CASE REPORTS

PHILIPPINE JOURNAL OF OTOLARYNGOLOGY-HEAD AND NECK SURGERY VOL. 26 NO. 1 JANUARY – JUNE 2011

Sinonasal Mucosal Melanoma: An Enigma

Hidayat Ullah, MBBS, MS[1]
Mirza Qaisar Baig, MBBS, MD[2]

[1]Department of ENT and [2]Radiotherapy, BRD Medical College, Gorakhpur, India

ABSTRACT

Objective: To report two cases of mucosal melanoma of the sinonasal cavity from India and review the literature emphasizing current important clinical and biologic aspects of this tumor.

Methods:

Design: Case Report
Setting: Tertiary Public Referral Hospital
Patients: Two

Results: Two patients presenting with progressive unilateral nasal obstruction over three to six months, respectively, were diagnosed to have sinonasal mucosal melanoma. The mass involved the nasal cavity and maxillary antrum in both patients. The first patient deferred radiotherapy for four months until pulmonary metastasis became evident, necessitating palliative chemotherapy; the second patient underwent surgical excision and radiotherapy.

Conclusion: In spite of aggressive therapy, the prognosis for people with mucosal melanoma is extremely poor. Surgery remains the mainstay of treatment, although adjuvant radiation therapy has recently had an increasing role in the treatment of mucosal melanoma. A clear understanding of the pathophysiology of this disease may yield more specific immunotherapy and chemotherapy techniques. A multicenter prospective study is required to objectively assess the optimal treatment regimen.

Keywords: *mucosal melanoma, sinonasal cavity*

Worldwide the incidence of melanoma has increased over the past 30 years and continues to do so at an alarming rate, with the number of cases increasing by almost 5% annually.[1] Although the head and neck accounts for only 9% of total body surface area, as many as 15-25% of all melanomas arise in the head and neck. Head and neck melanomas more commonly occur in men (2:1), with a median age at diagnosis of 55 years.[2]

Non-cutaneous melanomas are relatively rare lesions. In the head and neck, the commonest sites for mucosal malignant melanoma are the oral cavity (49%), followed by sinonasal (40%) and pharyngeal (11%) involvement.[3] The malignant mucosal melanoma of the nasal cavity and paranasal sinuses is a rare tumor of unknown etiology, unpredictable biologic behavior and poor prognosis.[4] We present two such cases and review the literature.

Correspondence: Dr Hidayat Ullah
House No 4M, Semra No 1
Chargawan
Gorakhpur, Uttar Pradesh
INDIA 273409
drhidayatullah@gmail.com
Reprints will not be available from the authors.

The authors declared that this represents original material that is not being considered for publication or has not been published or accepted for publication elsewhere, in full or in part, in print or electronic media; that the manuscript has been read and approved by all the authors, that the requirements for authorship have been met by each author, and that each author believes that the manuscript represents honest work.

Disclosures: The authors signed disclosures that there are no financial or other (including personal) relationships, intellectual passion, political or religious beliefs, and institutional affiliations that might lead to a conflict of interest.

Philipp J Otolaryngol Head Neck Surg 2011; 26 (1): 34-38

CASE REPORTS

Case 1

A 32-year-old Indian male farmer came to the otolaryngology ward complaining of left nasal obstruction for about three months. Gradual in onset, the obstruction progressively became complete about 15 days prior to this visit. He also complained of mucoid, clear rhinorrhoea for the past month that was not blood-tinged. There was no epistaxis, nor associated pain or numbness in the facial region. On anterior rhinoscopy an irregularly-surfaced, polypoidal, non-ulcerated black mass was visible in the left nasal cavity with surrounding secretions *(Figure 1)*. The mass was insensitive on palpation and did not bleed on probing. On endoscopy, it appeared to arise from the lateral wall of the nasal cavity, in the region of the middle meatus, with no apparent involvement of the choanae or nasopharynx. There was no apparent neck swelling and no palpable cervical lymph node enlargement. A biopsy was suggestive of a malignant melanoma *(Figure 2)* and Computed Tomography (CT) showed a mass in the left nasal cavity extending to the maxillary antrum on the left side with no signs of bony or cartilaginous destruction nor other sinus involvement *(Figure 3)*. A thorough search for distant metastasis was negative. A course of radiotherapy was advised but the patient only came back after four months with distant metastasis in the lungs. He is currently undergoing palliative chemotherapy.

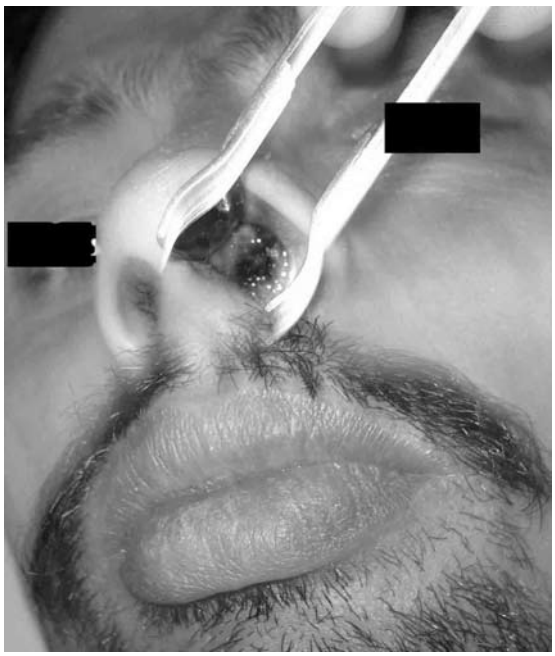

Figure 1. Photograph of first patient showing a black polypoidal mass in the left nasal cavity on anterior rhinoscopy.

Case 2

A 45-year-old male trumpet player, born and residing in India came to the otolaryngology clinic complaining of left nasal obstruction for about six months. The nasal obstruction was gradual in onset and had progressed slowly causing complete obstruction for 60 days, without complaints of epistaxis, rhinorrhoea or pain. On examination, a smooth, dry black mass was visible coming out of the left nasal cavity and expanding the vestibule *(Figure 4)*. It was insensitive on palpation and did not bleed on probing. It appeared to be arising from the nasal floor, completely filling the nasal cavity anteriorly, causing widening of the nasal ala. However, the choanae appeared free on posterior rhinoscopy.

A biopsy revealed malignant melanoma and the CT scan showed an extensive mass involving maxillary antrum and nasal cavity with no signs of bony or cartilaginous destruction *(Figure 5)*. A thorough investigation for distant metastases was negative. The mass was excised by lateral rhinotomy approach and a course of radiotherapy was given. However, the patient died due to systemic metastasis after 15 months.

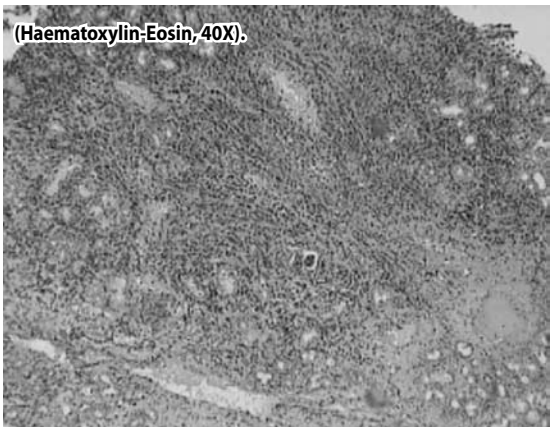

Figure 2. Histopathologic slide, Haematoxylin and Eosin stain (H & E) low power view (40 x) showing melanocytes infiltrating nasal mucosa.

DISCUSSION

Fifteen to twenty five percent of all malignant melanomas occur in the head and neck and of these, 6-8% involve the mucous membranes of the aerodigestive tract.[5] In the head and neck, the commonest sites for mucosal malignant melanoma are the oral cavity (49%), followed by sinonasal (40%) and pharyngeal (11%) involvement.[1] Malignant melanomas of the nasal cavity and the paranasal sinuses are uncommon, accounting for less than 1% of all malignant mucosal melanomas and 2-8% of all malignant neoplasms of the sinonasal tract.[5] Holdcraft and Gallagher[6] cited studies of sinonasal melanoma as representing 0.6-0.7% of all melanomas, 2-9% of melanomas of head and neck and 3.6-4% of all nasal tumors.

The incidence of cutaneous malignant melanoma is currently rising

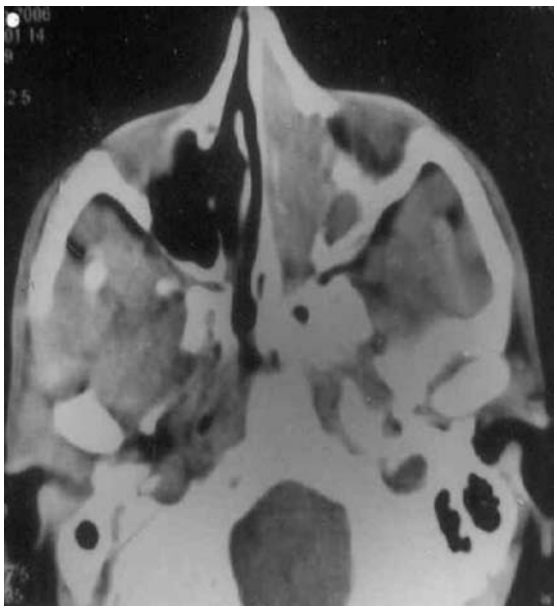

Figure 3. Computed Tomography (CT) scan of paranasal sinuses, axial view, shows a mass in the left nasal cavity extending to the maxillary antrum on the left side with no signs of bony or cartilaginous destruction

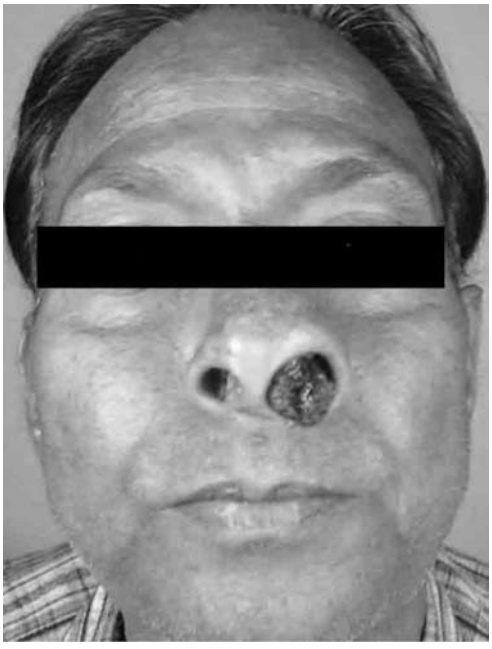

Figure 4. Photograph of second patient showing a black mass coming out of the left nasal cavity.

faster than any other cancer and has become an important public health problem. According to Rigel,[7] the lifetime risk of an individual in the United States to develop cutaneous malignant melanoma was 1:1500 in 1935. By 1980, the risk had increased to 1:250 and by 1991 it was 1:105. In contrast the trend of mucosal melanoma has remained

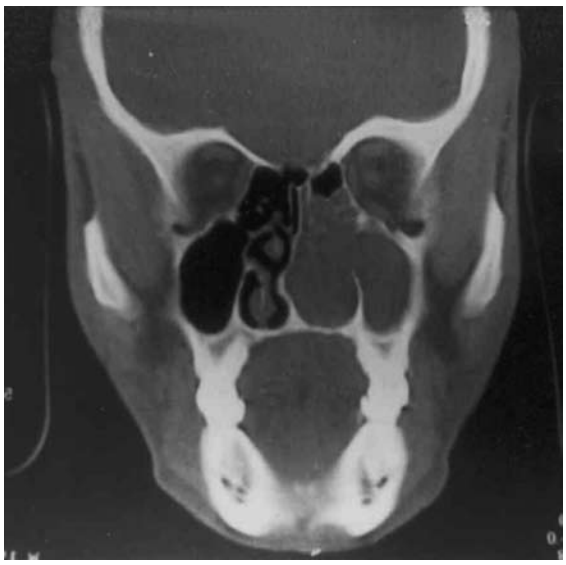

Figure 5. CT scan of paranasal sinuses, coronal view showing an extensive mass involving maxillary antrum and nasal cavity with no signs of bony or cartilaginous destruction.

remarkably stable over the last several decades.[3]

Most patients are older than 50 years at the time of diagnosis, the mean age of presentation being 60-70 years.[6,8] Only 10-20% occur in individuals younger than 50 years, as with both our patients. Most patients are white but 5-16% are black.[6]

Unlike its cutaneous counterpart, exposure to sunlight is not an etiologic factor for mucosal melanoma. There are however sporadic reports of mucosal malignant melanomas associated with preexisting melanosis or occurring somewhat more frequently in Ugandan Africans, suggesting possibilities that ectopic melanin production and race may be important factors.

Calderon-Garcideunas *et al.*[9] assessed 256 cases of nasal and paranasal sinus neoplasms, considering the idea that the etiology of these tumors may be related to air pollution in large cities, which could damage nasal respiratory epithelium DNA, although epidemiological studies have failed to prove this association. Mucosal melanomas of the sinonasal tract are thought to arise from the melanocyte precursors normally present within the mucosa, and occur more often in the nasal cavity than the sinuses, as in the case of both our patients. In a collective review of 407 cases, 73% arose in the nasal cavity, 19% in the sinuses and 8% involved both areas.[6,9] The most common site of origin within the nose is the nasal septum, followed by the inferior and middle turbinates. However, it is often difficult, particularly in bulky lesions to determine the exact site of origin.[10] When confined to the sinuses, the maxillary sinus is the most commonly involved, followed by the ethmoids. The frontal and sphenoid sinuses are rarely affected.[6]

Stammberger *et al*.[11] found involvement of the maxillary sinus in 47%, ethmoidal sinus in 18%, frontal sinus in 14%, nasal cavity in 14% and sphenoid sinus in 7% of all cases.

Because most of the mucosal melanotic lesions are painless in their early stages, the diagnosis is unfortunately often delayed until symptoms resulting from ulceration, growth and or epstaxis are noted.[4] On physical examination, the tumors are sessile or polypoid, pink, white, brown, or black and average 1-4 cm.[8]

Bone destruction may or may not be apparent on radiological imaging. Up to 20% have positive cervical lymph node metastasis, especially around the submandibular gland.[8] Biopsy is confirmatory; immunohistochemistry can be helpful. The traditional histologic staging for cutaneous melanoma (e.g., Clark level) cannot be applied to the mucosa because the mucosa lacks histologic landmarks analogous to papillary and reticular dermis. Breslow thickness, the single most important histologic prognostic factor in localized cutaneous melanoma, has not been found to be useful in head and neck mucosal melanoma.[12–14]

Mucosal melanoma is one of the great mimickers in pathology. Under appropriate conditions it can be mistaken for a variety of tumors. This is especially true in the sinonasal tract where the tumor is rare, often fails to show junctional activities, frequently is amelanotic and occasionally grows in spindle pattern.[15] Mucosal melanomas of the sinonasal tract resemble their cutaneous counterparts and, as such, are composed of epitheloid or spindle cells arranged in small clusters or sheets. Mitoses, pleomorphism, intranuclear inclusions of cytoplasm, necrosis, and lymphatic, vascular, and perineural invasion are additional, although inconsistent features.[16] Ten to thirty percent of tumors are also amelanotic, requiring special tissue stains (warthin-starry, s-100 protein, hmb-45) and a high index of suspicion for diagnosis.[17]

The treatment of choice in mucosal melanoma is a combination of surgery and radiation. Once considered radio-resistant, radiotherapy is now recognized as an important adjuvant and may even have merit as a primary modality.[18,19] Owens *et al.* did a comparable study at the University of Texas MD Anderson Cancer Center and showed that the addition of radiotherapy decreased the rate of local disease recurrence but did not significantly improve survival.[20]

A retrospective study conducted by Benlyazid *et al*. found that postoperative radiotherapy improves local control.[21] Lund *et al*.[17] made a retrospective analysis of 58 individuals diagnosed with nasal mucosa melanoma, followed over a period of 23 years. The patients received surgery alone, surgery with radiotherapy, with or without chemotherapy, radiotherapy or chemotherapy alone. The authors did not see any improvement as far as survival rates are concerned, regardless of the therapeutic method employed, whether single or combined.

The 5-year survival rate in head and neck mucosal melanoma-diagnosed patients was estimated to be 14% according to a retrospective study carried out by Manolidis *et al*.[22]The authors reported that the 5-year survival rate mentioned in the literature is 31%, if one considers the primary lesions of the nasal mucosa and it may drop down to zero in cases of primary tumors of the paranasal sinuses. Stammberger *et al*.[11] evaluated the possibilities and limitations of endoscopic nasal surgery in the treatment of malignant lesions. In the case of nose and nasal sinuses melanomas, five patients underwent endonasal surgery while two died between five and 14 months after surgery (patients in advanced stage and remote metastasis - T4), and the longest survival was 34 months in one patient with local recurrence.

A new therapy has been described as yielding benefits in the treatment of nasal mucosa melanomas. Seo *et al*.[23] reported three cases of this neoplasm in which hormonal chemotherapy led to a favorable clinical outcome. They used Tamoxifen, an anti-estrogen chemotherapeutic agent that competes for the estrogen receptor. Although its mechanism of action in mucosal melanomas has not yet been ascertained, the authors believe that this may prove to be one future option in the therapeutic approach to these lesions.

Immunotherapy in the form of bacillus Calmette-Guérin vaccine, dendritic cell vaccine or cytokines has been used as adjuvant therapy to treat isolated cases of mucosal melanoma, but with limited success.[24,25] Gene therapy is another area of active research.[26]

Melanoma arising in the mucous membranes is a rare clinical entity. Currently, despite aggressive therapy, the prognosis for people with mucosal melanoma is extremely poor. Local treatment failure is a significant problem for most treated patients. Local recurrence and distant metastases continue to be responsible for most treatment failures. Surgery remains the mainstay of treatment although adjuvant radiation therapy recently had an increasing role in the treatment of mucosal melanoma. A clearer understanding of the biology of this disease process may yield more specific immunotherapy techniques. A prospective study is required to assess objectively the optimal treatment regimen.

REFERENCES

1. Harris TJ, Hinchley DM. Melanoma of the head and neck in Queensland. *Head Neck Surg*. 1983 Jan-Feb; 5(3):197-203.
2. Thorn M, Adami H-O, Rinborg U, Bergstorm R, Krusemo U. The association with anatomic site and survival in mucosal melanoma. An analysis of 2,353 cases from Swedish cancer registry. *Eur J Cancer Clin Oncol* 1989 Mar; 25(3):483-491.
3. Conley JJ. Melanomas of the mucous membranes of the head and neck. *Laryngoscope* 1989 Dec; 99(12):1248-54.
4. Huang SF, Liao CT, Kan CR, Chen IH. Primary mucosal melanoma of the nasal cavity and paranasal sinuses: 12 years of experience. *J Otolaryngol* 2007Apr; 36(2):124-9.
5. Spiro JD, Soo KC, Spiro RH. Non squamous cell malignant neoplasms of the nasal cavity and the paranasal sinuses. *Head Neck*. 1995 Mar-Apr; 17(2):114-118.
6. Holdcraft J, Gallagher JC. Malignant melanomas of the nasal and paranasal mucosa. *Ann Otol Rhinol Laryngol*. 1969 Feb; 78(1):5-20.
7. Rigel DS. Epidemiology and prognostic factor in malignant melanoma. *Ann Plas Surg.* 1992 Jan; 28(1):7-8.
8. Kingdom TT, Kaplan MJ. Mucosal melanoma of the nasal cavity and the paranasal sinuses. *Head Neck*. 1995 May-Jun; 17(3):184-189.
9. Calderón-Garcidueñas L, Delgado R, Calderón-Garcidueñas A, Meneses A, Ruiz LM, Garza J, *et al*. Malignant neoplasms of the nasal cavity: A series of 256 patients in Mexico City and Monterrey. Is air pollution the missing link? *Otolaryngol Head Neck Surg*, 2000 Apr; 122(4): 499-508.
10. Bizon MJ, Newman RK. Metastatic melanoma of the ethmoid sinus. *Arch Otolaryngol Head Neck Surg*. 1986 Jun; 112(6):664-7.
11. Stammberger H, Anderhuber W, Walch C, Papaefthymiou G. Possibilities and limitations of endoscopic management of nasal and paranasal sinus malignancies. *Acta Otorhinolaryngol Belg*. 1999; 53(3):199-205.
12. Prasad ML, Patel S, Hoshaw-Woodard S,Escrig M, Shah JP, Huvos AG, Busam KJ. Prognostic factors for malignant melanoma of the squamous mucosa of the head and neck. *Am J Surg Pathol.* 2002 Jul; 26(7):883–892.
13. Prasad ML, Busam KJ, Patel SG, Hoshaw-Woodard S, Shah JP, Huvos AG. Clinicopathologic differences in malignant melanoma arising in oral squamous and sinonasal respiratory mucosa of the upper aerodigestive tract. *Arch Pathol Lab Med*. 2003 Aug; 127(8):997–1002.
14. Thompson LDR, Wieneke JA, Miettinen M. Sinonasal tract and nasopharyngeal melanoma: a clinicopathologic study of 115 cases with a proposed staging system. *Am J Surg Pathol*. 2003 May; 27(5):594–611.
15. Nakhleh RE, Wick MR, Rocomora A, Swanson PE, Dehner LP. Morphologic diversities in malignant melanomas. *Am J Clin Patho*. 1990 Jun; 93(6):731-740.
16. Chang ES, Wick MR, Swanson PE, Dehner LP. Metastatic malignant melanoma with "rhabdoid" features. *Am J Clin Pathol.* 1994 Oct; 102(4):426-431.
17. Lund VJ, Howard DJ, Harding L, Wei WI. Management options and survival in malignant melanoma of the sinonasal mucosa. *Laryngoscope*. 1999 Feb; 109(2):208-11.
18. Harwood AR Lawson VG. Radiation therapy for melanomas of the head and neck. *Head Neck Surg* 1982 Jul-Aug; 4(6):468-474.
19. Trotti A, Peters LJ. Role of radiotherapy in the primary management of mucosal melanoma of the head and neck. *Semin Surg Oncol* 1993 May-Jun; 9(3):246-250.
20. Owens JM, Roberts DB, Myers JN. The role of postoperative adjuvant radiation therapy in the treatment of mucosal melanomas of the head and neck region. *Arch Otolaryngol Head Neck Surg*. 2003 Aug; 129(8):864-8.
21. Benlyazid A, Thariat J, Temam S, Malard O, Florescu C, Choussy O, Makeieff, M, Poissonnet G, Penel N, Righini C, Toussaint B, Guily J L, Vergez S, Filleron F. Postoperative Radiotherapy in Head and Neck Mucosal Melanoma : a GETTEC Study. *Arch Otolaryngol Head Neck Surg.* 2010 Dec;136(12):1219-1225.
22. Manolidis S, Donald PJ. Malignant mucosal melanoma of the head and neck: review of the literature and report of 14 patients. *Cancer.* 1997 Oct; 80(8):1373-86.
23. Seo W, Ogasawara H, Sakagami M. Chemohormonal therapy for malignant melanomas of the nasal and paranasal mucosa. *Rhinology*. 1997 Mar; 35(1):19-21.
24. Nguyen NP, Levinson B, Dutta S, Karlsson U, Alfieri A, Childress C, Sallah S. Concurrent interferon-α and radiation for head and neck melanoma. *Melanoma Res* 2003 Feb; 13(1):67–71.
25. Yannelli JR, Wroblewski JM. On the road to a tumor cell vaccine: 20 years of cellular immunotherapy. *Vaccine* 2004 Nov; 23(1):97–113.
26. Liu M, Acres B, Balloul JM, Bizouarne N, Paul S, Slos P. Gene based vaccines and immunotherapeutics. *Proc Natl Acad Sci USA*. 2004 Oct; 101:14567–71.