would show lobulation separated by fibrous bands and forming irregular cords and syncytia with recognizable intercellular myxoid matrix and necrosis [9, 18]. In addition, bone destruction is noted. In BNCT, different cell morphologies can be recognized, including physaliphorous cells, clear adipose-like cells and eosinophilic cells with cytoplasmic globules. In contrast, chordoma physaliphorous cells are bubbly, atypical and pleomorphic with frequent mitosis. Both lesions benign and malignant can show similar immunohistochemical expression in regards to positivity to pancytokeratin (AE1/AE3), low molecular weight keratins, epithelial membrane antigen (EMA) and S100. However, Ki67 proliferation index is usually high in the malignant component [18]. In regards to the present case, histological features of adipocyte-like cells in the majority of the tumor, sheeting with lack of lobulation, fibrous septa, and necrosis in a radiologically well demarcated mass that is non-enhancing in its majority support the diagnosis of BNCT. In addition, the presence of multifocal intercellular myxoid matrix, nuclear atypia, tumoral heterogeneity and mitosis with radiological features of focal enhancement correlate with the presence of incipient malignant chordoma.

Rare reports are published about benign notochordal tumors in literature in the last 20 years, especially of clival location. Ma X et al. reported 11 cases of benign notochordal cell tumors in a series in 2014. The study documented cases in cervical, thoracic and lumbar vertebra, with correlation to patient gender, symptoms, fracture-association, MRI findings, treatment and follow-up [4]. Yamaguchi et al. reported incipient chordomas in a BNCT in the vertebra in two autopsy cases in which post-mortem examination done for other disease causes (hepatocellular carcinoma and prostate carcinoma) [1]. Case report by Riviere et. al. revealed an asymptomatic BNCT in vertebra in 52 years old female while bone staging for breast carcinoma [8]. A study done by Rizzoli Institute by Kreshak et. al. whom retrieved 174 chordoma cases from the period of 2008-2014, found only two cases with areas of both BNCT and chordoma, that are both involving the vertebra [6]. In addition, a symptomatic vertebral BNCT was diagnosed in a 59 years old female that histologically revealed a chordoma arising from a BNCT, as reported by Nishiguchi et. al. in 2010 [3]. In the clival location only rare publications are present. Peris-Celda et. al. reported 2 cases for clival incipient chordoma in a BNCT. The first case was for 18 years old female and the second for 38 years old male patients who both were asymptomatic and the lesions were incidentally found [2]. In contrary to our case, which was symptomatic clival mass.

Recognizing the notochordal benign entity and

differentiating it from malignant chordoma is essential as each would be managed differently [13]. BNCT would not require further management. Chordoma, on the other hand, should be treated by extensive resection to lower the risk of recurrence [16]. Knowing the ability of the tumor to spread and ensheath vital structures, surgery is usually accompanied by radiation.

The clivus, is part of the skull base situated between the foramen magnum and the dorsum sellae. It is a common site for involvement by both neoplastic processes and tumor-like conditions. Among the former, chordoma, multiple myeloma, lymphoma, chondrosarcoma, meningioma and metastasis are considered the most common conditions. While tumor-like lesions include fibrous dysplasia, Paget disease, Langerhans cell histiocytosis, and radio-necrosis. Lesions from paraclival location can also extend to involve the clivus like invasive nasopharyngeal carcinoma, juvenile angiofibroma, and invasive pituitary adenoma [5, 15]. Histologically, clearing of cells in this location will modify the differential diagnosis to chordoma, clear cell chondrosarcoma, clear cell meningioma, metastatic renal cell carcinoma and benign notochordal cell tumor. Clear cell chondrosarcoma usually shows at least focal chondroid differentiation and are S100 and IDH positive, while negative for EMA and cytokeratin. Clear cell meningioma similarly would show at least focal meningeal differentiation, in the form of whorls, syncytial pattern of growth, and meningeal nuclear features, in addition to positive reactivity for EMA and negativity for S100 and cytokeratin immunostains. Metastatic renal cell carcinoma histologically characterized by increased vascularity and lymphoid infiltrate among the clear vacuolated cells. These cells stain for PAX8 and CD10 and will be negative for S100 and cytokeratin stains. The panel of the immunohistochemical stains used is important and should always be directed by the tumor histology.

6. Conclusions

Notochordal rests and tumors are uncommon surgical specimens that might present to histopathology with different morphologies that are easily misdiagnosed if not entertained in the differential diagnosis. Correlation with radiology that indicates the core of the mass and its surrounding bone/soft tissue reaction has an integral part to the diagnosis. This paper states the rare association between benign notochordal cell tumor with incipient conventional chordoma, diagnosed histologically and supported by radiology.

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