Myxopapillary ependymoma: Lesser known cytomorphologic features

ABSTRACT
Myxopapillary ependymoma (MPE) is a rare and distinctive tumor which occurs in the sacrococcygeal area of young adults and children, often intradural in location. Histopathologic features have been well-described in the literature whereas cytological findings have been sporadically reported by various authors mainly as case reports. We report the features of a primary sacrococcygeal MPE on aspirate cytology in a 45-year-old female. Cytology smears displayed a papillary pattern with the presence of fibrovascular cores, rimmed by cuboidal to columnar cells sending fibrillary cytoplasmic processes forming pseudorosettes along with the presence of hyaline globules, and myxoid material. Intranuclear inclusions, nuclear grooves, cytologic atypia or mitotic activity was not evident, in this case. MPEs need to be differentiated from the other tumors occurring in this location which may also show myxoid material and papillary fronds. Hence, the recognition of the characteristic cytologic features plays an important role in establishing a preoperative diagnosis.

Key words: Cytomorphology; myxopapillary ependymoma, sacrococcygeal

Introduction
Myxopapillary ependymoma (MPE) is a rare variant of conventional ependymoma which arises from the ependymal cells lining the subarachnoid space. It most commonly affects young adults and children. The male-female ratio of this tumor is 2.2:1.2.

It is categorized by the World Health Organization as a Grade 1 lesion and is found predominantly in the sacrococcygeal region most often near the filum terminale or conus medullaris.

The tumor is usually slow growing, is often intradural although local extension into paravertebral soft tissue and adjacent bone is occasionally seen.

Myxopapillary ependymomas have also been described in extra-spinal locations including extradural/subcutaneous tissue, cervical thoracic spine, and the brain.

The prognosis is excellent especially for smaller lesions where complete resection is curative. Incomplete resection may lead to local extension into soft tissue and widespread dissemination into the subarachnoid space.

Distant metastases have been reported almost exclusively in tumors that invade lumbosacral soft tissue.

Case Report
A 45-year-old woman presented with pain and swelling in the lower back and buttocks for more than 8 years and had recently developed sciatica and bowel incontinence. There was no history of trauma. On examination, the region over L4-L5 and sacral spine was tender with a diffuse swelling measuring 11 cm × 10 cm. Magnetic resonance imaging scan showed a large heterogeneous presacral soft tissue mass lesion measuring 11.5 cm × 10.5 cm causing destruction of the L5 vertebra and sacrum with replacement of spinal and sacral canal contents. Left iliac bone was destroyed
posteriorly. Ano-rectum was displaced laterally, and the bladder and uterus compressed anteroinferiorly. L5-S1 disc showed partial involvement posteriorly by the mass lesion. A possible diagnosis of chordoma was suggested. The patient was referred for fine needle aspiration (FNA) cytology. The aspirate was mucinous. Slides were air-dried and fixed in alcohol and stained by Giemsa and Papanicolaou stain, respectively. Smears were highly cellular displaying a papillary pattern with fibrovascular cores; some clusters of cells were arranged in pseudorosettes with a central myxoid to hyaline area surrounded by a radial layer of cuboidal to columnar cells. Hyaline globules, fibrillary cytoplasmic structures, and myxoid material were also seen [Figures 1-3]. The nuclei of these cells were round to oval with speckled chromatin. Intranuclear inclusions, nuclear grooves, cytologic atypia or mitotic activity was not evident.

Based on these cytomorphologic features, a possibility of MPE was suggested, and the patient was taken up for surgery. The tumor, although adherent to several surrounding structures was resected. Histopathological examination confirmed the FNA diagnosis of MPE and demonstrated a branching papillary pattern characteristic of the tumor. Intercellular myxoid substance was present often surrounding central capillaries. The tumor was immunoreactive for vimentin and glial fibrillary acidic protein (GFAP) and negative for cytokeratin, excluding the possibility of chordoma as was suspected clinically and radiologically.

Discussion

Myxopapillary ependymomas were first described by Kernohan in 1932 and are now identified as a separate and distinct tumor.\[8\]

Previous authors have described the cytomorphologic features including pseudorosettes composed of myxohyaline material rimmed by neoplastic cells. The ependymal cells appear singly and in multiple layers surrounding the myxoid material, with prominent cytoplasmic processes. Additional findings were identified which included tumor cells appearing in a monolayer or sheet-like fashion, intracytoplasmic vacuoles, sparse mitotic figures, and intranuclear inclusions.

The differential diagnoses of myxomatous primary tumors can be confusing because of the overlapping cytomorphologic features. Careful attention to cell type, tinctorial qualities of the extracellular substance and architectural features allow accurate interpretation. The overall accuracy of FNA in the other spinal locations has been reported to range between 72% and 95% in different series.\[9\]

The cytologic differential diagnosis of MPE include paraganglioma, chordoma, neurofibroma, extraskeletal chondrosarcoma, metastatic papillary carcinoma, and metastatic mucinous carcinoma.\[10\]
Neoplasms consistently characterized by an abundance of myxoid, myxoid chondroid, or mucinous stromal substances also include myxoma, myxoid liposarcoma, myxoid neurofibroma, chordoma, extraskeletal myxoid chondrosarcoma, myxofibrosarcoma, and aggressive angiomyxoma. The cytomorphology of these neoplasms has been described by Wakely.\textsuperscript{[11]}

The tumor cells in MPE are immunoreactive for vimentin and GFAP. 50% of the cases stain positively for S100 protein. Ultrastructurally, the cells may contain nonciliated intracytoplasmic lumens or abnormal arrays of microtubules.

Paragangliomas may manifest a pseudopapillary pattern with mucoid vascular change, and cause a diagnostic difficulty. They, however, react positively for chromogranin and are negative for GFAP.

Fine-needle aspiration of chordoma often yields small, isolated clusters of epithelioid cells among a fibrillary, chondromyxoid background. The tumor cells have an abundant pale bubbly cytoplasm and well-defined cell borders. These cells express cytokeratin. Papillary fronds with central capillaries are not a feature. Ultrastructurally chordoma cells contain though nonspecific intracytoplasmic mitochondrial endoplasmic reticulum complexes.\textsuperscript{[12]}

None of the above-mentioned entities in the differential diagnosis express GFAP, which is typically demonstrated in MPE.

Ahuja \textit{et al.}\textsuperscript{[13]} studied cytomorphology of MPE along with immunocytochemical findings on alcohol fixed smears. The panel of immunocytochemical stains carried out included GFAP, S-100 protein (S100), pancytokeratin (CK), and epithelial membrane antigen (EMA). The tumor cells showed strong positivity for GFAP, which highlighted the cytoplasmatic processes. EMA and CK were negative, supporting the cytological diagnosis of MPE.\textsuperscript{[13]}

Takei \textit{et al.}\textsuperscript{[14]} reviewed touch imprint smears of 13 MPE cases. They observed variably cellular specimens composed of isolated and loosely aggregated tumor cells with round to oval or occasionally spindle-shaped nuclei, evenly distributed, finely granular chromatin and fibrillary processes admixed with occasional epithelioid tumor cells. Most of the cases showed prominent fibrillary processes and occasional epithelioid tumor cells with at least a focal myxoid background. Hyaline globules and hemosiderin-laden macrophages were often seen. Papillary structure, a histologic hallmark of MPE, was rarely observed.

Bradly \textit{et al.}\textsuperscript{[15]} studied cytological features of MPE's on crush preparations. The cytologic findings in six cases were reviewed. The epithelial component of MPE showing tumor cells appearing singly or in loose clusters, most with papillary branching. There was also presence of indistinct cell boundaries, tapered cytoplasmic prolongations, wispy/fragile cytoplasm, and uniform oval-to-fusiform shaped nuclei with an evenly distributed chromatin pattern. The stromal component was composed mainly of thick, metachromatic material and adenoid cystic-like areas. One case showed rosette-like structures.

A diagnostic algorithm with regard to immunohistochemical findings of myxoid and mucinous tumors of the sacrum and presacral tissues is discussed in Table 1.

The correct preoperative cytologic diagnosis is essential for surgical planning and patient counseling since it carries completely different prognostic significance. The prognosis of this tumor is good, with curability more dependent on resectability than histologic features. Local recurrence occurs in incompletely resected tumors. The tumor has potential to metastasize to the lung, liver, and lymph node. Prolonged postoperative follow-up is necessary as late recurrences may occur.

### Table 1: Immunohistochemical findings in myxoid and mucinous tumors of the sacrum and presacral tissues

| Tumor                          | S-100 | CEA | GFAP | Cytokeratin | AE1,3 | CAM 5.2 |
|-------------------------------|-------|-----|------|-------------|-------|---------|
| Chordoma                      | +     | ±   | +    | +           | +     | +       |
| Extraskeletal chondrosarcoma   | +     | −   | −    | −           | −     | −       |
| Myxopapillary ependymoma (50%)| +     | −   | +    | −           | +     | rare    |
| Adenocarcinoma                 | −     | +   | −    | −           | −     | −       |

GFAP: Glial fibrillary acidic protein, CEA: Carcinoembryonic antigen

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