Extraskeletal Myxoid Chondrosarcoma Of Oropharynx

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Abstract
Extraskeletal myxoid chondrosarcoma is a rare soft tissue neoplasm. We report such a tumor in an 80-year-old man, who presented with a 10-cm right tonsillar mass. Histologic examination of the tumor revealed an infiltrative growth pattern, focal hypercellularity, frequent mitosis, and areas of necrosis, in addition to features commonly seen in typical cases of extraskeletal myxoid chondrosarcoma.

INTRODUCTION
Extraskeletal myxoid chondrosarcoma (EMC) is rare, with an estimated incidence of 2.3% among all soft tissue sarcomas. It has characteristic ultrastructural, molecular and cytogenetic features, although morphology on routine hematoxylin & eosin (H&E) stained sections is not always specific for a definitive diagnosis. Most of the tumors occur in the soft tissue of the extremities, especially thigh and popliteal fossa. Occurrences in synovium, pleura, maxillary sinus, epiglottis, soft tissue of the chin, and retroperitoneum have been reported. Most of these tumors are deeply seated, but occasional tumors are confined to the subcutis. Histologically, these tumors exhibit a broad spectrum of morphologic features, which make distinction from other neoplasms difficult, particularly when the tumor occurs at an unusual anatomic location.

In this report, we describe a case of extraskeletal myxoid chondrosarcoma of the oropharynx, in an 80-year-old man. Unlike typical EMC, this tumor had focally increased cellularity, necrosis, and increased mitoses.

REPORT OF A CASE
An 80-year-old black man, with a history of prostatic adenocarcinoma (stage IV, Gleason's score 8) diagnosed 6 months before, presented to the Otolaryngology Clinic with one-month history of sore throat, dysphagia, and a 10-pound weight loss. He was referred following treatment for tonsillitis. His past medical history was significant for hypertension, chronic obstructive pulmonary disease, peptic ulcer disease, and asbestos exposure. He had a 20-year-history of smoking (2 packs a day), but quit 30 years before. He received hormonal treatment for his prostate cancer.

Physical examination was remarkable for cachexia. A smooth, round, firm, submucosal mass replaced the right tonsil and caused the soft palate to bulge anteriorly. There was no cervical lymphadenopathy. MRI with Gadolinium contrast of the orbit, face, and neck revealed a large, multinodular, heterogeneous, enhancing right-sided mass that extended laterally from the pharyngeal mucosa to the parotid space, anteriorly into the base of the tongue and right posterior nasopharynx, and medially into the left posterior pharyngeal mucosal space. The mass measured 6 cm in antero-posterior dimension, 6 cm in transverse dimension, and 10 cm in superior-inferior dimension (Figure 1).

Figure 1
Figure 1: Axial MRI STIR image (heavily T2-weighted image with fat suppression). The mass is seen involving the right base of tongue and tonsil.
wall. An incisional biopsy was performed. Over the following 14 days, he experienced progressive dysphagia, dysarthria and respiratory compromise leading to death. An autopsy was not performed.

MATERIALS AND METHODS

Histopathology. Hematoxylin and eosin stained sections were prepared from formalin-fixed, paraffin-embedded biopsy tissue. Colloidal Iron and Alcian blue stains with and without hyaluronidase were performed on the tumor sections to detect the presence of chondroitin sulfates.

Immunohistochemical stains. Four-µm tissue sections were stained by using an automated stainer (Dako, Capinteria, CA) after standard deparaffinization and dehydration. A standard avidin-biotin complex technique with diaminobenzidine as the chromogen was used. Commercially acquired monoclonal antibodies against pan-cytokeratin AE1/3 (Signet, Dedham, MA), CK20, epithelial membrane antigen (EMA), alpha-smooth muscle actin, S-100 protein, glial fibrillary acidic protein (GFAP), vimentin, desmin, neuron specific enolase (NSE), CD68, CD20, CD45, CD3 and myosin (Dako corporation, Carpinteria, CA) were used as primary antibodies, using our standard laboratory protocols routinely employed for surgical pathology diagnostics.

Electron microscopy. Tumor tissue was fixed in 2.5% glutaraldehyde, postfixed in osmium tetroxide, and embedded in epoxy resin for ultrastructural studies. Ultra-thin sections were stained with uranyl acetate and lead citrate and were evaluated using a Philips CM-100 (Mahwah, NJ) electron microscope.

Reverse transcriptase polymerase chain reaction. Total RNA was extracted from formalin-fixed, paraffin-embedded (PFPE) tissue block. Detection for type 1 and type 2 transcripts of the EWS-CHN fusion protein were performed by RT-PCR, as previously described, at Memorial Sloan-Kettering Cancer Center.

RESULTS

The incisional biopsy specimen consisted of multiple irregular fragments of soft tissue with areas of hemorrhage, measuring 7 x 6.5 x 2 cm in aggregate. Areas of mucoid appearance were also noted grossly. Microscopically, a multilobular, infiltrative tumor consisted of short cords or sheets of epithelioid cells situated in an abundant myxoid background (Figure 2A). The tumor invaded tonsillar tissue and the pharyngeal mucosa. Incomplete fibrous septae separated some of the lobules. Many tumor cells had moderately abundant eosinophilic cytoplasm, resembling rhabdoid cells (Figure 2A). In other areas, tumor cells had clear cytoplasm and were embedded in fibrillar eosinophilic matrix, suggesting chondroid differentiation (Figure 2B). The nuclei were round to oval, pleomorphic, hyperchromatic, and eccentrically located. Nucleoli were inconspicuous. There were frequent mitotic figures. Histochemically, the myxoid stroma stained deeply with colloidal iron (Figure 2C) and Alcian blue, which were not inhibited by pre-treatment with hyaluronidase. Foci of necrosis were noted.

Immunohistochemically, the tumor cells stained positive for vimentin (Figure 2D). However, stains for other markers, including cytokeratin (AE1/3, CK 20), S100 protein, GFAP, EMA, desmin, alpha-SMA, myosin, CD20, CD3, CD45 and CD68, were all negative, all with appropriate positive control.

Figure 2

Figure 2: Photomicrographs of the tumor. A. H&E stain. Epithelioid cells with abundant eosinophilic cytoplasm and eccentrically located nuclei, forming cords or loose sheets (X100). B. H&E stain. Chondroid area. (X100). C. Colloidal Iron staining showing blue myxoid matrix (X50). D. Immunostaining for vimentin (X50).
Representative areas of the tumor were selected for electron microscopy by examining the thin sections. Ultrastructurally, single or strands of tumor cells were in a fine matrix, which contained scattered collagen fibers (Figure 3A). The tumor cells were loosely arranged singly, in pairs, and in short cords. The cytoplasmic membranes were irregular in outline, some with a scalloping appearance. Occasionally, there were incomplete cell junctions between cell membranes, including macular or desmosome-like interface attachments without tonofilaments. However, well-formed tight junctions or desmosomes were not identified. Most of the cells had abundant cytoplasm, with an eccentrically located nucleus, which was often indented and contained evenly distributed chromatin (Figure 3A, 3B). There were no prominent nucleoli. The cytoplasm contained well-developed rough endoplasmic reticulin with many dilated cisternae, abundant mitochondria, and prominent Golgi apparatus. In addition, there were glycogen granules and lipid droplets in many cells. The EM findings were consistent with epithelioid chondrocytes, supporting the histologic diagnosis of chondrosarcoma.

**Figure 3**
Individual tumor cells in a loose matrix containing occasional collagen fibers (x8,113). Tumor cells contain eccentrically located nuclei that shown indentation, and cytoplasm containing abundant organelle and lipid (x8,113).
Total RNA was extracted from tissue retrieved from the formalin-fixed, paraffin-imbedded block. Adequate amount of RNA was obtained. However, RT-PCR did not result in the amplification of either type 1 or type 2 transcript of the EWS-CHN fusion gene.

The case was reviewed by the pathologists from the Oral and Maxillofacial Pathology and the Soft Tissue Pathology sections of the Armed Forces Institute of Pathology, Washington, DC. They considered myoepithelial carcinoma and extraskeletal myxoid chondrosarcoma as the principal entities in their differential diagnosis and agreed with our diagnosis of extraskeletal myxoid chondrosarcoma.

**DISCUSSION**

Extraskeletal myxoid chondrosarcomas are considered low-grade sarcomas, characterized by a protracted clinical course. The estimated 10-year survival is 70%, with 48% local recurrence and 46% metastases. Meis et al. in their review of 117 EMCs, concluded that clinical features such as tumor size, tumor site, patient age and metastases, rather than histological features, are significant predictors of survival. It was suggested that high-grade histologic features, such as necrosis, increased cellularity, high mitotic rate, pleomorphism, epithelioid or rhabdoid cells, and spindled foci, do not affect prognosis. All of their cases were tumors arising in limb girdle, limbs or trunk. Our patient presented at an advanced age (80 years), with a large tumor (10 cm) in an unusual location.

Many of the H&E-stained histologic features in this case are not specific for the diagnosis of an EMC. In fact, the diagnosis of myoepithelial carcinoma was considered initially, because of the extensive myxoid component and ovoid eosinophilic cells. However, myoepithelial carcinoma was excluded because this tumor usually expresses immunoreactivity for cytokeratin, S-100 protein, smooth muscle actin, and GFAP in addition to Vimentin. The abundant myxoid stroma stained strongly with colloidal iron and hyaluronidase-resistant alcin blue, indicating the presence of chondroitin sulfates. Among soft-tissue sarcomas with prominent myxoid stroma, EMC emerged as a strong possibility. However, EMC has been reported to focally express weak S-100 protein and NSE, which were negative in our case.

A non-random reciprocal translocation between chromosomes 9 and 22, t(9;22) (q22;31; q11-12), has been described in EMCs, resulting in fusion of the EWS gene to CHN (a member of the steroid/thyroid receptor gene superfamily) gene. Although this translocation appears specific for this tumor, it is not seen in all cases. RT-PCR for this translocation was performed on our case, but with a negative result. Another related cytogenetic abnormality has been described recently, t(9;17)(q22;q11.2), in a minority of EMCs. This later translocation results in the fusion of the entire coding region of CHN to the N-terminal transactivation domain of RBP56/h TAFII68, a protein with sequence homology to both EWS and TLS/FUS. We did not test for this translocation in our case.

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**References**

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