Chordomas are slow growing, malignant tumors of bone that are thought to be derived from the primitive notochord. As such, they are classically distributed in the axial skeleton, with approximately one half occurring in the sacrococcygeal region, one third in the spheno-occipital area, and the remainder elsewhere along the vertebral column. Other tumors with similar histologic appearances have been found in the soft tissues and bones outside the axial skeleton and include entities such as parachordoma, myxoid chondrosarcoma, and extra-axial chordoma. Some authors have used the term extra-axial chordoma to refer to these tumors located outside the axial skeleton and thought to have arisen from the notochord, whereas others use the term extra-axial chordoma to include tumors thought to arise at sites distant from the notochord. Currently, it is recommended that the term extra-axial chordoma should be reserved for tumors of classic chordoma histology that have been shown to occur at sites distant from the notochord. This usage is consistent with the current recommendations of the World Health Organization.4 In this report, we present what we believe to be the sixth case of extra-axial chordoma, and review the previous cases to date. 5–12 In this report, we present what we believe to be the sixth case of extra-axial chordoma, review the previous cases of extra-axial chordoma, and compare this group with classical axial chordoma.

OBJECTIVE

Our objective was to describe a case of extra-axial chordoma that is histologically identical to classical axial chordoma, and to review the previously reported cases of extra-axial chordoma.

METHODS

A 41-year-old woman presented for a routine physical examination, and an asymptomatic mass was detected in the right pelvis. A computed tomography scan identified a 5.5 cm smooth, ovoid mass in the right lower pelvis, separate from the ovary, and indenting the right lateral aspect of the urinary bladder. Nine months later, an ultrasound examination revealed a solid 8.3 cm pelvic lesion of uncertain origin. She underwent an exploratory laparotomy, and a circumscribed, solid, but soft, tan mass was found arising from the bone of the superior pubic ramus rather than the adnexa. The lesion was bluntly dissected from minor attachments to the bladder, mobilized off the bone, and removed. Postoperative workup revealed no evidence of metastatic disease. A surgical re-excision of the primary site was planned to eliminate any residual disease. A tissue expander was placed by laparotomy in the sacroccocygeal region, one third in the spheno-occipital area, and the remainder elsewhere along the vertebral column. Other tumors with similar histologic appearances have been found in the soft tissues and bones outside the axial skeleton and include entities such as parachordoma, 2–4 skeletal or extraskeletal myxoid chondrosarcoma, and extra-axial chordoma. We herein present another case of the rare extra-axial chordoma. A 41-year-old woman developed an 8.3 cm mass in the pubic bone. The gross, microscopic, and immunohistochemical findings were identical to those of a classic chordoma. Parachordoma and myxoid chondrosarcoma were excluded from the differential diagnosis. Five previously reported cases of extra-axial chordoma were reviewed and found also to demonstrate clinical and pathologic features specific to chordoma, despite arising in an extra-axial location. Although rare, extra-axial chordoma does exist and should be recognized and managed in a similar fashion to its well-described counterpart. It must be differentiated from other histologic mimics, because the treatment and prognosis can differ significantly.

Pathologic Findings

Representative sections were fixed in 10% neutral buffered formalin and embedded in paraffin, and 5-μm sections were cut and stained with hematoxylin-eosin. Immunohistochemical studies were performed using a labeled streptavidin biotin complex technique (Ventana Medical Systems, Tucson, Ariz). The following antigens were used: cytokeratin AE1/AE3 (Ventana, mouse monoclonal, 1:20 dilution of Ventana predilute), CAM 5.2 (mouse monoclonal, 1:20 dilution of a Becton Dickinson predilute, Becton Dickinson, Mississauga, Ontario), cytokeratin (CK) 1/10 (mouse monoclonal, 1:100, Dako Corp, Mississauga, Ontario), CK7 (Cell Marque, Hot Springs, Ariz; mouse monoclonal, 1:200), CK19 (Biogenex, San Ramon, Calif; mouse monoclonal, 1:25), CK20 (Cell Marque; mouse monoclonal, 1:20), epithelial membrane antigen.
Gross examination revealed a soft, tan mass measuring 7 × 7 × 4.5 cm, along with several smaller bony fragments. On sectioning, the tumor was composed of lobules of soft, glistening, hemorrhagic and myxoid tissue with a fibrous shell. Light microscopy showed lobules, sheets, and nests of variably sized, polygonal cells lying within a myxoid matrix (Figure 1). The lobules were divided by fibrous septa, and focal hemorrhage was present. The tumor cells contained clear to eosinophilic cytoplasm and demonstrated small, round, hyperchromatic nuclei with little atypia and a low mitotic rate (Figure 2). Scattered large, clear, multivacuolated cells (‘‘physaliferous cells’’) were found (Figure 3). No glomoid or spindle cells were seen, and there was no evidence of cartilaginous differentiation. The tumor cells stained with low and high molecular weight cytokeratins (AE1/AE3, CAM 5.2, CK1/10, and CK19), EMA, vimentin, and S100 protein (Figure 4). Immunohistochemical stains for cytokeratin 20, carcinoembryonic antigen, and type IV collagen were negative. Cytokeratin 7 was equivocal. The diagnosis was that of an extra-axial chordoma.

COMMENT

The clinical features of classic chordoma are well described. The mean age at presentation is 56 years, and the average tumor size is 8 cm. There is no sex predominance. Patients typically present with pain or with symptoms re-
lated to nerve or spinal cord compression. Approximately one half arise in the sacrococcygeal region, with the remainder occurring at the skull base or elsewhere along the vertebral column. Clinical information is available in 5 of the 6 reported EAC cases (Table). The age range was 36 to 77 years, and the average tumor size was 8.6 cm. Two patients were men, and 3 were women. Although 1 patient was asymptomatic, 4 presented with a mass. The 6 tumors were found in a variety of extra-axial locations; 3 in bone (ulna, tibia, and pelvis) and 3 in the deep soft tissue (region of the knee, gluteus maximus muscle, and posterior chest wall).

Grossly, chordomas tend to form large, multilobulated, grey-tan myxoid masses. Microscopically, they are composed of variably sized myxoid lobules separated by fibrous septa. Tumor cells are arranged singly or in cords or nests. The cells are variably sized, with abundant clear, eosinophilic, or multivacuolated cytoplasm (so-called physaliferous cells). Mild cytologic atypia may be present, and membrane-bound glycogen, intermediate filaments, and prominent rough endoplasmic reticulum are also found.3,4,8-13 Electron microscopy was undertaken in 4 of the 6 EAC cases and showed indistinguishable features, including desmosomes, intermediate filaments, and intracytoplasmic lumina lined by microvilli (not shown).

The immunohistochemical profile of chordoma includes positivity for cytokeratins (CK1/10, CK8/18, CK19), EMA, vimentin, and, occasionally, S100 protein and carcinomaembryonic antigen.3,4 Sporadic reactivity is seen for type IV collagen positivity.3,4 The profile of our tumor significantly lacks CK1/10 and CK19 staining while exhibiting type IV collagen positivity.3,4 The profile of our tumor (CK1/10+, CK19+, type IV collagen −), therefore, argues against parachordoma.

Cytogenetic studies of chordoma show a variety of abnormalities. Hypertriploidy, marker chromosomes, losses of or from chromosomes 1, 3, 4, 10, and 13, and partial or whole copy number gains of chromosomes 7 and 20 have all been described.15 No EAC cases were studied by cytogenetic analysis.

Although chordoma is considered a slow growing, indolent neoplasm, it is locally aggressive with a high propensity for local recurrence. Preferred treatment includes en bloc resection in conjunction with radiotherapy. Because of the location in the axial skeleton, local recurrences cause significant morbidity and mortality, and the mean survival is approximately 4 years. Distant metastases (usually to the lung) are seen in approximately 10% of cases, and a small number (<5%) dedifferentiate to high-grade sarcomas. Treatment information was given in 5 of 6 EAC cases. All cases were excised with wide margins. In none of the patients was preoperative adjuvant radiation or chemotherapy used. One case received postoperative radiation therapy. In the 4 EAC patients with documented follow-up, 2 demonstrated metastases. Both of these patients died of metastatic disease within 11 months of diagnosis. The other 2 patients remained free of disease at 2½ and 7 years.

Other entities in the differential diagnosis must be excluded before a diagnosis of EAC can be rendered. Parachordoma is a rare soft tissue neoplasm sharing some similarities with chordoma. It typically arises in a younger age group, however, and predominantly occurs as a small soft tissue mass rather than a large primary bone tumor. Microscopically, there is considerable overlap, including the presence of rare physaliferous cells. Three unique cell types, however, are described in parachordoma, including epithelioid, spindled, and glomoid cells.3 In addition, although parachordoma may express high molecular weight cytokeratins, EMA, vimentin, and S100 protein, it significantly lacks CK1/10 and CK19 staining while exhibiting type IV collagen positivity.3,4 The profile of our tumor (CK1/10+, CK19+, type IV collagen −), therefore, argues against parachordoma.
Myxoid chondrosarcoma is also a consideration. The majority of lesions in this group are the so-called extraskeletal myxoid chondrosarcomas (ESMC). ESMCs are deep-seated soft tissue tumors that can secondarily involve bone. Our tumor clearly had a primary origin in bone. ESMC occur in a similar age group to chordoma and may also attain a large size. Lobules of myxoid stroma and small, uniform cells can also be seen, but ESMC typically lacks physaliferous cells. ESMC is vimentin and S100 protein positive but does not demonstrate cytokeratin positivity, as was demonstrated in our case. ESMC is therefore also excluded.

In this study, we summarize 6 cases of what we believe to represent typical chordoma occurring outside the axial skeleton. The extra-axial lesions are identical in terms of their clinical presentation, gross and microscopic appearance, immunohistochemical phenotype, ultrastructural features, and clinical course. Cytogenetic analysis of EAC will no doubt shed further light on the relationship to its classic counterpart.

Although the numbers are small, the evidence appears to support the recognition of a rare but well-defined entity, the extra-axial chordoma. Despite the location, the origin of these tumors is also presumed to be from notochord remnants, albeit ectopic or migratory in nature. To avoid confusion with other similar but distinctive tumors, we propose the use of the term “extra-axial chordoma.” Because these tumors appear to have a similar biologic potential as their axial counterparts, care should be taken to arrive at the correct diagnosis so the treatment can be tailored accordingly.

References