Notochordal Differentiation

50

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50.1 Benign Notochordal Cell Tumor

Definition: A benign vertebral lesion of notochord origin (also called giant notochordal rest or ecchordosis physaliphora when localized in spheno-occipital region) recently introduced as benign counterpart of chordoma.

Epidemiology: The incidence is uncertain, although in a relatively small study an incidence of at least 20% of cadavers has been reported.

Location: Cervical and lumbar spine (clinical case); smaller lesions could also be found in the sacrum, coccyx, and clivus at autopsy.

Clinical: Most lesions are incidentally found on imaging examinations because they are usually asymptomatic. Lesions that fill the vertebral body may be symptomatic.

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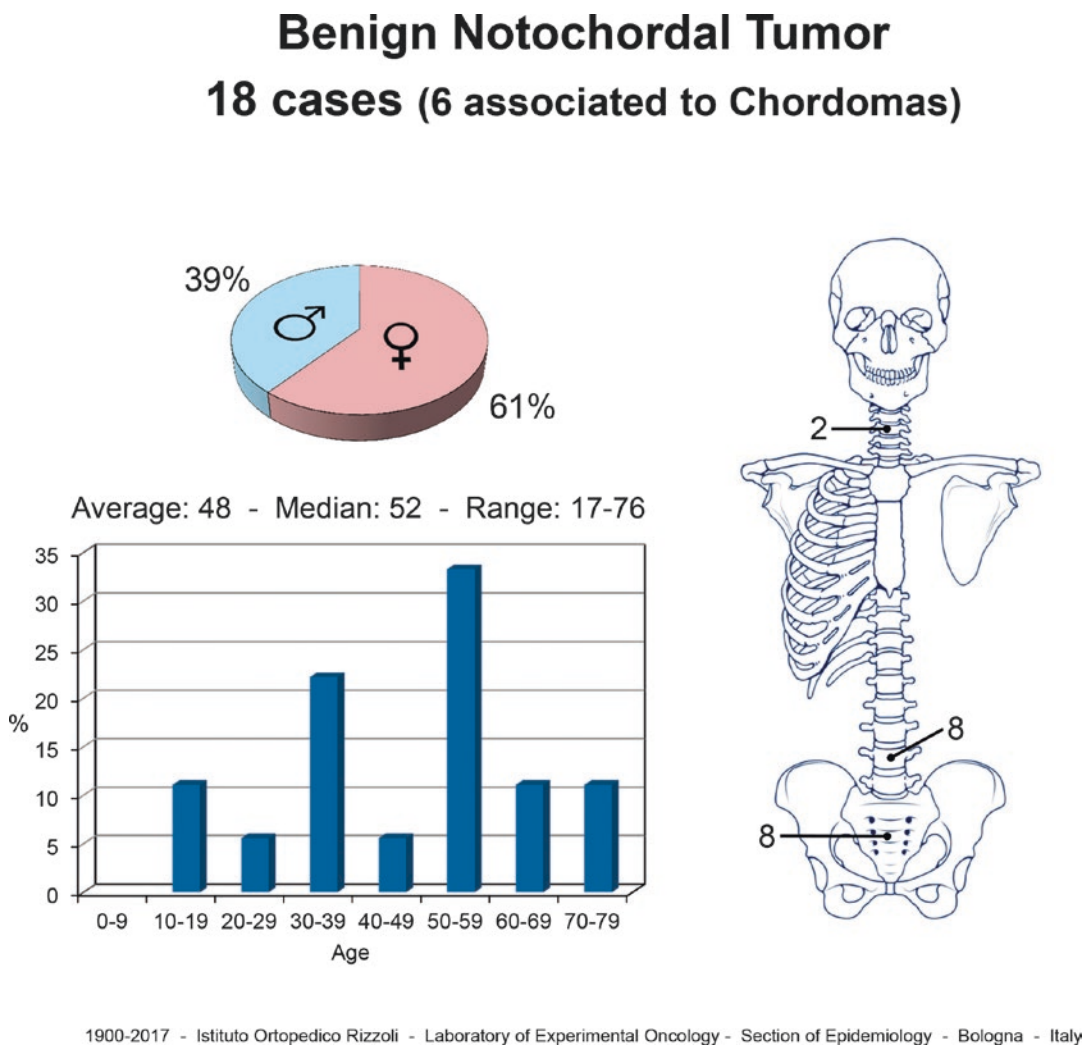
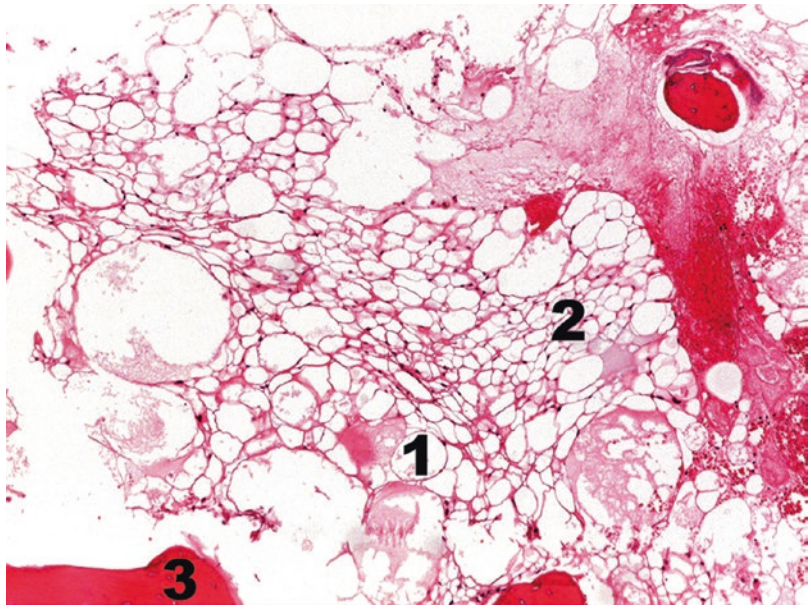


Imaging: Radiographs occasionally reveal mild osteosclerosis. Computed tomography scan shows an intraosseous sclerotic lesion without extraosseous tumor extension. Magnetic resonance imaging reveals homogeneously low signal intensity on T1-weighted imaging, homogeneously high signal intensity on T2-weighted imaging, and no contrast enhancement on gadolinium-enhanced.

Histopathology: Macroscopically, the cut-surfaces disclose an unencapsulated and well-demarcated tumor with a bright tan, glossy texture. Morphologically, the lesion consists of solid sheets of adipocyte-like vacuolated and eosinophilic tumor cells with bland nuclei without mitotic figures. Benign notochordal cell tumor lacks intercellular myxoid matrix, although some cystic spaces filled with colloid-like material can be seen. The involved bone trabeculae are mildly, occasionally markedly, sclerotic. Bone marrow islands may be seen within the lesion. A lobular configuration formation of fibrous septa are absent. The tumor cells are immunohistochemically positive for brachyury, epithelial markers, and S-100 protein.

Course and Staging: Prognosis is excellent and the clinical course is very indolent except for the very low risk of malignant transformation in chordoma.

Treatment: This lesion does not require any surgical intervention and a follow-up with imaging is necessary.

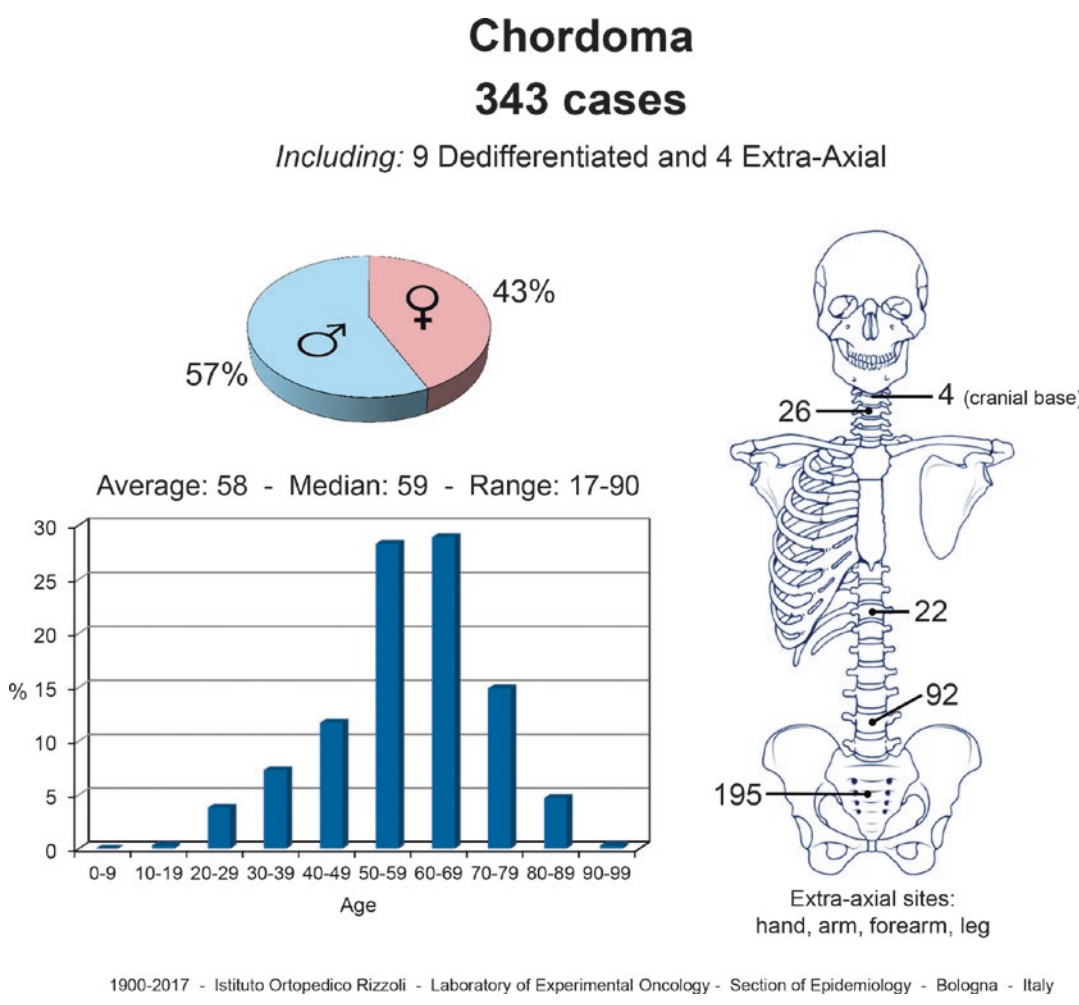


Benign notochordal cell tumor. Intraosseous tumor in the vertebral body composed of aggregates of large "adipocytes-like" cells. (1) Notochordal cells are large and show abundant clear cytoplasm. (2) The cells have well-defined cell membranes and centrally or peripherally placed nuclei with no atypia. (3) Affected bone trabeculae are often sclerotic

50.2 Chordoma

Definition: A rare, slow-growing, malignant bone tumor showing notochordal differentiation.

Epidemiology: The incidence is 0.08 per 100,000 people with a male prevalence (male to female ratio is 1.8/1). The tumor commonly develops in the fourth to seventh decades of life although all age groups are affected.



Location: 50–60% in the sacro-coccyx region, followed by skull base/spheno-occipital region (25–30%), vertebrae (15%) and with anecdotal reported extra-axial and extraosseous cases.

Clinical: Skull-based chordoma most commonly present with headache, neck pain, diplopia, or facial nerve palsy. Chordoma of the mobile spine and sacrum present with chronic low-back pain, constipation, hemorrhoids, dysuria, limping, hypoesthesia, and sphincteric paresis.

Imaging: On radiographs, osteolytic bone destruction lesion is usually evident. The outlines of bone and lines of the sacral foramina have disappeared. Faded radiopaque spots of intratumoral calcifications are frequent. The vertebral body chordomas show a relatively well-defined edge, with sclerotic rim, calcifications. CT evidences a destructive bone tumor with extraosseous tumor formation. In the sacrum, extraosseous mass protrudes more anteriorly than posteriorly with well-defined borders and infiltration of the adjacent muscles, dislocation of the viscera or of the dural sac. MRI reveals low homogeneous signal intensity on T1-WI, heterogeneously high signal intensity on T2-WI, and marginal or entire enhancement on Gd-enhanced T1-WI.

Histopathology: Most chordomas are conventional type, but there are three other rare subtypes: chondroid, poorly differentiated, and

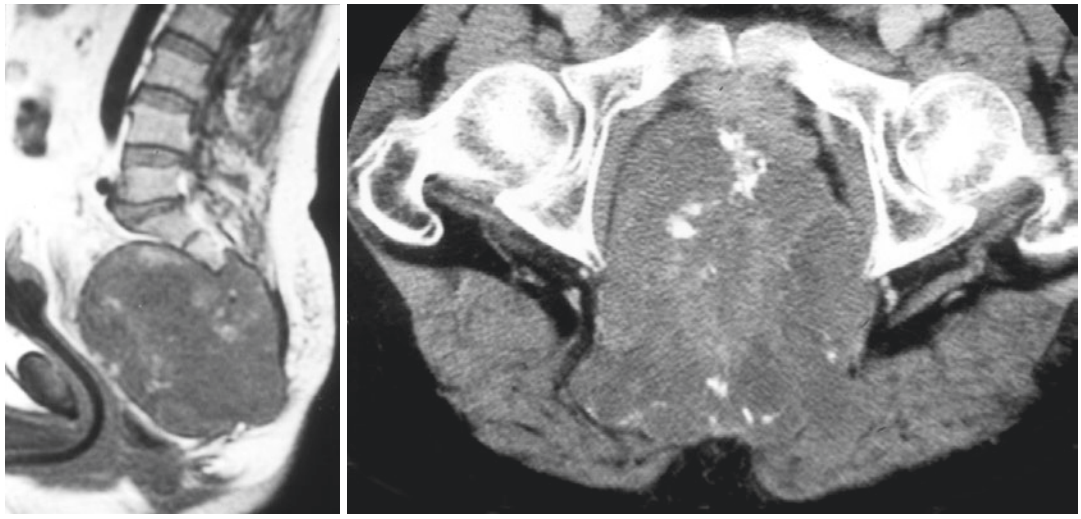
dedifferentiated chordomas. On macroscopy, the tumor, usually associated with a huge extraosseous tumor mass, is well demarcated and encapsulated with a thin fibrous capsule. Dedifferentiated chordoma is associated with a nonmyxoid tumor component with a fairly sharp margin. Morphologically, chordoma is an encapsulated lobular tumor composed of solid sheets and/or cords of epithelioid vacuolated tumor cells – so called "physaliphorous cells" – with a varying amount of intercellular myxoid matrix. Each lobule is separated by thin fibrous septa. The tumor cells show clear to eosinophilic cytoplasm. Poorly differentiated chordoma looks like pleomorphic spindle cell sarcoma but the tumor cells show signs of notochordal differentiation. Chondroid chordoma that has a predilection for the base of the skull shows chondrosarcoma-like components in addition to classic chordoma morphology. Dedifferentiated chordoma consists of two components: conventional chordoma and high-grade sarcoma, without notochordal differentiation. Immunohistochemically, all subtypes (except the dedifferentiated component in dedifferentiated chordoma) typically show positive staining for keratins, brachyury, S100, and EMA. Recently, a subset of chordoma (often poorly differentiated-subtype) shows an absence of INI1 / SMARCB1 expression.

Course and Staging: Chordoma recurrence rate is high at locations where surgical excision with sufficient tumor-free margins is not possible, which directly affects the long-term survival rate of these patients. Next to local recurrence, metastasis to the lung, bone, lymph nodes, and skin occurs in 5–43% of patients. The median overall survival is 4–7 years and the 10-year survival rate ranges from 40 to 60%. Poorly differentiated-type, that often affects children, appears to be more aggressive than conventional and chondroid chordoma in both the skull base and the spine, with a decreased mean overall survival. Dedifferentiated chordoma is lethal, with systemic spread occurring in approximately 90% of cases.

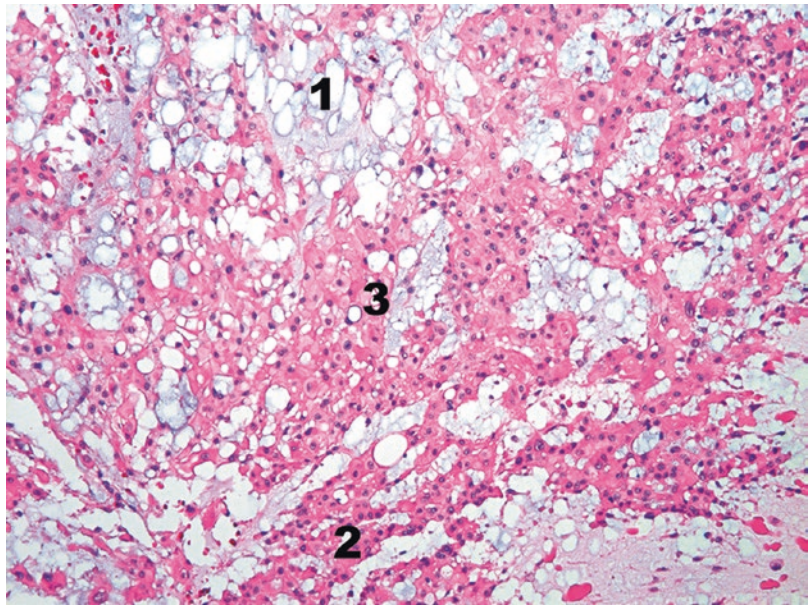
Treatment: Chordoma has been primarily managed by surgery for a long time. Wide resection is mandatory, but often impossible. Traditional chemotherapy has not been effective so far. Instead of chemotherapy, proton therapy has been primarily applied in combination with surgery. Carbon-ion radiation therapy has taken over from proton therapy to treat unresectable chordomas. The 5-year local control, overall survival, and disease-free rates of carbon-ion radiation therapy are 77%, 81%, and 50%, respectively. Despite the satisfying results, radiation therapy is not able to prevent distant metastasis even though it is effective in controlling local disease.

Key points	
• Clinical	Old patients, pain, and compression symptoms
• Radiological	Pure lytic lesion
• Histological	Lobular pattern with physaliferous cells
• Differential diagnosis	Bone metastasis, chondrosarcoma, and all other primary purely osteolytic lesions of adults—benign notochordal cell tumor

Immunohistochemical panel	
• CK	+
• EMA	+
• S-100	+/–
• INI1 (SMARCB1)	+/–
• Brachyury	+ (nuclear)



CT and sagittal T1 MR image. Huge tumor destroying the last sacral vertebrae, invading the anterior soft tissues, pushing the rectum, which remains free. On CT, remaining pieces of bone are well visible

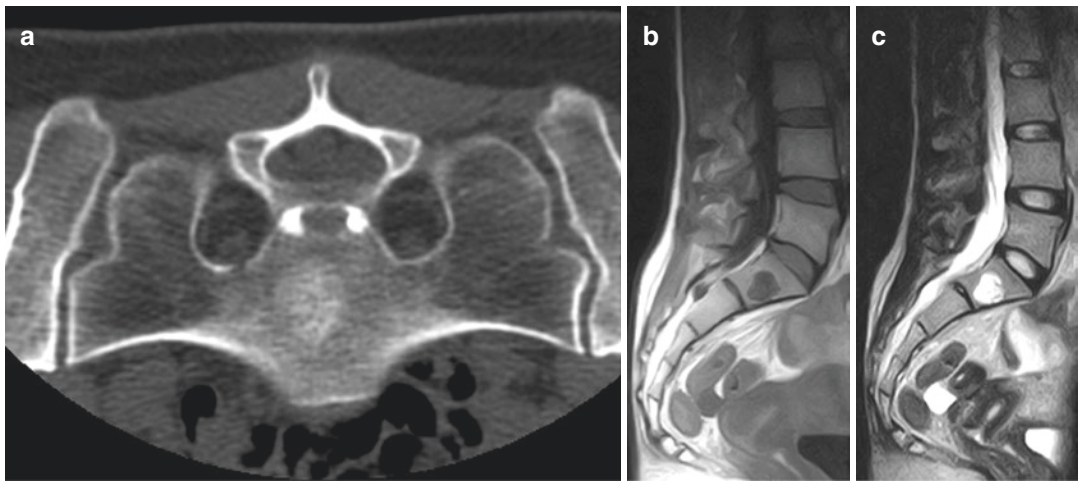


The histological picture of the tumor may vary from field to field. However, the architecture is usually characterized by cellular cords isolated and anastomized, producing mucin and contained in the mucoid substance accumulated on the outside. (1) Mucoid substance. (2) Large, deeply eosinophilic cells organized in cords. (3) Signet-ring cells and physaliphorous cells may be observed in more differentiated areas

50.3 Differential Diagnosis Between Benign Notochordal Cell Tumor and Chordoma

Differential diagnosis between chordoma and benign notochordal cell tumor is fundamental and represents a challenge for pathologist in particular on biopsy specimen because of an overlapping immunohistochemical profile. The radiograph features of benign notochordal cell tumor on CT (sclerotic lesion within bone, without lysis) and on MRI (a homogenous intraosseous lesion with a low signal on T1-weighted images and high signal on T2-weighted images, that does not take up contrast medium) allow differential diagnosis with chordoma. Morphologically, chordomas show fine fibrous capsules and/or septa with vasculature, lobular configuration, intercellular myxoid matrix, and bone destruction. The border of chordoma to bone marrow cells of host bone seems very smooth because of a thin fibrous membrane existed. In contrast, the border of benign notochordal cell tumor seems slightly zigzag along the contour of adjacent marrow adipocytes because of a lack of intervening fibrous membrane.

The distinction between benign notochordal cell tumor and chordoma applying the radiologic and histologic criteria is occasionally difficult, so recently some authors propose a designation of atypical notochordal cell tumors that should be used for the subset of notochordal-derived tumors that fail to fulfill current diagnostic criteria for either benign notochordal cell tumor or chordoma.



Incidental discovery. On TC (**a**) the lesion is medial, sclerotic. Cortex is normal and soft tissues are not involved. The lesion has a low signal on sagittal T1 (**b**) and high signal on T2 (**c**) MR images (there was no change after contrast medium injection)

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