

## Extraskelatal Myxoid Chondrosarcoma: A Case Report with Cytologic Features, Histopathology, and Variant Translocation

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### Abstract

Extraskelatal Myxoid Chondrosarcoma (ESMC) is a rare soft tissue sarcoma, of which its histopathologic and cytogenetic features have been thoroughly examined; however, limited reports on the description of the cytologic findings are present within the literature. We report a case of ESMC with typical cytomorphic and histopathologic features, and cytogenetic confirmation with expression of a variant translocation. A 75 year-old male presented with a large slow-growing right arm mass discovered on imaging studies upon initial work-up. Cytologic imprint preparations of image-guided needle core biopsies demonstrated groups of a monotonous population of round to oval cells, some with grooves, embedded within a myxoid-appearing stroma. Chromosome analysis performed on incisional biopsy tissue displayed the t (9:17) instead of the more common t (9:22) translocation, and resection of the mass provided additional histologic and immunophenotypic confirmation of the diagnosis. Although ESMC has distinctive cytologic features, these are not entirely specific, and ancillary cytogenetic studies can aid in confirmation of diagnosis resulting in the best-possible (and perhaps in the near-future, more individualized) treatment of these myxoid tumors.

**Keywords:** Extraskelatal myxoid chondrosarcoma; Variant translocation; T translocation; Myxoid tumors

### Introduction

Extraskelatal Myxoid Chondrosarcoma (ESMC) is a rare soft tissue sarcoma, first described by Stout and Verner [1], and later coined as a distinct clinicopathologic entity by Enzinger and Shiraki [2] in 1972 within a 34 case study. Patients with ESMC tend to be middle-aged adults (>35 years) with a median age in the fifth decade and a slight male predominance (approximately 2:1), although rare cases have been described in children [3]. The predominant sites are the proximal extremities and trunk. ESMC is considered a low-grade soft tissue tumor, which is usually slow-growing and well-circumscribed. However, recurrences and metastasis can occur several years after primary diagnosis. Few case reports describing the cytomorphic features of Extraskelatal Myxoid Chondrosarcoma have been reported in the literature [4-9]. We present a case with diagnostic findings on cytology with histologic and molecular confirmation.

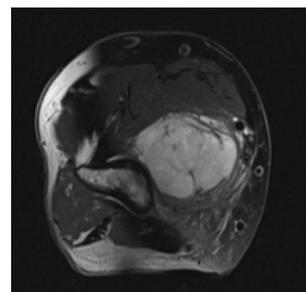
### Case History

The patient is a 75 year old male who initially presented with a right arm mass, proximal to the elbow joint. The patient reported that this mass was tender to the touch and slowly growing over several months. Imaging studies demonstrated a large heterogenous soft tissue density mass centered within the brachialis muscle, which extended from the level of the distal humeral diaphysis to the myotendinous junction. Contiguous non-contrast axial CT images showed the mass was predominantly hypo-attenuating in comparison to the adjacent skeletal muscle with no evidence for osseous invasion or invasion of the overlying neurovascular bundle. MRI with pre and post-contrast imaging demonstrated the lesion was iso to mildly T1 hyper-intense to the adjacent skeletal muscle and on T2-weighted imaging, the lesion was hyper-intense (Figure 1). Following gadolinium administration, there was enhancement of the solid component of the mass more proximally.

### Results

#### Cytology

Image-guided needle core biopsies of the mass were obtained and touch imprint preparations performed at the procedure demonstrated a relatively uniform population of round to oval cells with fine dark chromatin and inconspicuous nucleoli (Figures 2 and 3), and some with nuclear grooves to include “coffee bean” appearing nuclei (Figure 4). The tumor cells are arranged in clusters and occasional cords and embedded within a brightly metachromatic myxoid stroma (Diff-



**Figure 1:** T2-weighted MR images demonstrated a large hyper-intense nodular-appearing soft tissue mass located in the proximal right arm; (A) Axial, (B) Sagittal.

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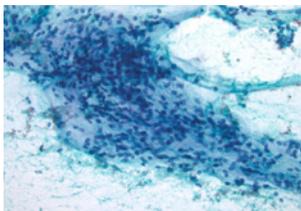
Quick stain) which is fibrillar in quality, reminiscent of pleomorphic adenoma of the salivary gland (Figure 5). On the Papanicolaou stain, the myxoid stroma exhibited a pale blue-green and more transparent appearance (Figure 6).

### Histopathology and Immunohistochemistry

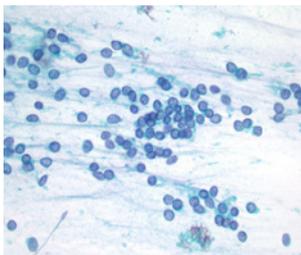
The patient later underwent resection of the tumor which measured 7.0 cm in greatest dimension and exhibited a gelatinous and nodular cut surface. Histologic examination revealed a multi-lobular tumor composed of uniform oval to elongated cells arranged in loose sheets and anastomosing cords, imparting a reticular appearance (Figures 7 and 8). The tumor cells were present in a background of abundant myxoid/mucoid material (Figure 8). The individual cells showed eosinophilic cytoplasm and vesicular nuclei with mild-to-moderate pleomorphism. Rare mitoses were identified, averaging 2 per 10 HPF. Immunohistochemical staining displayed a positive reaction for vimentin only. The CD31, CD99, Desmin, Myogenin, Smooth Muscle Actin (SMA), S-100, EMA, Lu-5 (pan-cytokeratin), Synaptophysin, and CD45 immunostains were all negative.

### Cytogenetic and molecular genetic analysis

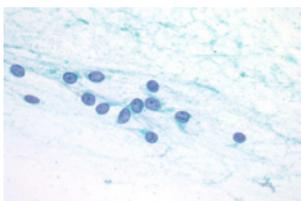
Paraffin embedded tissue from the surgical biopsy specimen was submitted for Fluorescence In-Situ Hybridization (FISH) and the tumor was found to be negative for ESWR1, FUS, and CHOP



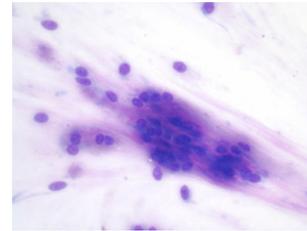
**Figure 2:** Abundant cellularity showing monotonous population of round to oval cells; Papanicolaou, X200.



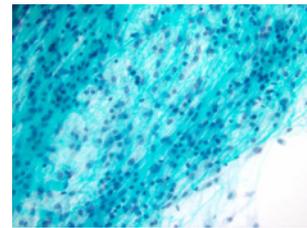
**Figure 3:** Cytologic imprint specimen demonstrates uniform cells with fine dark chromatin and inconspicuous nucleoli; Papanicolaou, X400.



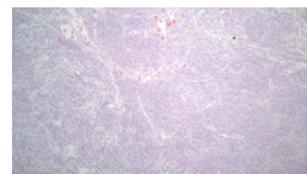
**Figure 4:** The tumor cells demonstrate occasional grooves and "coffee bean" shaped nuclei; Papanicolaou, X500.



**Figure 5:** Loose clusters of cells embedded within a metachromatic myxoid stroma with a fibrillary appearance. Diff-Quick, X400.



**Figure 6:** On Papanicolaou stain, the stroma has a blue-green pale, feathery appearance and is less prominent. Papanicolaou, X200.



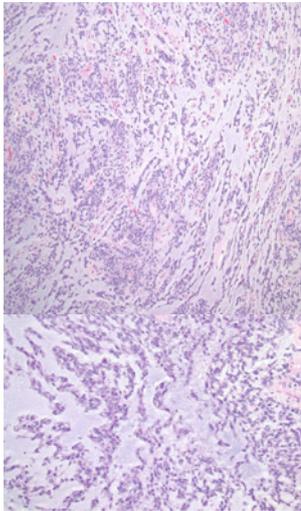
**Figure 7:** Microscopic appearance showing a lobular/nodular architecture at low power; H&E, X40.

rearrangements. However, chromosome analysis revealed a t (9;17) (q22; q11) variant translocation.

### Discussion

Extraskeletal Myxoid Chondrosarcoma is an uncommon tumor which arises predominantly in the soft tissues of the extremities with the most common location in the deep thigh. Other sites include the hand, retroperitoneum, head and neck, with rare cases arising in the retroperitoneum or the thoracic cavity. The cytologic features and immunohistochemistry, although far from specific and not entirely characteristic, can be helpful in distinguishing this entity from other neoplasms with myxoid features. More recently, ESMC has been found to demonstrate a consistent translocation, t (9; 22) (q22; q12), involving the Ewing Sarcoma (EWS) gene, resulting in a gene fusion product, and providing a more specific marker for this tumor.

Diagnostic cytomorphologic criteria for ESMC have been described in the literature among few case reports and small case series [4-9]. Common features include 1) a background myxoid matrix with embedded tumor cells, 2) anastomosing cords and lace-like arrangements or clusters of uniform round to spindle-shaped cells with bland appearing nuclei and inconspicuous nucleoli, and 3) grooved or cleaved nuclei suggesting chondroblast-like derivation; all of which were identified in our case. Other cell types have been reported to occur but only in rare cases, including epithelioid cells with vesicular nuclei, prominent nucleoli, and abundant cytoplasm;



**Figure 8:** The tumor cells are arranged in anastomosing cords imparting a reticular/lace-like appearance (A) within an abundant background stroma (B); H&E, (A) X100, (B) X200.

rhabdoid cells with hyaline cytoplasmic globules, or anaplastic cells (ranging from small blue cells to spindle cells to pleomorphic cells). However, other myxoid tumors of soft tissue should also be considered in the differential diagnosis based on cytology to include myxoid liposarcoma, myxofibrosarcoma, malignant fibrous histiocytoma, myxoid peripheral nerve sheath tumor, chordoma/parachordoma, and myxoma.

Our case demonstrated the typical ESMC histologic findings to support the initial cytologic impressions. The tumor was composed of multiple myxoid lobules, some separated by fibrous septa. The tumor cells demonstrated cord and strand-like arrangements forming netlike and linear interconnected patterns. The cells were round to stellate with hyperchromatic, uniform, round to oval nuclei and scant to moderately abundant eosinophilic cytoplasm. Mitotic activity was low and no significant pleomorphism was noted.

However, ESMC has no distinct diagnostic immunohistochemical profile and vimentin is generally expressed, as in our current case, with S-100 protein and EMA positivity reported in 20-50% and 30% of reported cases, respectively. There have been few reported cases of ESMC showing variable immunoreactivity with synaptophysin, chromogranin, and NSE, suggesting possible neuroendocrine differentiation [10].

Ancillary cytogenetic and molecular studies can be extremely useful in establishing a definitive diagnosis for ESMC. ESMC is marked by a reciprocal translocation: t(9;22)(q22;q12), generating a EWS/NR4A3 gene fusion, in approximately 75% of cases [11-13]. A variant (9;17)(q22;q11) translocation resulting in the fusion of NR4A3 gene at 9q22 with TAF15 gene at 17q11 has also been identified in ESMC [14,15]. Our case demonstrated negative FISH results with the EWSR1 and FUS probes, which correspond to rearrangements involving chromosomes 22 and 16, respectively. The negative EWSR1 FISH results corroborated the lack of the most common ESMC translocation in our case. This finding also aided in ruling out additional entities, such as Ewing's Sarcoma/PNET, which admittedly don't often demonstrate myxoid features microscopically, but can show small cell-type morphology with

rearrangements involving chromosome 22. Additionally, the negative FUS by FISH also assisted in ruling out myxoid liposarcoma (often involving rearrangements on chromosome 16), which can demonstrate myxoid features both cytologically and on histopathology, similar to those seen with ESMC. Finally, chromosome analysis performed on our case confirmed the presence of the variant t(9;17) translocation in support of the classic ESMC microscopic findings observed.

ESMC is a rare tumor which should be considered in the differential diagnosis when encountering a myxoid soft tissue neoplasm, especially given the large number of distinct entities which share the common feature of a myxoid background. Therefore, a multi-modal approach to include histopathologic correlation and the utilization of ancillary cytogenetic and molecular testing may be necessary in establishing a more definitive diagnosis, which may ultimately lead to a more targeted and specific treatment for patients.

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