



# Extraskelatal Myxoid Chondrosarcoma of Nasopharynx: An Oncologic Entity Rarely Reported

Abhishek Purkayastha<sup>1\*</sup>, Neelam Sharma<sup>1</sup> and Vibha Dutta<sup>2</sup>

<sup>1</sup>Department of Radiation Oncology, Army Hospital Research and Referral, New Delhi, India

<sup>2</sup>Department of Pathology and Molecular Science, Army Hospital Research and Referral, New Delhi, India

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## ABSTRACT

Extraskelatal myxoid chondrosarcoma (ESMC) is an extremely rare variant of chondrosarcoma accounting for less than 10% cases. It affects mainly the soft tissues of the proximal end of long bones. Its incidence in the head and neck region is less than 5%. This case presented in the nasopharynx, an exceedingly unusual site for ESMC in a 60-year-old female with left-sided nasal obstruction and occasional epistaxis of one-year duration. Biopsy from the nasopharyngeal mass was suggestive of low-grade chondrosarcoma. She underwent endoscopic resection of the tumor. Postoperative histopathology confirmed the diagnosis as myxoid chondrosarcoma of nasopharynx after performing a battery of immunohistochemical markers to rule out other possible differential diagnoses. We treated her with conformal adjuvant radiotherapy to a dose of 66 Gray in 33 fractions given residual disease to which she responded well with significant symptomatic and radiological improvement. The patient has been on regular follow-up for over two years without any evidence of recurrence or distant metastasis. This case is presented to highlight the extreme rarity, the clinicopathological findings of this disease, and to emphasize the role of radiotherapy as the primary adjuvant treatment affecting the final prognosis. A thorough review of the literature reveals that our case may be the second case of myxoid chondrosarcoma of nasopharynx ever reported in the world literature to date.

**E**xtraskelatal myxoid chondrosarcoma (ESMC) is a soft tissue malignancy with a predilection for soft tissues of long bones.<sup>1,2</sup> ESMC is exceedingly rare in the nasopharynx, posing a diagnostic and therapeutic dilemma due to its location, vast array of differential diagnosis, and only one previously reported case<sup>3</sup> without any definite therapeutic guidelines. Wide excision of the lesion is regarded as the initial treatment of choice.<sup>1</sup> Radiotherapy remains the cornerstone of adjuvant therapy due to the high probability of local recurrence<sup>1,2</sup> and also as a palliative option in metastatic or progressive cases.<sup>4</sup>

## CASE REPORT

A 60-year-old female presented with left-sided nasal obstruction and occasional epistaxis of one-year duration. Nasal endoscopy showed a pink, smooth, polypoid, fleshy growth occupying the whole of the nasopharynx. Biopsy suggested a low-grade tumor favoring myxoid chondrosarcoma. Magnetic

resonance imaging [Figure 1] showed a 3.5 × 3.4 × 6.7 cm well-defined hyperintense expansile soft tissue lesion arising from the nasopharynx, invading sphenoid and clivus. Cervical lymphadenopathy was absent. Metastatic workup was negative.

The patient underwent endoscopic resection with piecemeal excision of the tumor. Histopathological report (HPR) revealed tumor cells arranged in cords, reticulae, strands, and trabeculae interspersed within a myxoid stroma. The tumor cells were spindle- to stellate-shaped with round to oval hyperchromatic nuclei and scanty eosinophilic cytoplasm. Resection margins were positive for tumor. Immunohistochemistry was positive for vimentin and synaptophysin [Figure 2] while negative for pan-Cytokeratin (panCK), P-40, S-100, epithelial membrane antigen (EMA), chromogranin, melan-A, desmin, smooth muscle actin (SMA), neuron-specific enolase, CD99, CD56, CD20, CD45, and glial fibrillary acid protein (GFAP), thus confirming ESMC. Given the gross residual disease and positive resection margins, the patient



**Figure 1:** Sagittal section of T2-weighted magnetic resonance imaging showing well-defined hyperintense expansile soft tissue lesion arising from the nasopharynx, invading sphenoid and clivus (red arrow).

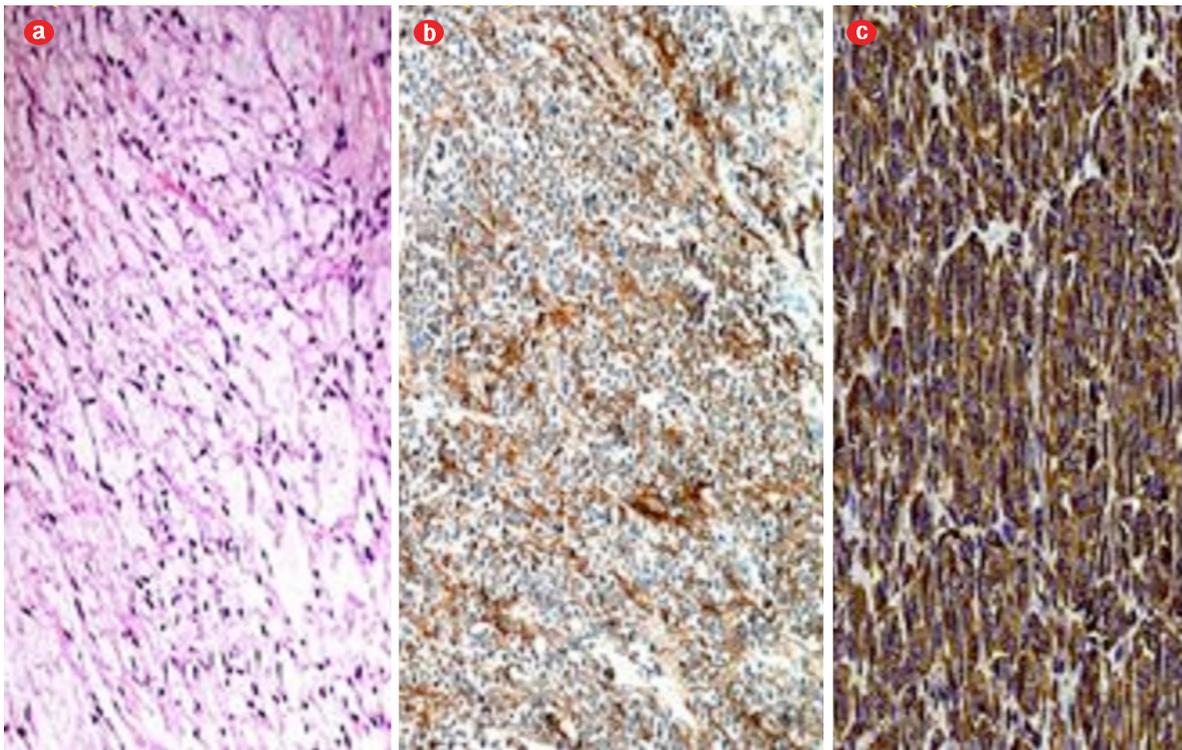
was treated with adjuvant conformal radiotherapy to a dose of 66 Gray (Gy) in 33 fractions to which she showed excellent symptomatic and radiological

improvement [Figure 3]. Presently she is on follow-up for over two years without any evidence of local recurrence or distant metastasis.

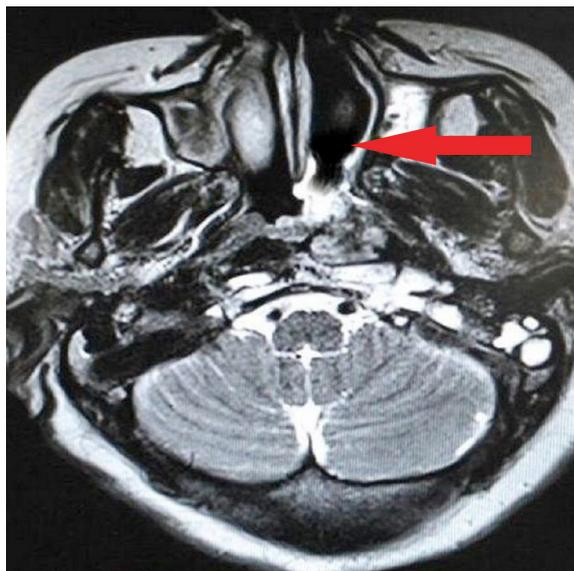
## DISCUSSION

Chondrosarcoma is a slow-growing malignant tumor of skeletal and extraskeletal origin comprising less than 1% of all head and neck tumors.<sup>4</sup> Chondrosarcoma has several histological variants, with the myxoid subtype having a predominant soft tissue origin accounting for less than 10% cases<sup>5</sup> and less than 5% of all head and neck malignancies.<sup>5</sup> ESMCs most commonly involve the soft tissue of long bones of lower extremities.<sup>1,2</sup> Other sites affected include the lung, spine, scrotum, testis, synovium, mammary gland, vulva, and abdominal wall.<sup>1</sup>

There have been few case reports of ESMC of the oropharynx, masticator space, infratemporal fossa, cerebellopontine angle, orbit, chin, nasal septum, nasal cavity, buccal space, and sphenoid sinus. Nimonkar et al,<sup>6</sup> treated a solitary case of ESMC of the maxilla in a 12-year-old girl with surgery and adjuvant radiotherapy with disease-free survival (DFS) of 10 months. Jérôme-Marson



**Figure 2:** Hematoxylin and eosin staining revealed (a) Histopathological report showing tumor cells arranged in cords, reticular pattern, strands, and trabeculae interspersed in a myxoid stroma, magnification = 40 ×. (b) Positive staining for vimentin, magnification = 20 × and (c) synaptophysin, magnification = 10 ×.



**Figure 3:** Axial section of magnetic resonance imaging post-adjuvant radiotherapy showing a significant radiological response.

et al,<sup>7</sup> reported two cases of ESMC involving nasal cavity and sphenoid sinus. In both cases curative surgery was not possible and adjuvant radiotherapy was given. Ganguly and Mukherjee<sup>1</sup> reported a case of maxillofacial ESMC managed with surgery and radiotherapy with DFS of one year while Zaki et al,<sup>8</sup> reported one case of ESMC of neck treated with chemoradiation. Following an extensive literature search, we could find only one case of nasopharyngeal ESMC reported in 2011 by Bhalla and Osipov.<sup>3</sup> Here, we present the second case of ESMC of nasopharynx reported to date.

The exact etiology of ESMC is still unknown.<sup>1,2</sup> Several theories like primitive cartilage forming mesenchyme, chondroblastic differentiation, synovial intimal cells, past surgical or traumatic insult, inhalation of chemical carcinogens,<sup>1</sup> multiple hereditary exostoses, intravenous thorotrast, previous irradiation, Maffucci syndrome, and Ollier disease<sup>4</sup> have been postulated, but none has been considered satisfactory. No association has been found with Epstein-Barr virus or consumption of salted fish.

ESMC is known to metastasize to lungs, bones, brain, lymph nodes, and testes.<sup>1</sup> Primary nasopharyngeal ESMC can often be misdiagnosed with squamous cell carcinoma nasopharynx, melanomas, lymphomas, soft tissue sarcomas, Ewing sarcoma, skeletal chondrosarcomas, chordomas, parachordomas, myoepithelial

carcinoma, myxopapillary ependymomas, chordoid meningiomas, and myxoid liposarcoma.<sup>1</sup>

Microscopic features of cords and lobules of neoplastic cells dispersed within a myxoid matrix are characteristic of ESMC.<sup>9</sup> Individual tumor cells are often round to oval with scant or moderate eosinophilic cytoplasm and pleomorphic nuclei with rhabdoid and epitheloid cells scattered at periphery.<sup>9</sup> ESMC expresses neuroendocrine differentiation with strong immunopositivity for vimentin and synaptophysin<sup>7</sup> and weak or focal positivity for EMA and S-100.<sup>7</sup> Myxoid matrix with lobulated neoplastic cells is also seen in chordoma, parachordoma, chordoid meningiomas, and myxopapillary ependymoma. However, chordomas stain positive for panCK and EMA and negative for GFAP while parachordomas are positive for EMA, S-100, panCK, and vimentin with abundant type IV collagen.

Chordoid meningiomas are positive for EMA, negative for panCK and GFAP while myxopapillary ependymomas are positive for GFAP and negative for EMA. Myxoidstroma with vimentin positivity is seen in myxoid liposarcoma, but the presence of lipoblasts rules out ESMC. An eosinophilic cytoplasm is also present in myoepithelial carcinoma, but it shows positivity for panCK, SMA, and p63 apart from vimentin, S-100, and EMA. Demonstration of two translocations  $t(9;22)$  and  $t(9;17)$  by reverse transcription polymerase chain reaction is required to confirm the diagnosis of ESMC.<sup>1</sup>

Surgical excision has been the initial treatment of choice as chondrosarcoma is traditionally regarded a radio-resistant tumor.<sup>1</sup> Since nasopharyngeal malignancies cannot be resected with wide surgical margins due to their anatomic location and proximity to critical structures, adjuvant radiotherapy plays a major role in treatment. Since no specific dosage schedule has been mentioned for nasopharyngeal ESMC, we used a dose of 66 Gy in 33 fractions given margin positivity. Chemotherapy has been effective in patients with metastatic or progressive ESMC<sup>2</sup> and mesenchymal chondrosarcomas.<sup>4</sup> Chemotherapeutic drugs like doxorubicin, ifosfamide, cisplatin, gemcitabine, dacarbazine, interferon-alpha, and imatinib have been utilized without any significant long-term effect.<sup>1</sup> Sunitinib has been used in metastatic ESMC expressing EWSR1/TAF15-NR4A3 translocation with satisfactory results.<sup>10</sup>

## CONCLUSION

The diagnosis of ESMC of nasopharynx should always be considered in patients presenting with nasal obstruction and epistaxis with a soft tissue mass on nasal endoscopy. A better interpretation of the molecular and biological mechanism of the disease process may help to devise therapeutic strategies to counter this entity. More sophisticated diagnostic techniques, improved cytogenetic analysis, novel targeted therapies, and optimal radiotherapy dosages should be devised to improve the disease-free and overall survival of patients.

### Disclosure

The authors declared no conflicts of interest.

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