

Notochordal cell tumors

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Introduction

Chordoma is a rare primary malignant neoplasm of bone that recapitulates the embryonic notochord. It almost exclusively arises in the axial skeleton, most commonly the sacrum, followed by the skull base and the mobile spine and almost always presents as a destructive bone lesion with soft tissue extension. Due to its similarity to the normal notochord, the assumption has been that chordomas may arise from notochordal remnants. In adults, notochordal remnants can be found in the nucleus pulposus of the intervertebral disc and at the base of the brain, outside the bone (the so called **ecchordosis physaliphora**). Chordomas, however are primary bone tumors and do not arise in the intervertebral discs or from ecchordosis. In the late 90s paper started coming out describing intraosseous lesions that were initially thought to be 'giant notochordal rests' or hamartomas. Then in the early 2000 Yamaguchi and his colleges in a series of articles recognized the possible origin of chordomas from these lesions and for which they coined the term **benign notochordal cell tumor** (BNCT).

Ecchordosis physaliphora

Ecchordosis physaliphora is an extra-osseous notochordal remnant that persists in the region of the base of the brain (intradural retroclival) as a well circumscribed round to oval gelatinous nodule. The lesion is usually few millimeters up to 2 cm in size. Clinically it is usually an asymptomatic lesion that is incidentally discovered on a CT scan or MRI that are obtained for non-specific symptoms. Histologically, it is similar to chordoma being composed of large cells

arranged in cords or clusters with a varying amount of extracellular myxoid matrix.

Immunohistochemically ecchordosis has the same immunohistochemical profile as chordoma, being positive for keratin, S100 and brachyury.

Benign Notochordal Cell Tumor (BNCT)

BNCT is an intraosseous, slow-growing notochordal cell proliferation that behaves in an indolent fashion. BNCT is the name that was introduced by Yamaguchi in 2002 to an intravertebral notochordal lesion that had first been described by Darby et al. in 1996 under then name of “Giant notochordal rest”. Several other names have been suggested to the same lesion like “Giant notochordal hamartoma” and “Notochordal inclusions”.

Radiographically, BNCT can be solitary or occasionally multiple and manifest as irregular areas of sclerosis within the vertebral body – mimicking intraosseous hemangioma radiographically.

BNCT is composed of a proliferation of univacuolated (adipocyte like) cells and multivacuolated (physaliphorous) or pale pink cells with no extracellular mucinous matrix or significant nuclear atypia. Some cells with pink cytoplasm contain round intracytoplasmic hyaline globules (PAS positive – diastase resistant). They are almost invariably located inside the bone without any extraosseous extension (very rarely can they extend through cortex and displace the periosteum, forming a small soft tissue component).

The immunohistochemical profile for BNCT is the same as for chordoma and ecchordosis, being positive for keratin, S100 and brachyury.

Chordoma

Chordoma is a primary malignant tumor of bone with a phenotype that recapitulates notochord and almost always arises within the bones of the axial skeleton. It accounts for approximately 5% of primary malignant bone tumors and is usually diagnosed during the 4th to 8th decades of life. Less than 5% develop in patients under the age of 20 and when tumors arise in children they usually involve the skull base. Chordoma almost exclusively arises within the bones of the axial skeleton with most cases arising in the sacrum, followed by the skull base and the mobile spine. The symptoms depend on the site of origin – skull base – mobile spine – sacrum.

Grossly, it is lobulated and gelatinous and well demarcated from the surrounding tissues. Skull based tumors are usually small at the time of diagnosis but sacral tumors are usually very large.

Histologically, chordoma can be classified into conventional chordoma, chondroid chordoma and dedifferentiated chordoma.

Conventional chordoma has a lobular growth pattern and demonstrates an infiltrative growth pattern, encasing preexisting bony trabeculae and is usually embedded in abundant extracellular myxoid matrix. The tumor cells are large and epithelioid and are arranged in nests and cords. The cells have an eosinophilic cytoplasm and may contain intracytoplasmic vacuoles (so called physaliphorous cells).

Chondroid chordoma contains areas of conventional chordoma as well as regions resembling low-grade hyaline-type chondrosarcoma. The chondroid areas are composed of neoplastic cells that are surrounded by matrix like hyaline cartilage. Chondroid chordoma

usually located at the skull base. On a small biopsy that does not contain the conventional chordoma areas, these tumors can be misdiagnosed as chondrosarcoma. This distinction is important as the prognosis and therapy for these two types of tumors are different. The prognosis for chondroid chordoma is however the same as for conventional chordoma. In the past, there were some issues with the regards to whether chondroid chordoma was a distinct entity and if it had a better prognosis than the conventional chordoma. One of the reason for this discussion was that many myxoid chondrosarcomas were misdiagnosed as chondroid chordoma – myxoid chondrosarcoma having a better prognosis than chordoma.

Dedifferentiated chordoma is the least common type. It is composed of conventional chordoma that is juxtaposed to a high grade (usually undifferentiated) sarcoma similar to what is seen in dedifferentiated liposarcoma and dedifferentiated chondrosarcoma. Dedifferentiated chordoma has the worst prognosis, much worse than conventional and chondroid chordoma.

Immunohistochemical stains can be very helpful in differentiating chordoma from other tumors in the differential diagnosis such as metastatic adenocarcinoma and chondrosarcoma. Conventional and chondroid chordomas express epithelial markers, keratin (including keratins 8 and 19) and epithelial membrane antigen and the majority also stain for S100 protein. The vast majority also show nuclear expression of T-brachyury which is a very specific and sensitive marker for notochordal differentiation (it is also expressed in normal notochord and benign notochordal lesions). Just as chordomas, chondrosarcomas express S100 protein but are negative for keratin and brachyury. The conventional chordoma, in dedifferentiated chordoma, expresses the same markers, whereas the high grade sarcomatous component loses the expression for these markers and has no specific immunohistochemical profile – the diagnosis

of dedifferentiated chordoma can only be made in the presence of the conventional component.

Atypical Notochordal Cell Tumor

Recently the concept of atypical notochordal cell tumor has been introduced for notochordal tumors that have the radiologic and/or histologic features that do not fit a classic benign notochordal cell tumor or chordoma. This will be discussed further in this short course.

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