Case Report

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Primary Mucosal Melanoma of the Nasal Cavity: A Rare Case Report

Ear, Nose and Throat Section

MANU S BABU[1], SAAHITI KOPPOLU[2], VINOD V SHINDE[3], GUNDAPPA MAHAJAN[4], YASH KALRA[5]

ABSTRACT

Mucosal melanoma of the nasal cavity and paranasal sinuses is a rare but increasingly reported malignancy, and typically diagnosed in patients aged 65-70 years. It commonly presents with unilateral nasal obstruction and epistaxis, often originating in the nasal septum or lateral wall. Diagnosis relies on immunohistochemical staining and is usually made at an advanced stage due to the tumour's aggressive nature. They behave more aggressively than skin melanomas. This case report discusses a 76-year-old female who presented with bilateral nasal obstruction (left>right) for two months, with difficulty in breathing for one month. The examination revealed a bluish bleeding mass in the left nasal cavity. Preoperative endoscopic incisional biopsy revealed non-keratinising squamous cell carcinoma. The patient was subjected to total maxillectomy, and the final histopathological report came as mucosal melanoma. Early suspicion, especially in elderly patients with unilateral nasal obstruction or epistaxis, is critical. Timely biopsy, accurate histopathological diagnosis, and aggressive surgical management with adjuvant radiotherapy can improve local control, though the overall prognosis remains poor. Multidisciplinary follow-up and evolving molecular therapies offer hope for better outcomes in the future.

Keywords: Head and neck neoplasms, Immunohistochemistry, Nasal cavity tumours, Radiotherapy, Surgery

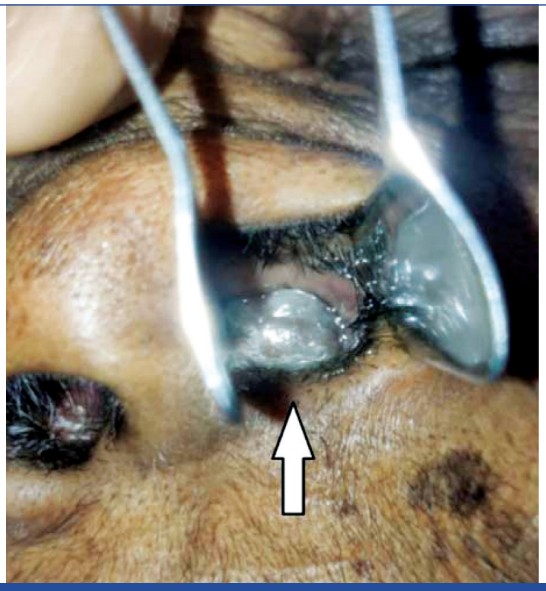
CASE REPORT

A 76-year old female patient, homemaker by occupation, presented with the chief complaint of bilateral nasal obstruction since two months (left>right), which was insidious in onset and gradually progressive. The patient also had a history of difficulty in breathing, epiphora, hyposmia, and intermittent epistaxis from the left nasal cavity since one month. There was no history of any nasal or facial trauma. No other significant history was present. The patient had no relevant past, personal, or surgical history.

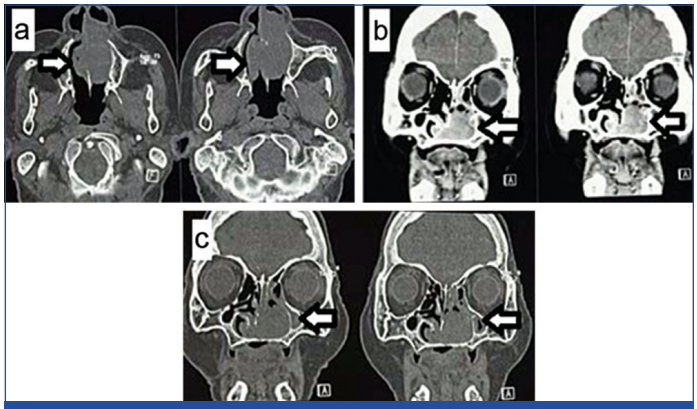
On clinical examination of the nasal cavity, anterior rhinoscopy revealed a bluish coloured mass between the nasal septum and the inferior turbinate in the left nasal cavity [Table/Fig-1]. On probing, the mass was non-tender, soft to firm in consistency, and bled on touch. The probe could be passed laterally, superiorly, and inferiorly to the mass but not medially. The right nasal cavity showed a deviated nasal septum to the right with congested nasal mucosa. Posterior rhinoscopy showed no mass in the nasopharynx and no other abnormality. There was no paranasal sinus tenderness, swelling in the maxillary sinus region, or skin changes. The examination findings were confirmed with a diagnostic nasal endoscopy. The oral cavity and oropharyngeal examination showed no palatal bulge and no other abnormality. No lymph nodes were palpable in the neck. The orbital examination and the remainder of the ear, nose, throat, and head and neck examination were normal.

Based on the clinical history and examination findings, a differential diagnosis of nasal polyposis, granulomatous diseases of nose, inverted papilloma, sinonasal malignancy like squamous cell carcinoma, adenocarcinoma, malignant mucosal melanoma was considered. All routine investigations of the patient were within normal limits.

Contrast Enhanced Computed Tomography (CECT) of the nasal cavity and paranasal sinuses showed a well-defined iso- to hypodense soft tissue lesion in the left nasal cavity measuring approximately 31×56×25 mm, showing moderate heterogenous enhancement [Table/Fig-2]. The lesion was causing complete obstruction of the left nasal cavity. Anteriorly, it was reaching up to the vestibule and posteriorly up to the choana medially it was eroding bony nasal septum with small extension in the inferior part



[Table/Fig-1]: White fill arrow showing bluish coloured mass in the left nasal cavity on anterior rhinoscopy.

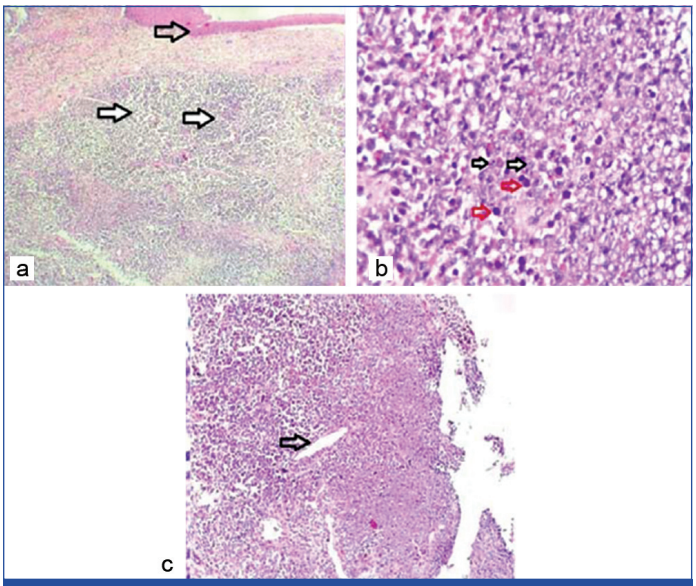


[Table/Fig-2]: Computed Tomography (CT) plain and contrast of nasal cavity and paranasal sinuses: a) Axial cuts with white fill arrow showing the mass in the left nasal cavity; b) Contrast CT coronal cuts with white filled arrow showing the mass; c) Coronal cuts with white fill arrow showing mass in the left nasal cavity with erosion of the bony septum and small extension into the right nasal cavity.

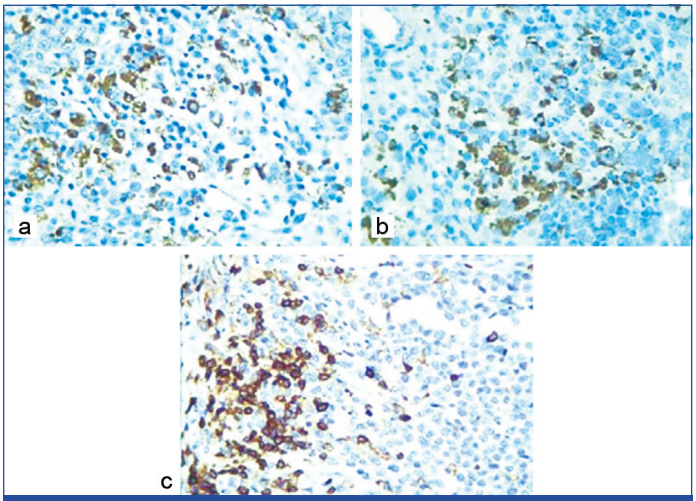
of the right nasal cavity. Laterally, it was causing thinning of the medial wall of the left maxillary sinus with compression and erosion of the inferior turbinate. Superiorly, it caused displacement of the left middle turbinate and was abutting the floor of the left ethmoid air cells. Inferiorly, it was causing small erosion in the hard palate at places. The impression made on Computed Tomography (CT) was the possibility of neoplastic aetiology.

Obstruction of the left ostiomeatal unit and frontal sinus drainage was noted.

Incisional biopsy of the mass was taken and sent for histopathologial examination which showed bits of tissue lined by stratified squamous epithelium. Some epithelial tissue showed loose sheets of undifferentiated tumour cells with vesicular nuclei and prominent nucleoli. Stroma showed fibrocollagenous tissue, lymphocytes with few lymphoid follicles with increased mitotic activity [Table/Fig-3]. Immunohistochemistry (IHC) markers Pan CK, CK5, CK6 and CK7 showed strong positive expression. Synaptophysin, chromogranin were negative and Ki67 was positive upto 50%. Hence, a diagnosis of non-keratinising squamous cell carcinoma was given [Table/Fig-4].



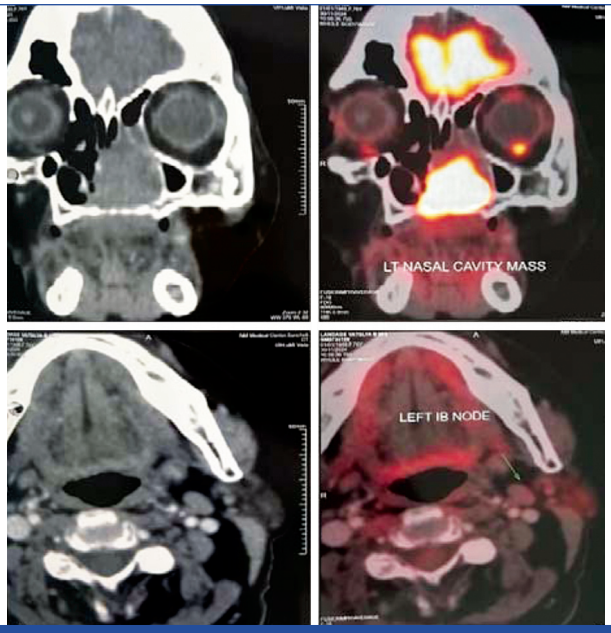
[Table/Fig-3]: Histopathological examination of the incisional biopsy of the mass indicating a non-keratinising squamous cell carcinoma; a) Arrow without fill showing stratified squamous epithelium; White fill arrows showing loose sheets of malignant cells; b) White fill arrows showing prominent nucleoli in the nucleus; Red arrows without fill showing cells with hyperchromatic nucleus; c) Arrow without fill showing blood vessel surrounded by malignant cells.



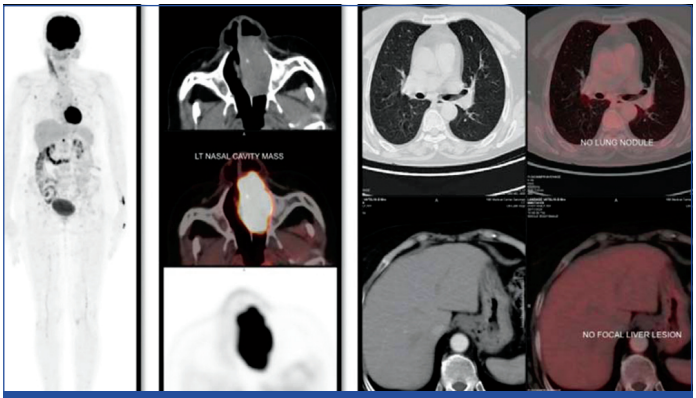
[Table/Fig-4]: IHC markers on incisional biopsy specimen: a) CK5, CK6 strong positive; b) CK 7 strong positive; c) Pan CK strong positive.

PET scan was done, which showed no definite evidence of distant metastasis [Table/Fig-5,6].

The patient was taken for left total maxillectomy with split thickness skin grafting and palatal obturator placement under general anaesthesia

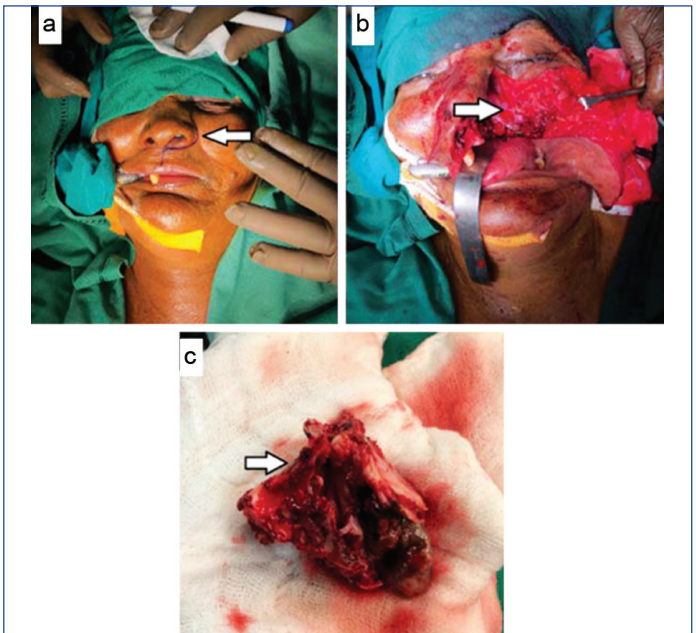


[Table/Fig-5]: Positron Emission Tomography (PET) scan showing large metabolically active mass almost occupying the entire left nasal cavity with erosion of the bony nasal septum.



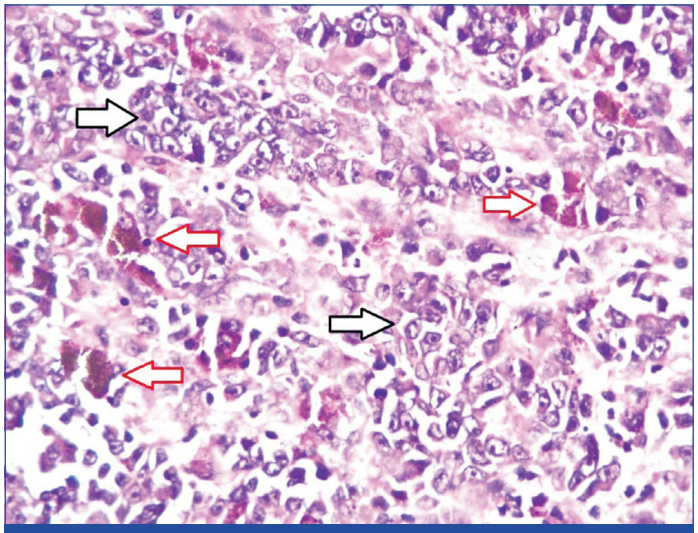
[Table/Fig-6]: Full body PET Scan showing no evidence of distant metastasis.

with Weber-Ferguson incision with subciliary extension with the osteotomies as follows: Zygoma beneath the infraorbital rim, across the frontal process of the maxilla, central upper alveolus and hard palate, maxillary tuberosity and pterygoid plates, orbital cut [Table/Fig-7].

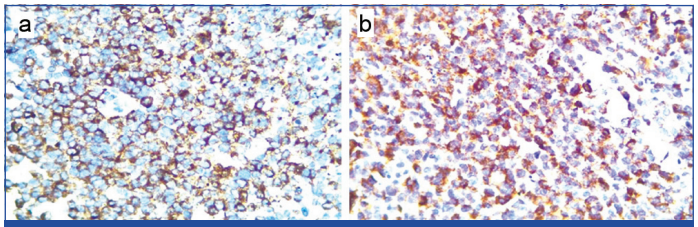


[Table/Fig-7]: Intraoperative images: a) White fill arrow showing Weber-Ferguson incision with subciliary extension; b) White fill arrow showing the plane after left total maxillectomy; c) White fill arrow showing the excised specimen after left total maxillectomy.

The specimen was sent for final histopathological examination, which revealed mucosal melanoma arising from left side of the nasal septum with no lymphatic, vascular and perineural invasion [Table/Fig-8]. The separately sent posterior revised mucosal and medial revised mucosal margins were involved by tumour. The staging according to the American Joint Committee on Cancer (AJCC) 8th edition was pT4a [1]. Amongst the IHC markers, HMB 45, S-100 and Vimentin were diffuse strong positive and LCA, CK5/6, Desmin were negative [Table/Fig-9].



[Table/Fig-8]: Final histopathological examination of the total maxillectomy specimen indicating a mucosal melanoma arising from left side of the nasal septum with no lymphatic, vascular and perineural invasion.
Black margin arrows showing melanocytes; Red margin arrows showing melanocytes with brown pigment melanin within



[Table/Fig-9]: IHC Markers of the excised specimen: a) HMB 45 positivity; b) S-100 positivity.

Postoperatively, the patient had no complications during wound healing. The sutures were removed on the 14th postoperative day. The patient was advised postoperative radiotherapy for the residual disease and prosthodontic follow-up for obturator management. The patient is under regular follow-up without any complications.

DISCUSSION

Sinonasal mucosal melanoma is a rare and aggressive malignancy originating from melanocytes located in the mucosal lining of the nasal cavity and paranasal sinuses. These tumours may present as polypoid or ulcerated lesions and may vary in colour from light tan to black due to melanin pigmentation. While it shares histological characteristics with cutaneous melanoma, its biological behaviour and response to therapy are distinct [2].

Melanoma constitutes approximately 3.6% of all malignancies in the sinonasal region, making, it a rare entity within head and neck cancers [2].

Sinonasal melanoma shows a female preponderance and tends to affect older individuals as seen in the present case, a 76-year-old female. The nasal cavity, particularly the lateral wall and turbinates, is the most commonly affected site (80%), while 20% are located in the paranasal sinuses, especially the maxillary sinus, followed by the ethmoid, frontal, and sphenoid sinuses [2]. This case involved the left nasal cavity with the tumour extending into the right nasal cavity and the left maxillary sinus.

Melanocytes are dendritic neuroectodermal cells that originate from the neural crest and reside at the dermoepidermal junction of all mucosal membranes. Mucosal melanomas develop from these melanocytes, and the sinonasal region has a relatively high melanocyte density. In contrast to cutaneous melanoma, no specific environmental or lifestyle risk factors (e.g., UV exposure) have been identified [3]. Mutations involving tyrosine kinase receptor pathways may play a role in tumourigenesis [3]. The precursor lesion for mucosal melanoma has not been identified, but atypical melanocytic hyperplasia and coexisting melanosis may be predisposing conditions [4].

The presentation of sinonasal melanoma varies based on tumour location and extent. Common symptoms include epistaxis, nasal obstruction, and diplopia or proptosis in advanced disease, most of which were seen in the present case. In oral cavity melanomas, pigmented lesions, ulceration, and ill-fitting dentures may be noted [4].

The nasal cavity, particularly the lateral wall and turbinates, is the most commonly affected site (80%), while 20% are located in the paranasal sinuses, especially the maxillary sinus, followed by the ethmoid, frontal, and sphenoid sinuses [5].

These tumours typically consist of epithelioid and/or spindle cells. Recognised variants include plasmacytoid, rhabdoid, small cell, giant cell, balloon cell, neurotropic, and desmoplastic forms. The cells are highly pleomorphic. Nucleoli are prominent, and intra-nuclear inclusions are common. An adjacent inflammatory infiltrate and necrosis may be present. Melanocytic atypia or melanoma in situ can be observed in the surrounding mucosa. The cells exhibit nuclear and cytoplasmic immunoreactivity for S100 protein. MelanA, HMB-45, and SOX10 are typically positive [2,5]. The present case showed positivity for S-100, HMB-45 and Vimentin.

Diagnosis involves clinical examination, endoscopic evaluation, imaging (Computed Tomography {CT}/Magnetic Resonance Tomography {MRI}), biopsy with histological and immunohistochemical evaluation. Imaging plays a critical role in diagnosis and staging. CT and MRI assess locoregional extent and resectability. On MRI, sinonasal melanomas typically appear as low-signal intensity on T2-weighted images and show enhancement on T1-weighted sequences [6]. PET/CT is useful in detecting distant metastases and in treatment planning due to high Fluorodeoxyglucose (FDG) uptake [6]. Although its routine use in initial assessment remains controversial, it was included in the diagnostic plan for the present case [7].

Staging is done using the AJCC system or a simplified classification: Stage I: tumour confined to primary site, Stage II: regional lymph node involvement and Stage III: distant metastases [8].

The differential diagnoses of sinonasal mucosal melanoma include sinonasal undifferentiated carcinoma which lacks melanocytic markers (negative for S100, HMB-45), olfactory neuroblastoma that is typically positive for neuroendocrine markers and negative for melanocytic markers. The pigmented squamous cell carcinoma was ruled out based on histology and negative melanocytic immunoprofile, and metastatic melanoma from a cutaneous site was also ruled out via thorough skin and systemic examination and absence of primary cutaneous lesion.

The cornerstone of treatment for sinonasal melanoma is surgical resection of the tumour with an adequate safety margin to ensure it is free of invasion, which was the management plan opted in this case. Unlike squamous cell carcinoma, sinonasal melanoma rarely metastasises to lymph nodes, but more commonly spreads to the lungs and brain. Thus, radical neck dissection is not recommended for patients who do not show clinical or radiological evidence of cervical metastases. Recent observations indicate that radiotherapy plays a significant role in treatment. The literature reports an initial response rate of 50-75% for radiotherapy alone when used to

Study	Case presentation	Treatment method	Histopathology	Diagnosis	Outcome
BhaRtiya R and Prasad KM (2015) [13]	A 51-year-old male presented with nasal swelling, blockage and with occasional nasal bleeding from last 5 months	Surgical resection	Hyperplastic squamous epithelium, medium to large spindle cells in diffuse pattern, pleomorphic nuclei, prominent nucleoli, both intra and extra cellular brown-black pigment, scattered mitosis, tumour giant cells and ulcerated overlying epithelium. IHC: S-100 and HMB 45 positive	Malignant melanoma	No complications, alive 1 year after surgery
Alves IS et al., (2017) [14]	A 64-year-old male patient with nasal obstruction and epistaxis	Chemotherapy followed by concurrent chemoradiotherapy	Initial incisional biopsy: undifferentiated carcinoma of the right maxillary sinus, staged T4aN0M0. Review IHC: vimentin, S100, and HMB45 positive	Malignant melanoma	In the 21 months of 3 monthly follow-up, no complications, no recurrence, with almost complete resolution of the lesions
Długosz-Karbowska A and Wąsowicz B (2020) [15]	An 89-year-old female patient with epistaxis and nasal obstruction since 3 months	Surgical resection: Lateral rhinotomy approach followed by radiotherapy	Initial excisional biopsy: malignant tumour tissue, 70% with necrotic lesions, focal surface ulceration, pT4, IHC: S-100 and vimentin positive Final IHC after surgery: HMB-45, Ki-67, Melan A, S-100 positive	Malignant melanoma	Complete healing of the nasal skin, normal nasal patency with smooth mucosa without signs of recurrence two months after radiotherapy
Present case	A 76-year-old female with nasal obstruction since two months, epiphora, hyposmia, epistaxis since 1 month	Left total maxillectomy with split thickness skin grafting and palatal obturator placement under general anaesthesia with Weber-Ferguson incision with subciliary extension followed by radiotherapy	Incisional biopsy: stratified squamous epithelium, loose sheets of undifferentiated tumour cells, vesicular nuclei, prominent nucleoli, fibrocollagenous tissue. IHC: Pan CK, CK5, CK6, CK7 strong positive Final histopathology after surgery: mucosal melanoma arising from left side of the nasal septum, no lymphatic, vascular and perineural invasion, posterior revised mucosal and medial revised mucosal margin were involved by tumour. Staging: pT4a. IHC: HMB 45, S-100 and vimentin diffuse strong positive	Malignant mucosal melanoma	No complications, discharged safely and started with radiotherapy with prosthodontic follow-up for obturator care

[Table/Fig-10]: Similar cases from literature [13-15].

treat localised mucosal melanomas. However, long-term survival continues to be a major challenge [9].

Radiotherapy plays a crucial role, especially when surgical margins are inadequate. Postoperative radiation helps improve local control, though it has not shown a survival benefit [10]. In this case, as the posterior revised mucosal and medial revised mucosal margins were involved by tumour postoperative radiotherapy was given to the patient.

The prognosis of sinonasal melanoma is poor, with limited long-term survival, despite aggressive locoregional therapy. Survival rates are significantly lower than those of cutaneous melanoma, mainly due to early distant metastasis, particularly to the lungs and brain. Local recurrence occurs in about 50% of cases and often precedes the development of distant metastases [10].

Due to the high recurrence rate and complex anatomy, management is particularly challenging. Postoperative radiation is more commonly employed in sinonasal cases compared to oral melanomas, owing to difficulty in achieving negative margins [11].

Despite aggressive locoregional treatment, recurrent disease is common, and management is difficult. Emerging technologies, such as whole exome sequencing, show promise in improving outcomes in rare and aggressive cancers like mucosal melanoma by identifying therapeutic targets [12].

The patient in this case presented with bilateral nasal obstruction and epiphora, symptoms consistent with reported cases such as those by BhaRtiya R and Prasad KM and Długosz-Karbowska A and Wąsowicz B but the presence of contralateral nasal extension and septal erosion adds a unique anatomical complexity not emphasised in earlier reports [13-15]. Similar to prior reports, this case showed strong HMB-45, S-100 and vimentin positivity as seen in [Table/Fig-10], however, the initial incisional biopsy suggested a non-keratinising squamous cell carcinoma, highlighting a diagnostic dilemma not prominently noted in the earlier cases. Unlike Alves IS et al., where chemotherapy was the primary modality, this case was managed surgically via total maxillectomy followed by radiotherapy [14], aligning more with the approach by Długosz-Karbowska A and Wąsowicz B though reconstruction and prosthodontic strategy provide an additional dimension to long-term care in the present case [15]. In contrast to previous cases, the multidisciplinary surgical planning and prosthetic rehabilitation in the present case emphasise comprehensive oncologic and functional management, especially critical in extensive mid-facial resections.

CONCLUSION(S)

Early detection of mucosal melanoma in the nasal cavity is a vital prognostic factor. The occurrence of unilateral symptoms, such as nosebleeds or nasal blockage, in individuals over 60-year-old should be regarded with suspicion. Diagnosis is confirmed through histological and immunohistochemical analysis of a biopsy sample. The primary treatment involves extensive surgical removal, potentially supplemented with radiotherapy. Achieving a complete resection with clear margins initially is crucial for survival. The overall prognosis of these tumours is very poor. However, there is hope for improved survival rates through advancements in radiotherapy techniques and ongoing research into cell and gene therapies.

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PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Otorhinolaryngology, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.
2. Resident, Department of Otorhinolaryngology, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharastra, India.
3. Professor, Department of Otorhinolaryngology, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.
4. Professor, Department of Otorhinolaryngology, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.
5. Resident, Department of Otorhinolaryngology, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Saahiti Koppolu,
Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pimpri,
Pune-411018, Maharashtra, India.
E-mail: sahiti.koppolu@gmail.com

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