

Mucosal Malignant Melanoma of the Maxillary Sinus

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SUMMARY

Mucosal malignant melanoma (MMM) is an aggressive tumour occurring in the upper respiratory tract. It is rare compared to malignant melanoma of the skin. We report a case of a 53-year-old man with left paranasal swelling. A biopsy showed high-grade spindle cell tumour. Subsequently a subtotal maxillectomy was performed. Histopathological examination revealed a hypercellular tumour composed of mixed spindle and epithelioid cells with very occasional intracytoplasmic melanin pigment. The malignant cells were immunopositive for vimentin, S-100 protein and HMB-45. It was diagnosed as mucosal malignant melanoma (MMM). This article illustrates a rare case of MMM where the diagnosis may be missed or delayed without proper histopathological examination that include meticulous search for melanin pigment and appropriate immunohistochemical stains to confirm the diagnosis. Malignant melanoma can mimic many other types of high-grade malignancy and should be considered as a differential diagnosis in many of these instances.

KEY WORDS:

Mucosal malignant melanoma, Paranasal swelling, Melanin, S-100 protein, HMB-45

INTRODUCTION

Primary mucosal malignant melanoma (MMM) is relatively rare compared to cutaneous malignant melanoma and has more aggressive clinical course. This case illustrates MMM that can masquerade other high-grade malignant tumours such as undifferentiated carcinoma, anaplastic large cell lymphoma, and various sarcomas. High index of suspicion and thorough histopathological examination together with immunohistochemical stains are essential to arrive at an accurate diagnosis.

CASE REPORTS

A 53-year-old man presented with left cheek swelling for one month. A biopsy performed was diagnosed as high-grade malignant spindle cell tumor. Extraoral examination revealed a soft and tender left paranasal swelling extending to the left medial canthal region. Neck lymph nodes were not palpable. Intraorally, there was left buccal sulcus swelling crossing the midline from right upper central incisor to left first molar region. A repeat biopsy was reported as high-grade malignant

spindle cell tumour. Subsequently endoscopic subtotal maxillectomy via degloving approach and reconstruction of the palatal defect with dental obturator was performed. [Figure 1]

The specimen showed an irregular tumour measuring 55x50x40 mm occupying the left maxillary sinus. This was a polypoidal brownish tissue extending from the floor of the maxillary sinus infiltrating into the facial tissues and muscles laterally, to the hard palate inferiorly and protruding through the antrum superiorly and medially. Microscopically, there were hypercellular mixed spindle and epithelioid malignant cells interspersed by large areas of necrosis. Mitoses were 20 per 10 high power fields. Vascular and perineural invasion and occasional osteoclastic type giant cells were identified. All resected margins were free from the tumour except the margin at the facial muscle. There were occasional intracytoplasmic brown pigments. [Figure 2] The differential diagnoses included malignant melanoma, fibrosarcoma, leiomyosarcoma, malignant peripheral nerve sheath tumour (MPNST) and spindle squamous cell carcinoma. Immunohistochemical stains were performed to determine the phenotype of these spindle cells. The malignant cells were immunopositive for vimentin, S-100 protein and HMB-45 [Figure 3] and were negative for cytokeratin, epithelial membrane antigen, leucocytes common antigen, smooth muscle actin, synaptophysin, chromogranin, CD31 and desmin. The pigment was confirmed as melanin by Masson Fontana stain. The final diagnosis was mucosal malignant melanoma. Post-operatively, the patient was recommended for adjuvant radiation therapy with the goal of improving local control. He was treated with 900 Rads, external beam radiotherapy at a private hospital. Three months post-operatively, a new swelling was noted on the same surgical site and biopsy confirmed recurrent mucosal malignant melanoma.

DISCUSSION

MMM is derived from the melanocytes that had migrated as neuroectodermal derivatives in ectodermally derived mucosa. It is also known as 'mucosal-lentiginous' melanoma as it is analogous to acral melanoma in histologic appearance and aggressiveness.

The incidence of MMM is higher in Asians and Japanese and low among Caucasians¹. There is no sex predilection. More

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Fig. 1: A subtotal maxillectomy specimen with a swelling of left buccal sulcus. (arrow)

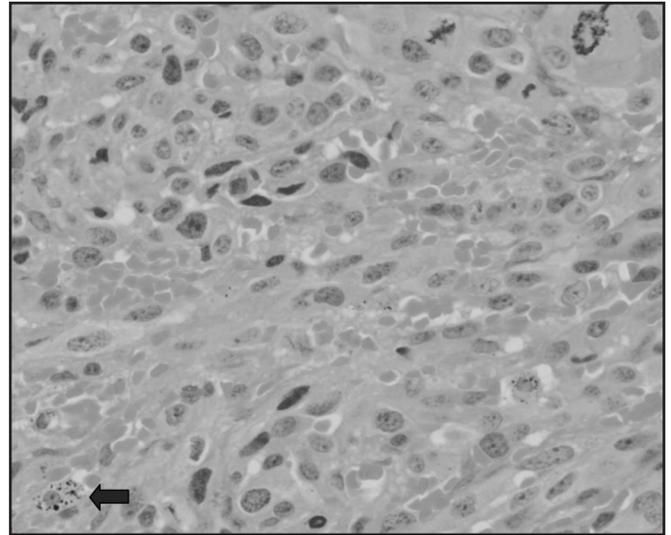


Fig. 2: Malignant spindle cells with occasional malignant cells containing intracytoplasmic melanin pigment (arrow). (Hematoxylin and eosin stain, original magnification x400)

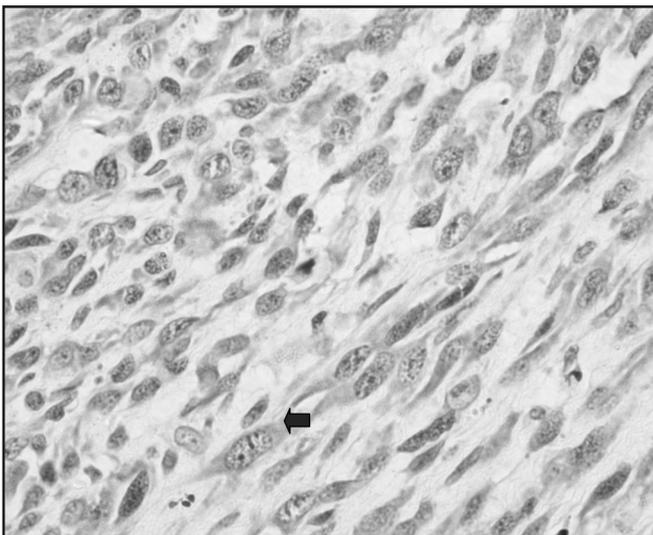


Fig. 3: The malignant cells show strong diffuse cytoplasmic staining to HMB 45. (Immunohistochemical stain, original magnification x400)

than 50% of cases occur in the sixth to eight decades of life². MMM is extremely rare below the age of 20. There are no specific etiologic factors though formaldehyde exposure and tobacco smoking have been implicated in the pathogenesis.

MMM always arise in juxtacutaneous mucous membranes such as oral mucosa, nose and nasal sinuses. It affects the nasal cavity more often than paranasal sinuses. Concurrent nasal cavity and paranasal sinus melanomas are common, either as a direct extension or as multicentric tumours. A primary site of involvement in the paranasal sinuses is the maxillary antrum.

Symptoms of MMM vary according to the site of occurrence. Sinonasal melanoma causes unilateral nasal obstruction and epistaxis. Pain, ulceration and nodular growth are common presentations in oral cavity lesions. The duration of symptoms ranges from weeks to years with majority of patients reported symptoms between one and five months. Most cases usually are advanced at initial presentation.

MMM may present as polypoidal or sessile, friable to rubbery lesions with or without ulceration. The size varies from 10 mm to >50 mm. The colour ranges from brown, black, pink or white, depending upon the amount of melanin production.

MMM varies in histology and comprises epithelioid, spindled, plasmacytoid, rhabdoid, and/or multinucleated tumour cells. The tumour cells are medium to large size with high nuclear to cytoplasmic ratio, prominent eosinophilic nucleoli and intranuclear cytoplasmic inclusions. The cytoplasm is usually eosinophilic and contains intracellular melanin pigment in 50-70% of cases³. Necrosis and increased mitoses with atypical mitotic figures are common. MMM usually invade into the subepithelial tissue and extend into the bone, cartilage or skeletal muscle as seen in our case. Occasionally, intraepithelial melanocytic atypia (melanoma in-situ) occurs in the overlying epithelium. About 40% of cases show vascular and perineural invasion.

A diagnosis of melanoma depends on identification of melanin pigment that is confirmed by Fontana-Masson silver stain and the appropriate immunohistochemical staining pattern that included HMB-45 antibodies, Melan-A, tyrosinase and antimicrophthalmia transcription factor. S-100 protein is always positive in melanomas.

Amelanotic and highly undifferentiated MMM are difficult to diagnose as it mimics a variety of neoplasms, such as "small

blue round cell" neoplasms, pleomorphic neoplasms (sinonasal undifferentiated carcinoma, anaplastic large cell lymphoma, angiosarcoma) and various sarcomas. A panel of antibodies including melanocytic markers and other relevant immunohistochemical stains to exclude the differential diagnoses are essential for definitive diagnosis. In our case, leukocyte common antigen and cytokeratin are performed to rule out lymphoma and carcinoma. Smooth muscle actin, desmin, synaptophysin, chromogranin and CD31 were performed to exclude leiomyosarcoma, MPNST and fibrosarcoma. In a small proportion of malignant melanoma, the tumour cells are non-reactive to the melanocytic markers and useful in these situations to demonstrate melanosomes and premelanosomes to confirm the diagnosis.

There is no universal staging system for MMM. Clark's level of staging and Breslow's depth of invasion are no longer appropriate as the tumour thickness and depth of invasion are difficult to assess due to lack of well-defined reference point for the surface in the respiratory mucosa, ulceration, tissue fragmentation and poorly oriented specimen.

There is no definite treatment for MMM. In many centers, irrespective of the site of origin, aggressive radical surgery with palliative radiotherapy is the mainstay of treatment. Despite radical treatment, 5-year disease specific survival rate is low ranging from 17-47%³. Up to two thirds of patients

have local recurrence in the first postoperative year as seen in our patient. MMM metastasizes to the lungs, lymph nodes, and brain and less frequently to regional lymph nodes. Poor prognostic factors include advanced age, obstructive symptoms, tumour size >3 cm, paranasal and nasopharyngeal tumour, invasion into skeletal muscle, bone and vessels, high mitotic count, marked cellular pleomorphism and distant metastasis².

In conclusion, MMM is an uncommon yet aggressive malignant tumour of the upper respiratory tract. High index of suspicion, meticulous histopathological examination to look for melanin pigment with the appropriate immunohistochemical stains is very essential as this tumour is a great mimicker of other high-grade malignancy. Prompt and definite diagnosis is essential to avoid delay in treatment, as the prognosis becomes very poor with an advanced tumour stage.

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