28 Chordoma

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INTRODUCTION

Chordomas are unusual tumors with seemingly unconventional traits. Most notably, they are malignant primary bone tumors but not sarcomas. They derive from embryologic cell remnants but predominantly affect late-middle-age adults, and they behave aggressively but grow slowly. Chordomas present with long-standing symptoms related to local mass effect or invasion. At the skull base, they often cause headaches and cranial neuropathies. In the spine, they incite low-grade pain and either weakness, numbness, constipation, or incontinence. Imaging interpreters play an important role in initial diagnosis, treatment response, and surveillance for recurrence.

EVOLUTION: OVERVIEW

The majority of malignant bone tumors derive from the cells that compose the building blocks of bone: matrix (osteosarcoma), cartilage (chondrosarcoma), fibrous tissue (fibrosarcoma), neural crest cell (Ewing sarcoma), and hematopoietic marrow (lymphoma). Chordomas, however, arise from vestiges of the primitive notochord, an evolutionarily conserved structure regarded as one of the defining characteristics of the entire chordate phylum. Although several cellular, genetic, and epigenetic markers have been identified, the exact molecular pathogenesis of chordoma remains poorly understood.[1] It is unclear what mutations, environmental insults, molecular signals, or other triggers transform benign notochord

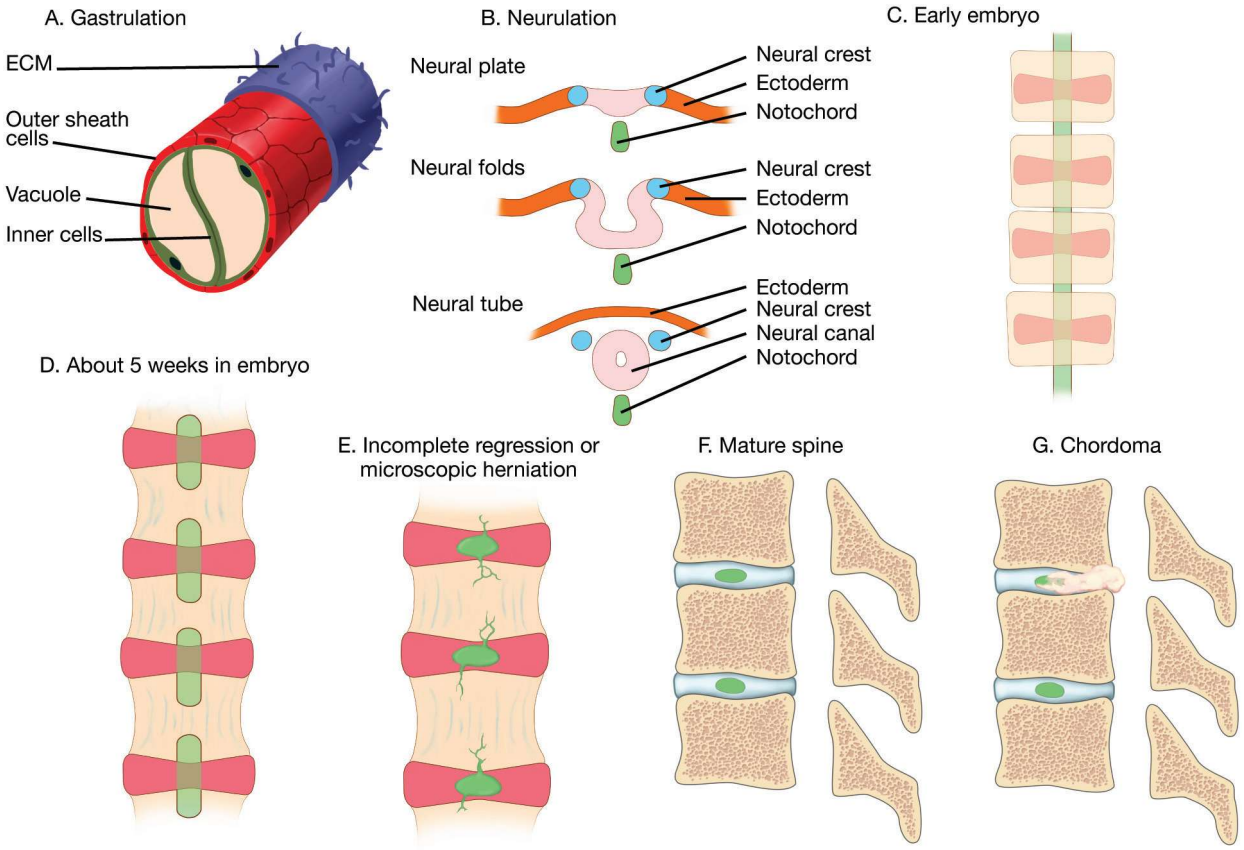

Figure 28.1. This illustration depicts the role and fate of the notochord in the embryo and later life. Shortly after gastrulation the two layers of the notochord provide structural support for the early embryo (A). The notochord also releases signals to induce neurulation and tissue differentiation (B). In the early embryo, the notochord canal extends from the anterior pituitary gland and sella to the coccyx (C). Around 5 weeks, the notochord gradually regresses to segmented levels between developing somites or vertebral body precursors (D). However, if this regression is incomplete or if notochord-derived cells herniate away from their intervertebral levels, then ectopic notochord rests may be found within the developing vertebral bodies or adjacent structures (E). By the late embryonic stage, notochord-derived cells form the nucleus pulposus (F). In most people, these notochord-derived cells remain benign and clinically insignificant throughout life. In about one in one million persons (in the United States), or approximately 300 people annually, unknown factors transform these notochordal cells into chordoma tumors (G). *ECM,* Extracellular matrix.

rests into malignant tumors later in life. It is also unclear whether malignant cells arise solely from these rests, or whether another pathway to malignancy exists. Regardless, an understanding of the notochord in the embryo can help explain two common attributes of well-differentiated chordoma: T2 high signal and midline location.

The notochord forms a flexible rod-like skeleton before regressing as the spinal column develops. The opposing pressures of its two internal cell layers provide critical mechanical support for the embryo. An outer layer of notochord cells maintains a basement membrane by secreting an extracellular matrix rich in glycogen and mucin.[2] An inner layer of notochord cells contains large, fluid-filled, intra-cytoplasmic vacuoles that inflate the inner cells against the more constrictive basement membrane.[2] While the exact molecular composition and function of these lysosome-related vacuoles remain unclear, they, along with the mucin and glycogen in the extracellular matrix, endow well-differentiated notochord remnants with their characteristic gelatinous T2 bright signal.

The notochord also serves as the principal longitudinal axis of the embryo, signaling the directional positioning (e.g., dorsal—ventral, left—right) and tissue patterning of adjacent cells. In adults, the notochord leaves cellular remnants along its canal, which traverses the nucleus pulposus and vertebral bodies.[3] This central positioning explains why all notochord remnants establish themselves along the midline and why these lesions can emerge anywhere from Rathke pouch to the coccyx. Notochord remnants are never found outside the neural axis in the extremities or ribs.

The role and fate of the notochord in the embryo and later life is depicted in Fig. 28.1.

Chordomas are closely monitored with imaging after initial therapy because they are locally aggressive tumors located next to many vital structures that frequently recur (Fig. 28.2). Their unique location makes them difficult to completely resect or treat with radiation, and it increases the chance that even a small recurrence will be clinically devastating. Recurrences tend to develop along the margins of the treatment bed or as directly seeded metastases along the surgical tract.

SPECTRUM: OVERVIEW

Most chordomas display a few characteristic imaging traits: high T2 signal, midline location, aggressive bone changes, and dual bone/soft tissue components. If the imaging interpreter is fortunate enough to encounter the most common appearance of chordoma, recognizing these cardinal clues will lead to a straightforward diagnosis.

In clinical practice, chordomas do not necessarily follow the rules or "read the textbook." Real-world tumors do not always have high T2 signal; rather, many express intermediate T2 signal. Several factors can explain this signal variability. First, the amount

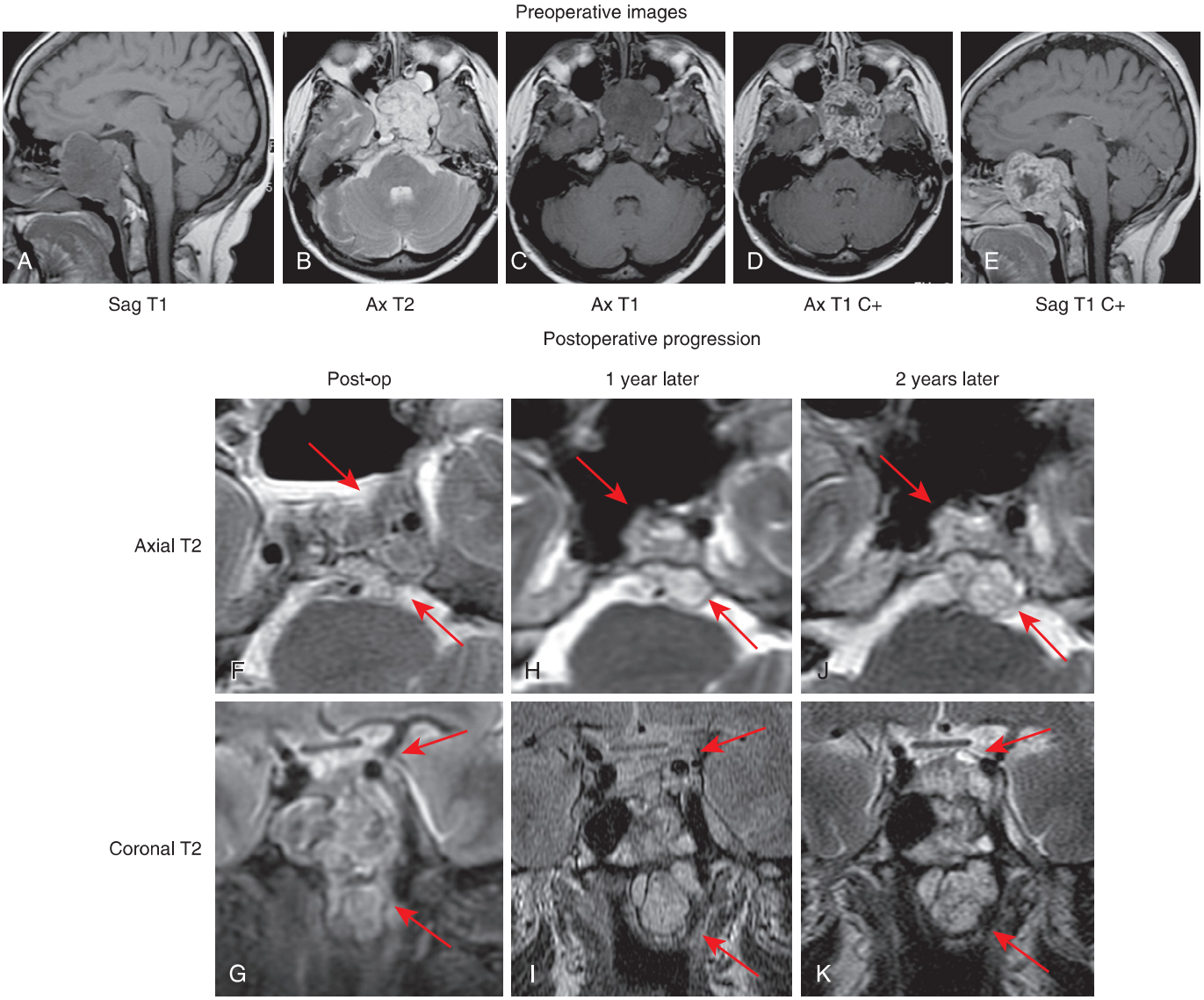

Figure 28.2. Preoperative appearance of chordoma and postoperative progression of recurrent tumor. Preoperative sagittal T1 (A), axial T2 (B), axial T1 (C), axial T1 postcontrast (D), and sagittal T1 postcontrast (E) images demonstrate a large, T2 hyperintense, heterogeneously enhancing chordoma centered within the clivus. Postoperative axial and coronal T2 images (F and G) show residual unresectable T2 hyperintense chordoma surrounding the cavernous carotid artery, posterior to the clivus, and extending into the nasopharynx *(arrows)*. Axial and coronal T2 images 1 year (H and I) and 2 years (J and K) after initial resection clearly show gradual enlargement *(arrows)*.

of fluid associated with the vacuoles and proteinaceous extracellular matrix differs with each tumor. Second, tumors grow slowly reaching medium to large sizes before they are discovered, and this allows time to evolve, bleed, or internally degenerate. Third, the pathologic subtype of the tumor can influence its imaging properties.

SPECTRUM: IN GREATER DEPTH

Accurately identifying the correct pathologic variant of chordoma on imaging is difficult, and, thankfully, this step is not required for initial clinical management. Nevertheless, understanding the pathologic spectrum of disease clarifies why chordomas do not all look the same. Currently, two pathologic subtypes are recognized: classic and dedifferentiated. The classic variant (Figs. 28.3–28.5) is the most common type and generally follows the standard imaging rules. The dedifferentiated or anaplastic variant (Fig. 28.6) is more straightforward. It displays relatively more diffusion restriction compared to the other variants, and it expresses intermediate rather than high T2 signal. As might be expected, the anaplastic variant behaves much more aggressively compared to the other two subtypes.

MIMICS AND DIFFERENTIAL DIAGNOSIS

Chordomas are confused with other tumors when they deviate from their classic appearance. The relative proportion of the bone component and the soft tissue component ranges considerably, and imaging interpreters may be misled when only one of the two components is identified. In other cases, the off-midline component of the tumor is larger than its midline component. If image interpreters fix the tumor center incorrectly, they may be led down an inappropriate differential pathway. When encountering these unconventional appearances, other nuances will help the image interpreter arrive at the correct diagnosis. A definitive diagnosis cannot always be made on imaging, however, and in these cases, a biopsy is required.

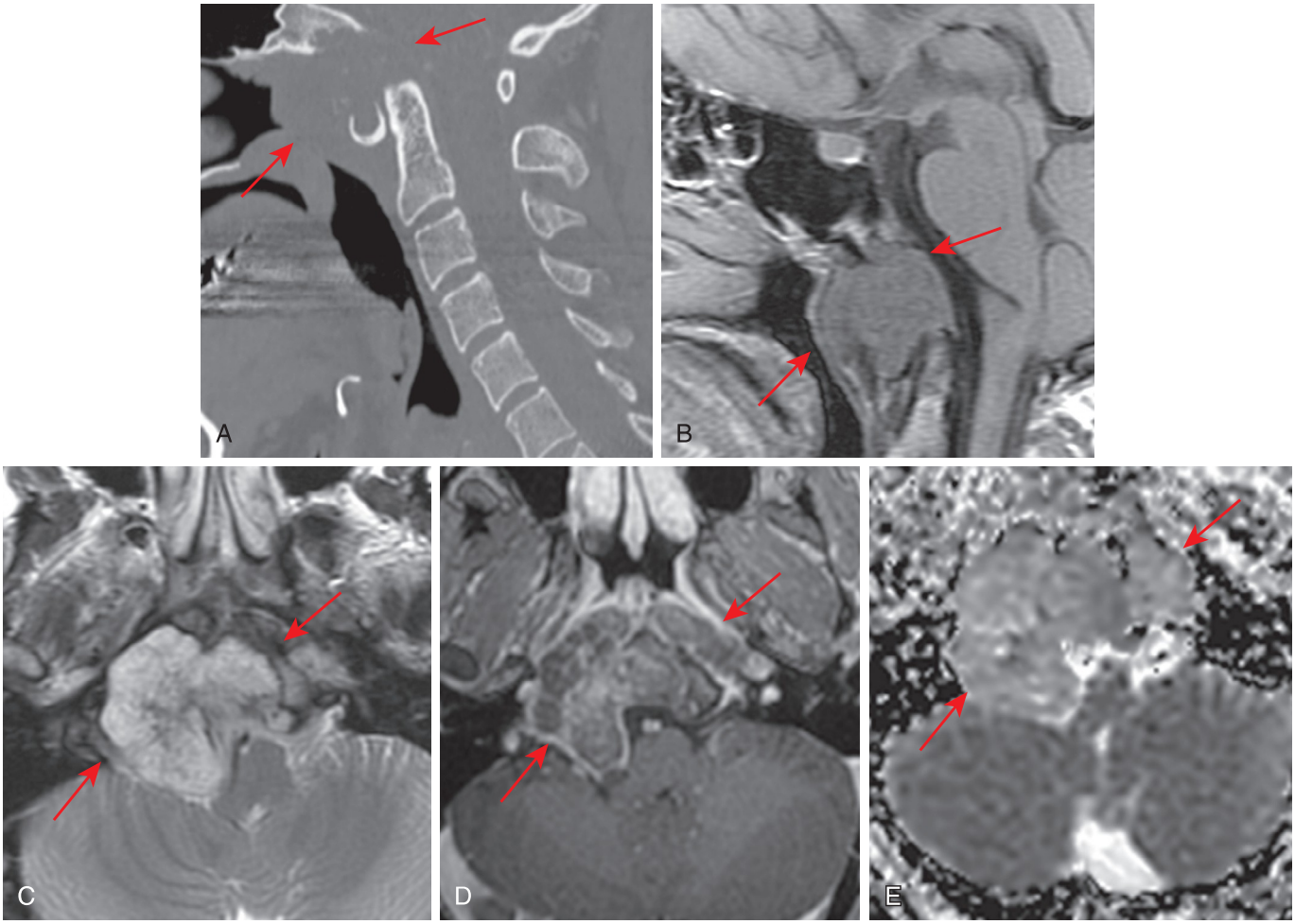

Figure 28.3. Classic appearance of clival chordoma. Sagittal CT (A), sagittal T1 (B), axial T2 image (C), axial T1 postcontrast (D), and apparent diffusion coefficient (E) images demonstrate a clival chordoma with classic appearance including high T2 signal, mild enhancement, mild restricted diffusion, and lytic bone destruction *(arrows)*. Both bone and soft tissue components are evident. Note how the chordoma displaces the adjacent basilar artery and medulla.

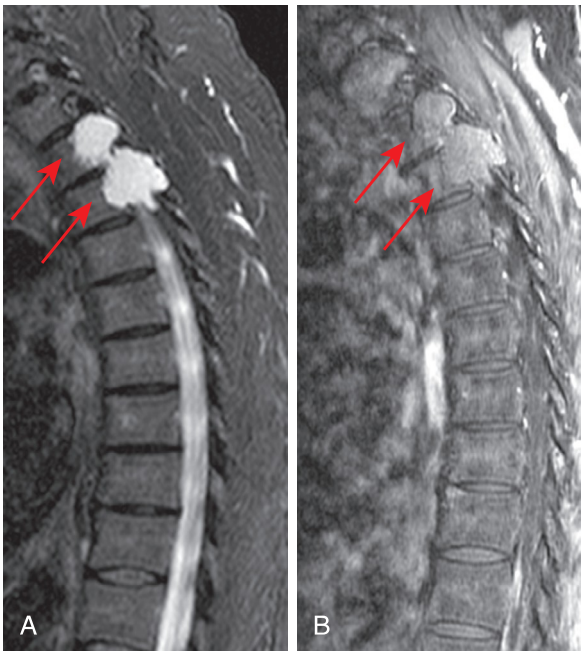

Figure 28.4. Classic appearance of a thoracic chordoma. Sagittal STIR (A) and T1 postcontrast fat-suppressed (B) images demonstrate a thoracic chordoma *(arrows)* with bone destruction, a narrow zone of transition, high T2 signal, enhancement, and dual bone/soft tissue components.

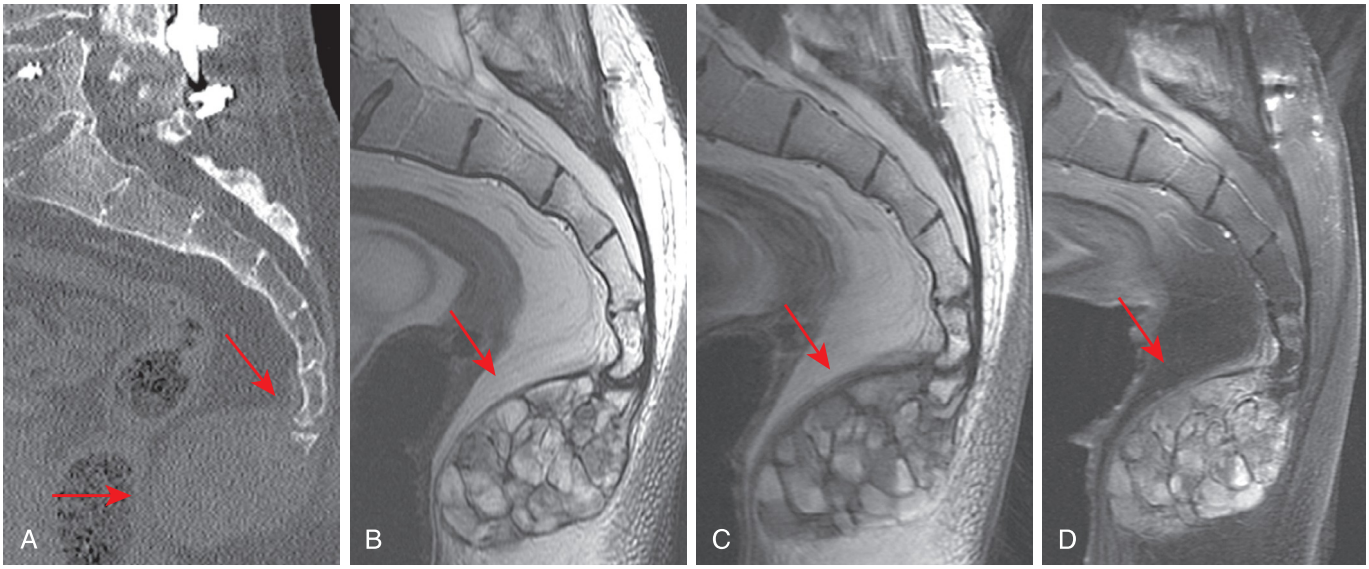

Figure 28.5. Classic appearance of sacral chordoma. Sagittal CT (A), T2 (B), T1 (C), and T1 postcontrast fat-suppressed (D) images of the sacrum and coccyx demonstrate a sacrococcygeal chordoma *(arrows)*. The chordoma has a dominant soft tissue component composed of multiple internal lobulations separated by fibrous septa. Each lobule contains mucoid material and blood products. The bone component of the tumor shows destructive tumor with a narrow zone of transition.

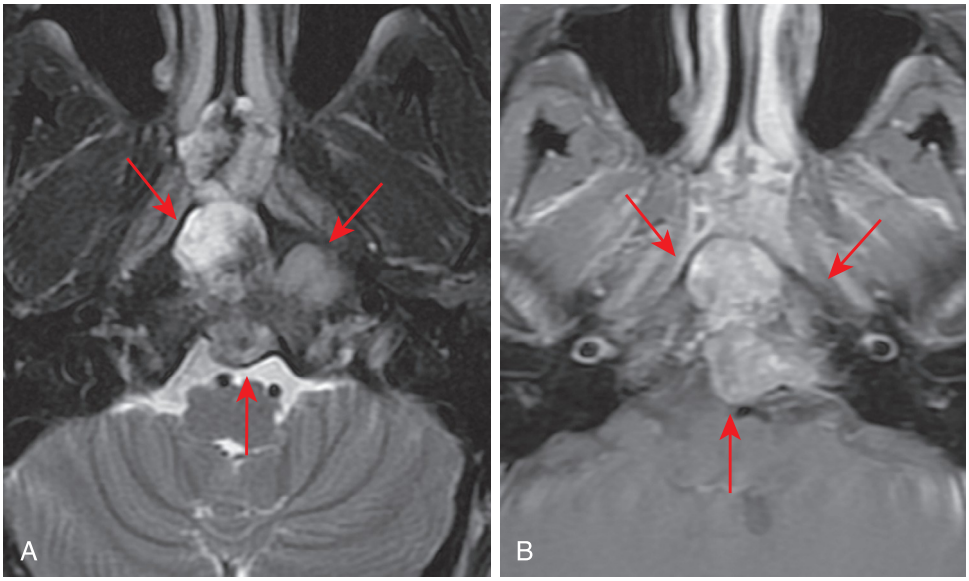

Figure 28.6. Anaplastic chordoma. Axial T2 (A) and T1 postcontrast fat-suppressed (B) images demonstrate a heterogeneous chordoma centered within the clivus *(arrows)*. Note the clival destruction and soft tissue components extending both anterior and posterior to the clivus. The chordoma has T2 intermediate signal in many areas, enhances, and has mildly restricted diffusion (not shown).

Although chordomas are confined to the neural axis, they are not evenly distributed from nasopharynx to coccyx. Thirty-five percent of chordomas are located in the head/neck and skull base region; 15% of chordomas originate within the cervical, thoracic, and lumbar spine; and 50% of chordomas occur in the sacrum and coccyx. When a chordoma arises in the nasopharynx, ethmoid air cells, and nasal cavity at the most rostral end of the neural axis, it is often excluded from the differential altogether. Here, a chordoma may resemble both nasopharyngeal carcinoma and chondrosarcoma.[4] In these cases, evaluating for lymph node metastases is helpful because 85% of nasopharyngeal carcinomas present with lymph node metastases in the neck.[5] While hematogenous chordoma metastases to lymph nodes are possible and have been published in case reports, they are rare and mostly found in advanced or recurrent disease.[6]

At the skull base, chordomas may be mistaken for dermoids, epidermoids, plasmacytomas, and chondrosarcomas. Benign dermoids and epidermoids have a high T2 signal like chordomas, but they will not enhance or cause destructive bone changes. Plasmacytomas can inhabit the midline and may have either intermediate or low T2 signal. The plasmacytomas with low T2 signal will probably not be confused for chordomas, but the plasmacytomas with T2 intermediate signal may appear indistinguishable.

Chondrosarcomas resemble chordomas due to their high T2 signal, internal septa, and local aggression. They derive from the chondroid line of cells, which may produce "ring and arc" chondroid matrix mineralization on computed tomography (CT). While internal mineralization increases the likelihood that a skull base tumor is a chondrosarcoma rather than a chordoma, it does not reliably discriminate between the two entities for several reasons.

Approximately 50% of chondrosarcoma do not mineralize. Thus the absence of mineralization does not imply chordoma. Furthermore, chordomas frequently acquire lysed native bone fragments, a by-product of their local aggression, and these fragments may mimic chondroid mineralization. Fortunately, these two tumors can be separated by their location. As a general rule, chondrosarcomas have a predilection for the petroclival synchondrosis (off-midline) while chordomas arise at the midline (often at the spheno-occipital synchondrosis).

In the cervical spine, a chordoma may be mistaken for a pharyngeal tumor if its soft tissue component extends in front of the vertebrae. Pharyngeal tumors advanced enough to transgress two fascial planes and advanced enough to invade or abut the vertebrae will have spread to multiple lymph nodes in the neck. In contrast, chordomas are unlikely to present with lymph node metastases. A chordoma may also be mistaken for a nerve sheath tumor if its soft tissue component extends laterally to the neural foramen. To distinguish chordoma from a nerve sheath tumor, scrutinize the adjacent vertebral artery. A chordoma will displace the artery away from the midline, while a nerve sheath tumor will displace the artery toward the midline.

In the sacrococcygeal spine, chordomas typically have a smaller bone component and a larger soft tissue component. They often exhibit multiple lobules with layering fluid or blood separated by internal septa, and consequently may be mistaken for benign entities such as aneurysmal bone cysts, plasmacytomas, or giant cell tumors. Aneurysmal bone cysts are expansile like chordomas, but they thin the cortical bone and remain entirely contained within the bone. In contrast, chordomas cause bone destruction and have a soft tissue component outside the bone. Giant cell tumors are harder to differentiate from chordomas because both can have dual bone/soft tissue components. Statistically, fewer than 3% of giant cell tumors occur in the spine or sacrum, unlike chordoma, which regularly involves the sacrum.[7] If the mass is centered off-midline, giant cell tumor should be primarily considered. If sequestered bone fragments are identified, chordoma should be favored.

At any location, benign notochord rests such as ecchordosis physaliphora are difficult to distinguish from chordoma because both have a similar underlying cellular composition (Fig. 28.7). Although the imaging features of benign notochord rests overlap considerably with chordoma, they are "do not touch" lesions because their clinical behavior is not malignant or aggressive (Fig. 28.8). Unfortunately, no single imaging feature can reliably differentiate these benign notochord remnants from chordoma. The key is to search for multiple clues indicating benign or nonaggressive behavior, such as smaller size (<2 cm), absent clinical symptoms,

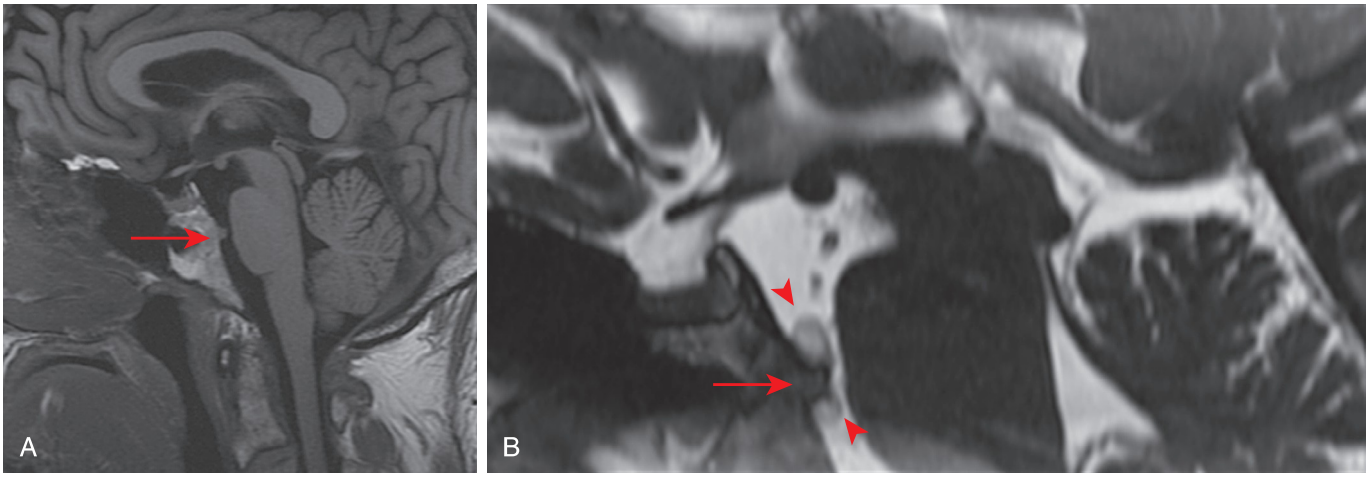

Figure 28.7. Ecchordosis physaliphora of the skull base and spine. A sagittal T1 spin echo (A) image shows a bony spicule arising from the posterior margin of the clivus *(arrow)*, a key characteristic of this benign notochord remnant at the spheno-occipital synchondrosis. This lesion was only evident on a heavily T2-weighted sagittal FIESTA image (B), and indistinguishable from surrounding CSF on T2-weighted spin echo images. Note the characteristic T2 hyperintense, small, cystic lobulations *(arrowheads)* surrounding the bony spicule *(arrow)*. The lesion did not enhance (not shown), another key imaging feature. Chordomas are associated with destructive bone components rather than hyperostotic bone components.

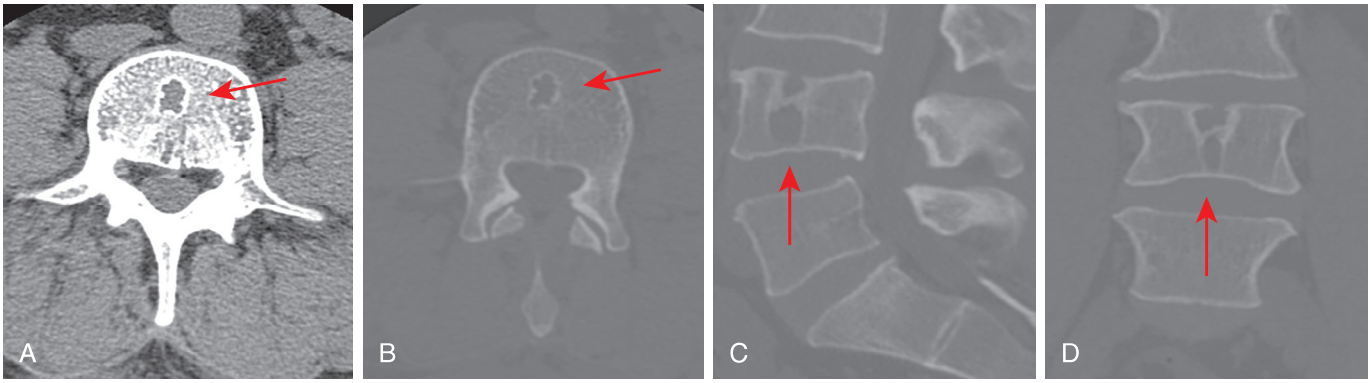

Figure 28.8. Benign notochordal remnants of the lumbar spine. Axial soft tissue window (A) and bone window axial (B), sagittal (C), and coronal (D) CT images of the lumbar spine demonstrate an L4 notochordal remnant *(arrows)*. Note the elongated contour of this lucent lesion spanning the entirety of the vertebral body. Also note the benign appearance of the lesion with a well-defined sclerotic narrow zone of transition. This lesion was unchanged for several years.

minimal or no enhancement, a bony spicule, and absent erosive/permeative bone destruction. Ultimately, stability on follow-up imaging may be the only way to ensure the notochord remnant is not aggressive. Even in these cases, it is still difficult to exclude the small subset of less aggressive chordomas that demonstrate minimal or no growth over time.[8]

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