Open Journal of
Clinical & Medical
Case Reports

Volume 7 (2021)
Issue 04

ISSN: 2379-1039

Rare case series of sinonasal malignant melanoma: The role of immunohistochemistry in the diagnosis of malignant melanoma

Deepa Mohan*; Mohamad Khir Abdullah; Noorizan Yahya; Siti Halimahtun Sahab

***Corresponding Author: Deepa Mohan**
Department of Otorhinolaryngology, Hospital Pakar Sultanah Fatimah, Muar, Johor, Malaysia.
Email: drdeepamohan87@gmail.com

Abstract

Malignant melanoma of the head and neck region are rare. Malignant melanoma involving the nose and paranasal sinuses are aggressive and classically presented at an advanced stage. It has a 5-year survival rate ranging between 20-30%. Malignant melanoma arising from the maxillary sinuses are very uncommon and the diagnosis can be established by Immunohistochemistry (IHC). A classic melanoma case is immunoreactive for HMB 45, S-100 protein, Melan-A, tyrosinase, Microphthalmia Transcription Factor (MITF), and vimentin staining.

Keywords

Malignant melanoma; Immunohistochemistry; HMB 45; S-100 protein; Vimentin.

Introduction

Malignant melanoma is a rare malignancy and constitutes approximately 1-2% of all malignancies arising in the body. 90% of the cases occur in the skin. Primary malignant melanoma of the nasal and paranasal sinuses are rare, accounting for less than 1% of all the melanomas and subjects to a poor prognosis due to local nodal involvement, local recurrence, and distant organ metastasis occurring months or years after the initial diagnosis [1].

Malignant melanomas arise from melanocytes, which derived from the neural crest cells grouped under dispersed Neuroendocrine System (DNES) tumors.

Malignant melanoma is highly curable when discovered early and fully excised. However, as the disease metastasizes, the treatment options are becomes limited and the survival rate decreases to months [2]. There is a delay in diagnosis due to the nonspecific clinical features. The exact site of the tumor origin

is occasionally difficult to identify due to the extensive local destruction it causes and the large size of the tumor [3].

Patients with malignant melanoma usually presents with nasal mass, nasal obstruction, bloody discharge and rhinorrhoea. Unlike it's cutaneous counterparts, sinonasal melanoma can present as a gray-white or pink-to-black, firm and ulcerated mass. Black discolouration is rare, and its absence doesn't rule out melanoma. Histologically, melanoma's appearance varies; therefore, it is in the differential diagnosis of almost everything. It is identified through the prominent melanin pigmentation, its junctional activity, nuclear grooves, marked cytological atypia, folds and pseudoinclusions, abundant mitotic figures and large eosinophilic nucleoli [4]. The cells may have multiple appearance such as spindle shaped, epithelioid, or extremely bizarre. The cell size can range from small (lymphocyte like) to giant multinucleated forms. The cytoplasm seen can be basophilic, foamy, eosinophilic, signet ring type, oncocytic, or completely clear (balloon cell melanoma). The melanin can be scanty, abundant, or absent (amelanotic melanoma). Immunoperoxidase studies are very useful and include the use of HMB-45, S100, Melan A, and one of the newest diagnostic markers, which is the Pigment Epithelium Derived Factor (PEDF). Immunohistochemically, sinonasal malignant melanomas are positive for S100 and markers for melanomas includes HMB45, Mart-1, and tyrosinase. Most of them do not produce sufficient amount of melanin. HMB-45 is more specific but less sensitive than S-100 protein as a melanoma marker. It is found to be positive in 80-86% of metastatic deposits and in 90-100% of primary melanomas. It is useful in the diagnosis of amelanotic melanomas. S-100 protein is a highly sensitive marker for melanoma however it lacks in specificity. It is also found to be positive in 94-100% of primary and metastatic tumors. However, it is also known to be positive in a variety of mesenchymal cells and their tumors, including Schwann cells, myoepithelial cells, adipocytes, chondrocytes, and Langerhans cells [5].

Case Report 1

A 68-year-old gentleman presented with right sided nasal blockage for a duration of 1 month. The patient also had a painless nasal mass increasing in size which gradually occupied the whole nasal cavity. The patient also had intermittent minimal bloodstained nasal discharge.

Nasoendoscopy was performed over bilateral nostrils showed aggressive looking blackish fungating mass occupying the whole right nasal cavity. Left nasal cavity was normal looking. The histopathological examination revealed malignant melanoma with marked ulceration of the overlying squamous epithelium and covered with necrotic tissue.

CT of paranasal sinus showed a heterogenous enhancing lobulated mass occupying the right nasal cavity extending superiorly till the right ethmoid sinus causing expansion of the right nasal cavity. The mass measures approximately 4.3 X 2.6 X 5.5 (AP x W x CC) causing obliteration of the right middle and superior meatus with no clear demarcation of the turbinates. There is extension onto the right osteomeatal complex with obliterated and enhancement within the right maxillary infundibulum. Fluid retention also seen in right maxillary sinus.

Right modified medial maxillectomy and ethmoidectomy was performed and the tumor was removed and sent for histopathological examination. On gross examination, multiple pieces of brownish tissue measuring 65 X 65 mm with separated bony tissue measuring 25 X 25 X 10 mm in size were obtained. Microscopically, the biopsy material showed malignant tumor infiltrating the nasal mucosa. The cells exhibit plump to spindle shaped nuclei some with prominent nucleoli. Mitosis is increased. Abundant intra and extracytoplasmic pigment seen. IHC showed positive staining for HMB 45, Vimentin and S100 protein confirming the diagnosis of malignant melanoma (Figure 1A,B,C,D,E,F). Patient was referred to Oncology Clinic and planned for radiotherapy. However, the patient defaulted the follow up.

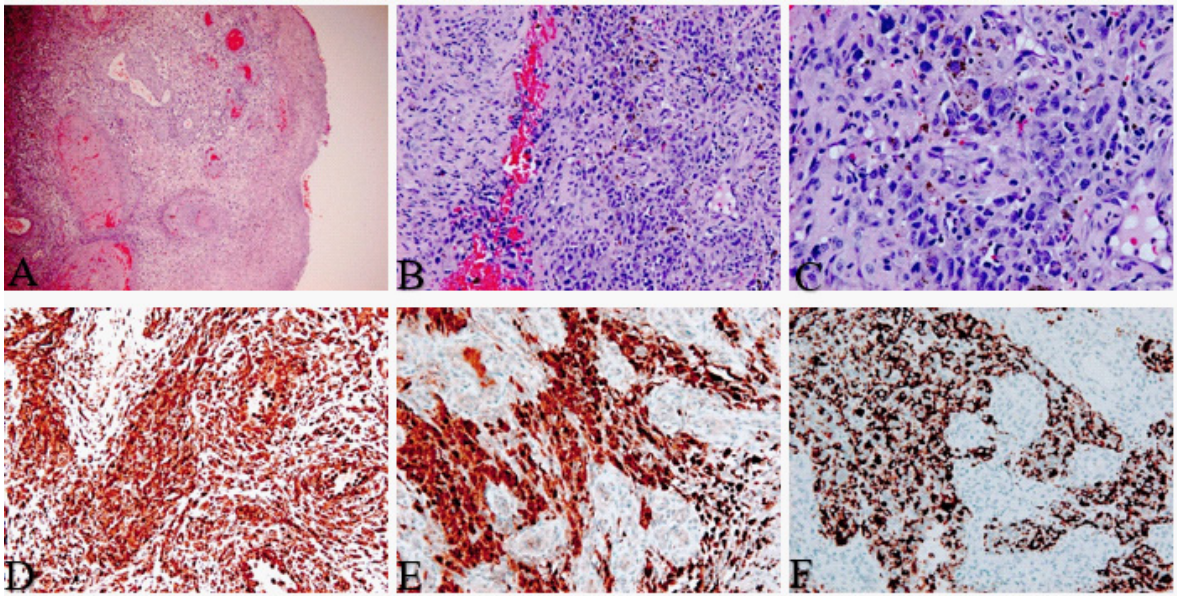

Figure 1: (A) HMB45 positive (x20), **(B)** Vimentin positive (x20), **(C)** S100 protein positive (x20), **(D)** Diffuse sheets of tumor cells exhibiting enlarged pleomorphic nuclei, **(E)** High power view of tumour cells with intra and extracellular pigments, **(F)** Diffuse sheets of tumor cells exhibiting enlarged pleomorphic nuclei.

Case Report 2

A 46-year-old gentleman presented with intermittent epistaxis, aggravated by sneezing for a duration of 3 month. The patient also had right sided nasal blockage. He has no facial pain, no anosmia or headaches.

Nasoendoscopy showed reddish fungating mass from right middle meatus mixed with mucous and blood stain extending to the posterior choana. Left nasal cavity was normal. The histopathological examination showed malignant mesenchymal tumor (Sarcoma). The malignant cells were positive for vimentin and actin with patchy weak positive for CD 56 and S100 protein. The cells were negative for HMB 45.

CT of paranasal sinus showed right heterogenous enhancing mass with local extension into right posterior choana, right ethmoid sinus, right sphenoid sinus, right maxillary sinus and through the right inferior orbital fissure resulting in extraconal mass at floor of right orbit. Laterally, it extended to the maxillary sinus results in widening of right osteomeatal complex and infundibulum.

Right total submaxillectomy was done and the excised tumor was sent for histopathological examination. On gross examination, a piece of maxillary bone and tissue measuring 60x40x30mm with brownish

hemorrhagic and friable mass within the maxillary sinus. Multiple pieces of brownish and greyish tissue measuring 40 X 35 X 20 mm with friable and hemorrhagic tumor was obtained. Microscopically, the biopsy material showed fragments of respiratory mucosa with underlying stroma showing diffuse sheet of malignant infiltrates. The tumor cells exhibit large round nuclei with fine chromatin pattern, prominent nucleoli, indistinct cell border and frequent mitosis. There is extensive tumor necrosis and focal bone involvement noted. The tumor cells were positive for vimentin and actin staining confirming the diagnosis of malignant mesenchymal tumor (sarcoma), with differentials include rhabdomyosarcoma, dedifferentiated sarcoma and leiomyosarcoma.

Further IHC staining performed, whereby S100 protein, Melan A, HMB 45 (focal), CD56 and Bc12 staining confirmed the diagnosis of malignant melanoma with focal area suggestive of bony involvement (Figure 2A,B,C,D). Patient was referred to Oncology department and planned for IMRT and chemotherapy due to distant metastasis. However, patient was unable to complete chemotherapy and passed away.

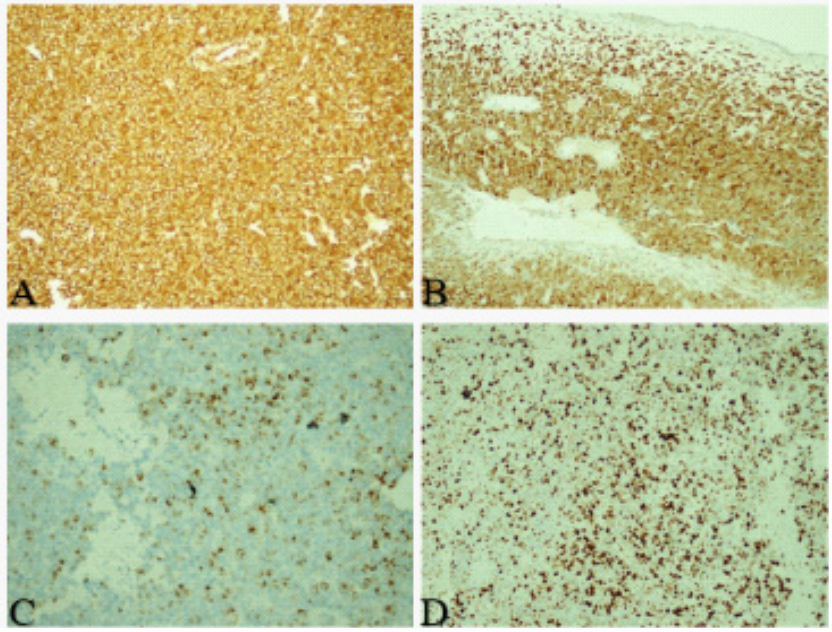

Figure 2: (A) HMB45 positive (x20), **(B)** Vimentin positive (x20), **(C)** S100 protein positive (x20), **(D)** Diffuse sheets of tumor cells exhibiting enlarged pleomorphic nuclei, **(E)** High power view of tumour cells with intra and extracellular pigments, **(F)** Diffuse sheets of tumor cells exhibiting enlarged pleomorphic nuclei.

Discussion

Sinonasal malignant melanoma is a rare, aggressive, and quirky tumour which results in 4% of sinonasal malignancies. This tumour arises from melanocytes derived from neural crest tissue (ICD-O 8720/3) [6]. Unilateral nasal blockage, epistaxis and visible nasal mass are the most common features. The lesion may appear pigmented but can be amelanotic in at least 10% and often appears as a vascular friable mass. The tissue is usually obtained by performing biopsy endoscopically and histopathology is essential to differentiate sinonasal malignant melanoma from sinonasal undifferentiated carcinoma, nasopharyngeal carcinoma and lymphoma. We discuss 2 cases of sinonasal malignant melanoma, with a typical presentation and another with atypical presentation which leads to a histological dilemma. Both the cases presented with unilateral nose block and intermittent epistaxis. The 1st case showed blackish fungating mass occupying

the whole nasal cavity whereas the 2nd case showed reddish fungating mass. The case was diagnosed as malignant melanoma based on IHC. The 1st case discussed showed positive staining for HMB 45, S100 protein and Vimentin confirming the diagnosis of malignant melanoma. However, the 2nd case was positive for vimentin and actin staining confirming the diagnosis of malignant mesenchymal tumor(sarcoma). However, IHC was advised and IHC markers S100 protein, Melan A, HMB 45(focal), CD56 and Bc12 confirmed the diagnosis of malignant melanoma.

Definite diagnosis is based on immunohistochemistry, however no single antibody probe has been described that is both 100% sensitive and specific to diagnose melanoma. At this point of time, every tested antibody has had cross-reactivities [7]. The immunohistochemical profile is identical to skin melanoma. Markers include HMB-45, S-100 protein, melan-A, MITF, tyrosinase, cytokeratin and vimentin [8]. Study shows only 91% were S-100 protein immunoreactive, suggesting that a panel of melanoma markers is necessary to avoid misdiagnosing [9]. S-100 protein, tyrosinase, and HMB-45 would correctly identify all tumors even when the tumors are spindled or undifferentiated types. In majority cases, malignant melanoma shows strong cytoplasmic positivity for HMB-45 marker and it is more specific than a S-100 protein as it recognizes the melanosomal oligosaccharide side chain of a glycoprotein (gp100) [10,11]. When HMB-45 and S 100 protein gives ambiguous results, Melan-A which is a specific melanoma marker is usually used and it has proven to be very specific in differentiating melanoma from other malignancies like carcinomas, plasmacytomas and sarcomas [12]. Vimentin is also useful in the differential diagnosis because olfactory neuroblastoma and sinonasal undifferentiated carcinoma are usually nonreactive. MITF is identified by nuclear positivity and can be identified in about 30% of nuclei in about 90% of metastatic melanomas [10]. MITF is relatively specific for melanoma, however it is not as sensitive as S-100 and specific or sensitive as tyrosinase.

References

1. Yoshika H, Kamda T et al. MRI of mucosal malignant melanoma of the head and neck-J.Comput assistant Tommogr. 1998; 22; 492-497.

2. Strauss JE, Strauss SI. Oral malignant melanoma: A case report and review of literature. J Oral Maxillofac Surg. 1994; 52: 972–976.

3. Thompson AC, Morgan DA, Bradley PJ. Malignant Melanoma of the nasal cavity and paranasal sinuses. Clin Otolaryngol Allied Sci. 1993; 18: 34–36.

4. Gupta S, Singh PA, Misra V, Jain S. Malignant melanoma of maxillary sinus. J Clin Diagn Res. 2009; 3: 1801–1804.

5. Dharam Ramnani. Webpathology visual survey of surgical pathology. Melanoma immunohistochemistry. 49-55

6. Lund VJ. Sinonasal Malignant Melanoma. Anterior Skull Base Tumors. 2020; 185–196.

7. Smoller BR. Immunohistochemistry in the Diagnosis of Malignant Melanoma: Clinics in Dermatology. 1991; 9; 235–241.

8. Alves ISS, Berriel LGS, Alves RT, Pinto MB, Oliveira CFP, Cazzotto AC, et al. Sinonasal Melanoma: A Case Report and Literature Review. Case Reports in Oncological Medicine. 2017; 1–6.

9. Thompson LDR, Wieneke JA, Miettinen M. Sinonasal Tract and Nasopharyngeal Melanomas: A Clinicopathologic Study of 115 Cases With a Proposed Staging System. The American Journal of Surgical Pathology. 2003; 27: 594–611.

10. Miettinen M, Fernandez M, Franssila K, et al. Microphthalmia transcription factor in the immunohistochemical diagnosis of metastatic melanoma: Comparison with four other melanoma markers. Am J Surg Pathol. 2001.

11. Leong ASY, Cooper K, Leong FJWM, HMB-45 (melanoma marker). In: Leong ASY, Cooper K, Leong FJWM, Manual of diagnostic antibodies for immunohistology, Greenwich Medical Media. 1999; 172–175.

12. Eudy GE, Carlson GW, Murray DR, Waldrop SM, Lawson D, Cohen C. Rapid immunohistochemistry of sentinel lymph nodes for metastatic melanoma, Hum Pathol. 2003; 34: 797–802.

Manuscript Information: Received: January 11, 2021; Accepted: April 16, 2021; Published: April 30, 2021

Authors Information: Deepa Mohan*; Mohamad Khir Abdullah; Noorizan Yahya; Siti Halimahtun Sahab
Department of Otorhinolaryngology, Hospital Pakar Sultanah Fatimah, Muar, Johor, Malaysia.

Citation: Mohan D, Abdullah MK, Yahya N, Sahab SH. Rare case series of sinonasal malignant melanoma: The role of immunohistochemistry in the diagnosis of malignant melanoma. Open J Clin Med Case Rep. 2021; 1741.