Case Report

Nasopharyngeal melanoma: An unusual entity

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Abstract Nasopharyngeal melanoma is a rare condition with an estimated incidence of about 0.3/10 lac per year and has a slight female predominance. It can arise from stem melanocytes and mature melanocytes of the submucosa that have acquired genetic alterations, may be due to tobacco, trauma and oxidative stress. It resembles other common polypoidal lesions; therefore, histopathological examination with immunohistochemistry plays a pivotal role in confirming the diagnosis. Lack of specific clinical features often leads to a delay in diagnosis.

Keywords: Melanoma, mucosal, nasal obstruction, nasopharynx, primary

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INTRODUCTION

Primary mucosal malignant melanomas of the head—and-neck region account for 0.8%–3.7% of all melanomas and 0.03% of all cancers. Nasopharyngeal melanoma (NM) is a rare condition with an estimated incidence of about 0.3 million per year. Weber reported the first case of mucosal melanoma of the head-and-neck region in 1856. In 1965, Kully and Shreedharan reported the first case of NM in India. It can arise from stem melanocytes and mature melanocytes of the submucosa that have acquired genetic alterations, may be due to tobacco, trauma and oxidative stress. At times, these tumors are amelanotic and are often mistaken for ordinary nasal polyposis resulting in a broader differential diagnosis at this site.[1,2]

Here, we describe a rare case report of NM in a 72-year-old female.

CASE REPORT

A 72-year-old female presented to ENT OPD with chief complaints of progressive left side nasal obstruction, headache and sporadic episodes of epistaxis for 3 months. Clinical examination revealed a large, fleshy, bluish-red and friable mass completely blocking the left nasal cavity. Investigations including blood counts were within normal range and no significant abnormality was noted on the chest X-ray. On contrast-enhanced computerized tomography paranasal sinus (PNS), a polypoidal soft tissue mass was noted obliterating the left choana and protruding into the nasopharynx on the left side. The clinical differential diagnoses were inverted papilloma and sinonasal carcinoma.

Endoscopic biopsy was done subsequently and tissue from the mass in the left nasopharynx and nasal cavity was sent in two separate containers for histopathological examination. Grossly, multiple creamy white to dark brown soft-tissue pieces were received in 10% neutral buffered formalin in both the containers, measuring 2 cm × 1 cm × 0.5 cm and 1 cm × 0.5 cm × 0.2 cm, respectively. Whole tissue was processed following the standard protocol and hematoxylin and eosin-stained sections were examined.

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On microscopic examination, tumor tissue bits from the left nasopharynx revealed predominantly ulcerated epithelial lining. Occasional bits showed a lining of parakeratinized stratified squamous epithelium. Stroma showed tumor cells in sheets. These cells were polygonal having large vesicular nuclei, prominent nucleoli and a moderate amount of ill-defined cytoplasm [Figure 1a and b]. Focally, cells showed cytoplasmic brown pigment melanin, which stained positive with Masson Fontana. Many pigment laden macrophages were admixed with tumor cells. Necrotic bits showed inflammatory cell infiltrate. Hence, Histopathological diagnosis of NM was considered, which was confirmed with immunohistochemistry (IHC).

On IHC, the tumor cells showed positivity for S100 and HMB45 [Figure 2a and b]. The tumor cells were negative for pancytokeratin AE1/AE3 [Figure 2c].

The patient was referred to a higher center for radiotherapy. Her condition on completion of therapy was satisfactory. No evidence of metastases was observed.

DISCUSSION

Mucosal malignant melanomas are a rare type of neural crest-derived neoplasms that originate from melanocytes that are normally present in the mucous membrane of PNSs and nasal cavities in about 20% of the population.[1] They are also found in the brain where they produce neuromelanin. There is no definite sex predominance, although females are slightly more commonly affected than males. The median age of presentation is 64.3 years (range: 50–80 years).

Molecular alterations in melanomas vary by site of origin. The molecular profile of mucosal melanomas is dissimilar in comparison to cutaneous and uveal melanomas. The mucosal melanomas have higher rates of KIT mutations/amplification (25%) followed by NRAS mutations (15%–20%) and rare BRAF mutations (<6%). In contrast, ocular melanomas have higher rates of BAP1 (50%) and GNAQ mutations (50%), whereas the frequency of BRAF mutations is 0% in them.

Grossly, a variety of appearances may be seen, including polypoid or sessile, brown, black, pink or white, friable to rubbery masses ≥1.0 cm, which results in obstructive signs and symptoms. Histologically, surface ulceration is often present, but when the surface epithelium is intact, junctional or pagetoid changes may be present. The cells are round to oval and tend to be markedly pleomorphic. They have increased nuclear-to-cytoplasmic ratio, vesicular to hyperchromatic nuclei, prominent eosinophilic nucleoli, and eosinophilic to clear-appearing cytoplasm. Nuclear pseudoinclusions and nuclear molding are present. The epithelioid cells may have plasmacytoid features with eccentrically located nuclei and eosinophilic cytoplasm, but in contrast to plasma cell proliferation the nuclear chromatin pattern is more densely hyperchromatic and there is no para nuclear clear zone.

As many as 50% of lesions are amelanotic, resulting in a broader differential diagnosis at this site and delay in the diagnosis. IHC evaluation is necessary, particularly in amelanotic tumors. S100 and melanocytic markers (HMB45, Melan-A, tyrosinase, MITF and SOX10) show variable sensitivity depending on the morphological type. For both S100 protein and HMB-45, the intensity of staining is strong and the extent is diffuse. HMB-45 reaches 100% specificity for melanoma. It is often difficult to distinguish a metastasis from a primary neoplasm. However, a *de novo* primary NM is much more likely than a metastasis. At the time of the diagnosis, up to 50% of patients with primary

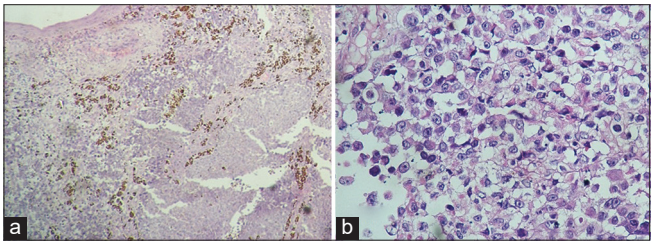

Figure 1: (a) Photomicrograph from the nasopharyngeal tissue showing infiltrating tumor cells and brown pigment ?melanin (H&E, ×100), (b) photomicrograph showing sheets of polygonal tumor cells having large vesicular nuclei, prominent nucleoli and ill-defined cytoplasm (H&E, ×400)

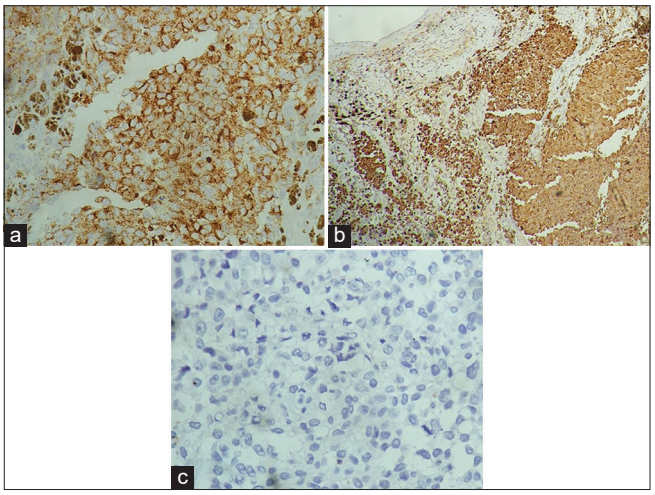

Figure 2: (a) Tumor cells showing strong cytoplasmic and nuclear S-100 positivity (immunostaining S100, ×100), (b) tumor cells showing strong cytoplasmic positivity of HMB-45 (immunostaining HMB-45, ×400), (c) photomicrograph showing negative immunoexpression of AE1/AE3 in tumor cells (immunostaining pancytokeratin AE1/AE3, ×400)

NM develop distant metastases to the brain, liver and lungs.[1] Computed tomography and positron emission tomography are the necessary investigations to detect any systemic involvement and guide appropriate management. Differential diagnoses are undifferentiated small blue cell tumors of sinonasal tract, olfactory neuroblastoma, sinonasal undifferentiated neuroendocrine carcinoma, Ewing's sarcoma, peripheral neuroendocrine tumor and rhabdomyosarcoma. Other differentials include squamous cell carcinoma and non-Hodgkin lymphoma.[1]

Surgical excision of the tumor is considered as the gold standard treatment.[1-5] Local recurrence is common within a year of surgery. Although re-excision can be considered, it is usually followed by disseminated disease. Radiotherapy is indicated in cases of local recurrence or positive surgical margins. Radiation after the surgery improves local control. Systemic treatment includes immunotherapy and targeted therapy, which offers scope for modifying the course of disease. Conventional chemotherapy is now rarely given in melanoma[6]. Most of the head-and-neck mucosal melanomas are T3-4 and associated with poor overall survival (<30%) at 5 years.[3,7-9] Hence, a close follow-up for 5 years is recommended.

CONCLUSION

NM is a rare tumor with a poor prognosis. It should be considered in differential diagnosis during clinical evaluation of nasal polyposis or epistaxis to provide early diagnosis and timely management of the patient.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. 1. Paolino G, Didona D, Macri G, Calvieri S, Mercuri SR. Nasopharyngeal Melanoma. In: Scott JF, Gerstenblith MR, eds. Noncutaneous Melanoma. Chapter 4. Brisbane (AU): Codon Publications; 2018.
2. Grewal DS, Lele SY, Mallya SV, Baser B, Bahal NK, Rege JD. Malignant melanoma of nasopharynx extending to the nose with metastasis in the neck. J Postgrad Med 1994;40:31-3.
3. Naggar AK, Chan JK, Grandis JR, Takata T, Slootweg PJ. World Health Organization Classification of Head and Neck Tumours. 4th ed. France: International Agency for Research on Cancer; 2017. p. 106-17.
4. Mardi K. Primary mucosal malignant melanoma of nasopharynx: A rare case report. J Cancer Res Ther 2014;10:416-8.
5. Maza-Salano JM, Sanchez-Gomez S, Herrero-Salado TF, Estrada-Molina F. El melanoma nasofaringeo: Una enidad infrecuente. Acta Otorhinolaringol Esp 2014;65:314-6.
6. Tyrrell H, Payne M. Combatting mucosal malignant melanoma: Recent advances and future perspectives. Melanoma Manag 2018;5:MMT11.
7. Bachar G, Loh KS, O'Sullivan B, Goldstein D, Wood S, Brown D, *et al*. Mucosal melanomas of the head and neck: Experience of the Princess Margaret Hospital. Head Neck 2008;30:1325-31.
8. Dauer EH, Lewis JE, Rohlinger AL, Weaver AL, Olsen KD. Sinonasal melanoma: A clinicopathologic review of 61 cases. Otolaryngol Head Neck Surg 2008;138:347-52.
9. Lund VJ, Chisholm EJ, Howard DJ, Wei WI. Sinonasal malignant melanoma: An analysis of 115 cases assessing outcomes of surgery, postoperative radiotherapy and endoscopic resection. Rhinology 2012;50:203-10.