CASE REPORT

UDC: 616.214/.216-006.81
DOI: 10.2298/VSP140414075A

Melanoma of the sinonasal mucosa: A report on the two cases and a review of the literature

Mukozni melanom nosnosinusne sluznice

Aleksandra Aleksić*, Radoslav Gajanin†, Dejan Djurdjević‡, Zorica Novaković*, Dalibor Vranješ*, Slobodan Spremo*, Dmitar Travar*, Nataša Guzina-Golac*, Vesna Tomić-Spirić§

***Department of Ear, Throat and Nose, †Department for Pathology; ‡Department of Maxillofacial Surgery, Clinical Center, Banja Luka, Republic of Srpska, Bosnia and Herzegovina; §Clinic of Allergy and Clinical Immunology, Clinical Center of Serbia, Faculty of Medicine, University of Belgrade, Belgrade, Serbia**

Abstract

Introduction. Primary mucosal melanoma of the sinonasal tract is a rare neoplasm, accounting for less than 1% of all melanomas. It has an aggressive and unpredictable biologic behavior characterized by frequent incidence of local recurrence, local and distant metastasis of the disease. **Case report.** This report summarizes the results of the previous research concerning sinonasal mucosal melanoma, and by the example of the two patients suffering from mucosal melanoma, we described clinical and histopathological features of this rare neoplasm and our experience in its diagnosis and treatment. **Conclusion.** Only histopathological analysis complemented by immunohistochemical analysis contributes to early and accurate diagnosis of the disease.

Key words:
melanoma; nose; paranasal sinuses; diagnosis; neoplasms staging; oral surgical procedures; radiotherapy; treatment outcome; prognosis.

Apstrakt

Uvod. Primarni mukozni melanom nosnosinusnog regiona je retka neoplazma i čini svega 1% svih melanoma. Biološko ponašanje melanoma karakteriše agresivan i nepredvidiv rast, česti lokalni recidivi, lokalne i udaljene metastaze. **Prikaz bolesnika.** Rad sumira rezultate prethodnih studija mukoznog melanoma nosnosinusne sluznice, a kroz prikaz dva bolesnika opisane su kliničke i patohistološke karakteristike ove retke neoplazme i naša iskustva sa dijagnostičkim i terapijskim postupcima. **Zaključak.** Naši rezultati pokazuju da patohistološke i imunohistohemijske analize doprinose postavljanju rane i tačne dijagnoze ovog oboljenja.

Ključne reči:
melanom; nos; paranazalni sinus; dijagnoza; neoplazme, određivanje stadijuma; hirurgija, oralna, procedure; radioterapija; lečenje, ishod; prognoza.

Introduction

Mucosal melanoma is a rare neoplasm accounting for less than 1% of all melanomas. However, head and neck region is the most frequent primary site for mucosal melanomas and consists of 55.4% of all mucosal melanomas. Among head and neck anatomical locations, sinonasal tract is the most common primary site for this malignancy [1–5]. Primary sinonasal mucosal melanoma is a rare entity, which constitutes about 1.5–9% of all malignancies in this site [1, 2]. In an exhaustive review, Manolidis and Donald [5] found 1,000 cases reported in the literature up to 1997.

The etiopathogenesis of this form of melanoma is poorly understood. It is clear, however, that sinonasal mucosal melanoma is derived from melanocytes present in the mucosa of nasal cavity [1, 3, 5]. Approximately 80% of sinonasal melanomas are believed to occur in the nasal cavity, whereas about 20% originate in the sinuses. According to the available literature the most frequent primary site is the lateral wall of the nasal cavity (inferior and middle turbinate), and then nasal septum [2–4]. Epistaxis and unilateral nasal obstruction are the most frequent presenting symptoms, in the most reported series. Pain and deformities in the face region with proptosis, diplopia and epiphora rarely occur (in 9–12% of cases) most frequently in advanced stages of the disease [3–6].

Correspondence to: Aleksandra Aleksić, Department of Ear, Throat and Nose, Clinical Center Banja Luka, Koste Jarića 14b, Banja Luka, Republic of Srpska. Phone: +387 65 535 109. E-mail: alexandraaleksic@gmail.com

One of the difficulties in diagnosing mucosal melanoma relates to its clinical rarity and variable histological presentation. In histopathological sense, especially in case of amelanocit lesions, differential diagnosis includes other epithelial and mesenchymal tumors [6, 7]. One of the key histologic features of melanoma is the identification of intracellular melanin. Hence, crucial for making an accurate diagnosis of mucosal melanoma is immunohistochemical staining analysis for S-100, HMB-45, Melan-A, microphthalmic transcription factor, tyrosinase Mart-1 [6, 7]. In other words, immunohistochemistry is invaluable in making an accurate diagnosis [1, 2, 7].

The staging system for mucosal melanoma has not been well established. Therefore, oncologists use different systems to stage mucosal melanoma [3–5]. Some are considered that the current American Joint Committee on Cancer (AJCC) sinonasal staging system should be the primary staging system for patients with mucosal melanomas of the sinonasal tract [2]. Widely used is Ballantyne's clinical staging system: the lesions confined to the primary site – stage I, regional cervical lymph node involvement – stage II, distant metastasis – stage III [8]. According to Ballantyne's clinical staging system, 76–95% of patients with mucosal melanomas of the sinonasal tract present with stage I disease [1, 2, 5].

In the recent literature there are numerous controversies concerning treatment of mucosal melanoma [1, 2, 9, 10]. In view of this locally aggressive growth pattern, even seemingly early, localized lesions may require radical surgery with planned reconstruction for optimal tumor control. The treatment of choice in mucosal malignant melanoma is radical craniofacial resection followed by radiotherapy, particularly in cases of small or doubtful radically reseced surgical margins [1–6, 9, 10]. Postoperative radiotherapy is usually considered for the majority of patients with sinonasal mucosal melanoma [10–12]. Management of disseminated melanoma includes adjuvant and palliative chemotherapy, in an effort to improve systemic disease control and survival [10–12]. In one pooled analysis from five different case series, patients with nasal mucosal melanoma had a 31% 5-year survival rate, whereas sinus melanoma patients had a 0% 5-year survival rate [1, 5].

We presented two cases suffering from primary mucosal melanoma of the sinonasal region taken from our own experience in diagnosis and treatment of this rare disease. Clinical information retrieved included demographic data, presenting symptoms, results of diagnostic procedures, staging, treatment and outcome. The two patients were retrospectively staged according to the Ballantyne's clinical staging system and to the AJCC staging system for sinonasal tumors [8, 13]. All the available clinical information, such as clinical presentation, radiological data, and intraoperative findings, were used for staging purposes.

Case report

Case 1

A female patient, 82-year-old presented with complaints of persistent unilateral nasal congestion for 6 months. She had also been noticing blood streaks in her mucus for several weeks. Clinical examination revealed a proptosis, nasal deformity and large grayish-black solid mass within the left nasal cavity (Figure 1).

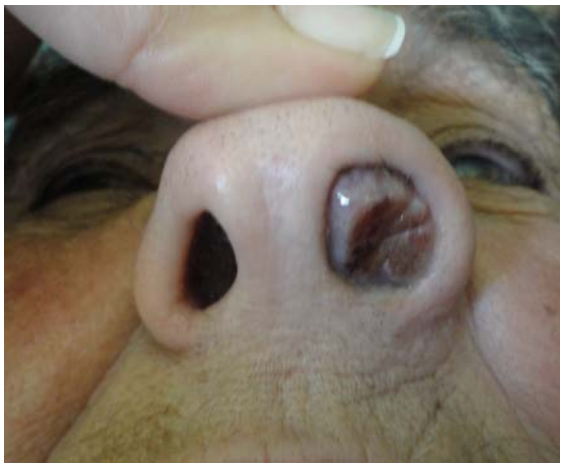


Fig. 1 – Tumor in the left nasal cavity.

A biopsy was obtained and the sample was sent for histopathological analysis. Computed tomography (CT) scan showed an enhancing mass invading the left nasal cavity, left maxillary, ethmoidal and frontal sinus, with destruction of the left medial orbital wall (Figure 2).

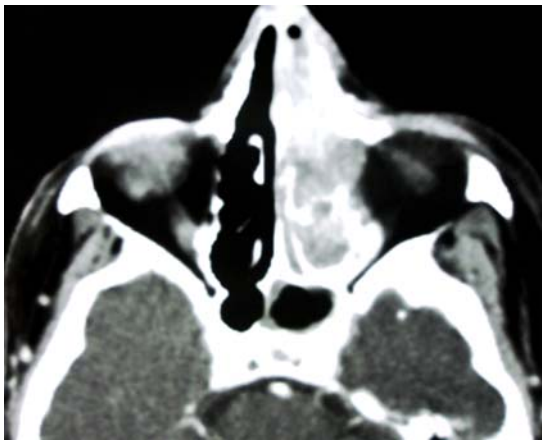
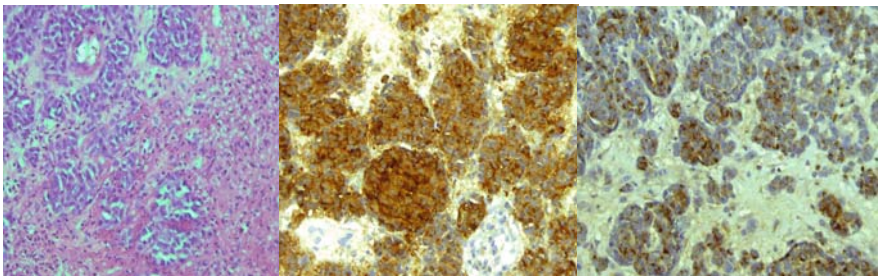


Fig. 2 – Axial computed tomography (CT) image showed an enhancing mass invading the left ethmoid sinus.

CT scan also showed enlarged regional lymph nodes. Histopathological findings were as follows: tumor composed by a cohesive nodule and small nests of tumor cells that have a "pushing" or "expansile" pattern of growth. Tumor cells were of epitheloid type. The cell population was polymorphous, with appearance of cellular enlargement, nuclear enlargement, variation in nuclear size and shape, hyperchromatism, prominent nucleoli, high mitotic count. Immunohistochemistry analysis were : tumor cells positive for CK 7, EMA, S-100, HMB-45 (Figure 3). Antibodies, CK 7 and endomysial antibodies (EMA) were not essential for diagnosis. According to imunohistochemical analysis we confirmed the diagnosis of mucosal melanoma. Meanwhile, a CT scan of thorax showed a distant metastasis in the lung. The findings indicated stage III, T3N2aM1. Taking into consideration the age,



a b c

Fig. 3 – Mucosal melanoma, histopathological findings with imunohistochemical analysis. a) HE, ×200; b) Diffuse cytoplasmic positivity for S-100 (anti- S 100, × 200); c) Diffuse cytoplasmic positivity for HMB-45 (anti-HMB 45, × 200).

advanced stage of the disease (unresectable primary tumor), the presence of regional and distant metastasis, the treatment consisted of radiotherapy. The patient received paliative chemotherapy, but the prognosis was very poor.

Case 2

A 75-year-old male patient presented with complaints of persistent unilateral nasal congestion and nose bleeding for 1 month. Clinical examination revealed a proptosis soft reddish mass on the interior floor of the nasal cavity, partially obstructing the nasal cavity, with adhesion to the nasal septum and inferior turbinate. A biopsy was obtained and the sample was sent for histopathological analysis. CT scan showed a tumor on the floor of the left nasal cavity, with adhesion to the nasal septum and inferior turbinate (Figure 4). Histopathological findings revealed tumor cells of epitheloid type. The cell population was polymorphous with the appearance of cellular enlargement, nuclear enlargement, variation in nuclear size and shape, hyperchromatism, prominent nucleoli, high mitotic count. We performed immunohistochemical analysis and the positive immune response was present at the antibodies S-100 and HMB 45 (Figure 5). According to the clinical examination and immunohistochemical analysis we confirmed

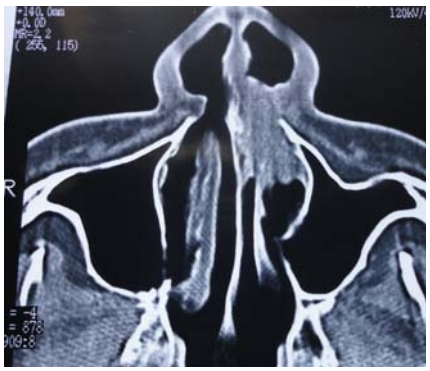
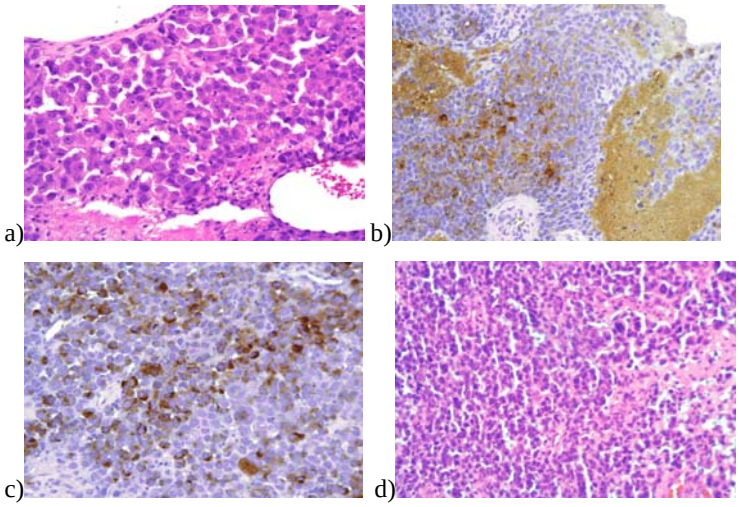


Fig. 4 – Axial computed tomography (CT) image showed tumor in the left nasal cavity, with the adhesion to the nasal septum and inferior turbinate.



a) b) c) d)

Fig. 5 – Mucosal melanoma, histopathological findings with imunohistochemical analysis. a) HE, ×200; b) Cytoplasmic positivity for S-100 (anti-S 100, ×200); c) Cytoplasmic positivity for HMB-45 (anti-HMB 45, × 200); d) HE, ×200.

the diagnosis of mucosal melanoma of the nasal cavity. The findings indicated stage I, T1N0M0. Taking into consideration the stage of the disease, the patient underwent medial maxillectomy and partial septectomy (Figure 6). The final pathology confirmed the diagnosis of sinonasal melanoma. The patient was followed-up fur ther. At a 3-month follow-up, the patient showed no evidence of local reccurence. Then he was receiving postoperative radiotherapy.

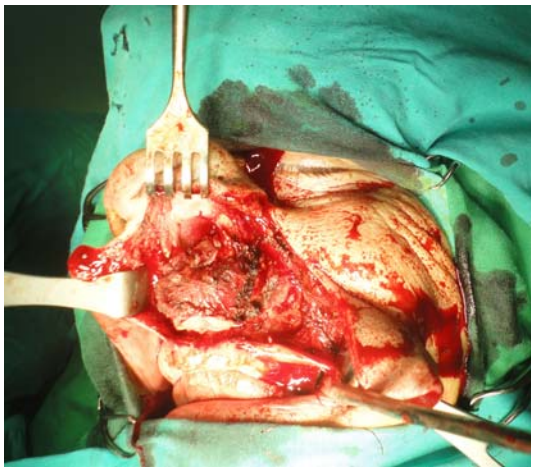


Fig. 6 – Medial maxillectomy and partial septectomy in patient with mucosal melanoma in the nasal cavity.

Discussion

Primary mucosal melanoma of the sinonasal tract has an aggressive and unpredictable biologic behavior characterized by frequent incidence of local recurrence, local and distant metastasis of the disease, despite radical surgical resection [2–7]. Many studies have noted a long time from the appearance of symptoms to evaluation by health care professionals from several weeks to as long as 1–5 months [1–7]. The exact origin is often difficult to ascertain due to anatomic limitations and, for older patients, due to lack of fiberoptic endoscopy and accurate modern anatomic and radiologic diagnostic techniques [1, 2, 5]. Because of its hidden location and rich vascularization, mucosal melanoma is usually diagnosed at a more advanced stage. In a review by Manolidis and Donald [5], 18.7% of patients with malignant mucosal melanoma of the head and neck presented with lymph node metastasis while other reported series showed 26% to 52% [2, 3–10]. The pathologic diagnosis of melanoma hinges on the identification of intracellular melanin [5]. In histopathological sense, especially in case of amelanocit lesions, differential diagnosis includes other epithelial and mesenchymal tumors [6, 7]. Immunohistochemical staining analysis for S-100, HMB-45, Melan-A, microphthalmic transcription factor, tyrosinase Mart-1 are often required to diagnose malignant melanoma [3, 6, 7]. Histopathological features of this neoplasma are as follows: tumor site, specimen, specimen integrity, specimen size, tumor focality, tumor size, maximal tumor thickness, growth phase, histologic type, margins, lymph-vascular invasion, perineural invasion, lymph nodes with metastases [6, 7, 14]. Pathologically, fewer mitoses and the absence of ulceration predict better outcomes and should be reported as part of routine histological profiles of mucosal melanoma [15]. Prasad et al. [14] defined microstaging classification based on histological findings on level I as mucosal melanoma *in situ* (without invasion of the *lamina propria* or with only microinvasion), level II as invasion into the *lamina propria* only, and level III as invasion into deep tissue structures, such as bone, muscle, and cartilage.

There are no randomized trials studying treatment modalities such as surgery, radiotherapy, or chemo and immunotherapy specifically in mucosal melanoma [1–6, 9, 10, 16]. Unfortunately, complete resection achieving melanoma-free margins is often difficult in primary mucosal melanoma of the sinonasal tract because of the close proximity of critical anatomic structures [9, 10, 16]. This likely contributes to the high local recurrence rate, which has been reported to be 50–90% [5, 17]. A study by Dauer et al. [6] which included 61 patients in the period from 1953 to 2003 showed that 50% of patients, despite radical surgical excision, experienced local recurrence. To date, there is no consensus regarding the indications for postoperative radiation therapy, although most authors agree regarding its use in patients with positive and close margins, especially as these have been recently identified as negative prognostic factors [10–12, 16, 17]. In a review of 69 patients with mucosal melanoma, Temam et al. [12] found that the local control rates were 26% with surgery alone and 62% with postoperative radiation therapy, even though the individuals in the radiotherapy group had much more locally advanced tumors. A considerable morbidity in high doses of radiotherapy to the head and neck region, requires new radiographic modalities with better precision [9–12, 16].

Chemotherapy/immunotherapy is usually used with an adjuvant or palliative intention. Combination chemotherapy or biochemotherapy results in higher response rates, in the range of 35–45%, but is associated with significant toxicity and has not been proven to increase overall survival [18]. According to Monolidis and Donald [5] patients with nasal mucosal melanoma have a 31% of 5-year survival rate, whereas sinus melanoma patients fare poorly, with a 0% rate of 5-year survival. One of the prognostic factors is the problem of local recurrence. Of 484 patients in 14 series, 258 (53,3%) patients had local recurrence [1, 2, 15, 19]. Shuman et al. [15] reviewed 52 patients with mucosal melanoma of the head and neck and they demonstrated extremely poor prognosis among patients presenting with advanced primary disease or regional and/or distant metastases.

Conclusion

Primary mucosal melanoma of the sinonasal region is a rare neoplasm with variable clinical and histopathological presentation, invasive growth, frequent local recurrence and poor prognosis despite the implementation of adequate treatment modalities. Immunohistochemical analysis in histopathological diagnosis contributes to early and accurate diagnosis of mucosal melanoma. Most frequent controversies regarding treatment modalities are negative surgical margines, reconstruction of surgical defects and role of radiotherapy. Its location and relatively nonspecific features frequently delay diagnosis, and its rarity avoids an optimal treatment guideline setting.

R E F E R E N C E S

1. *Clifton N, Harrison L, Bradley PJ, Jones NS*. Malignant melanoma of nasal cavity and paranasal sinuses: report of 24 patients and literature review. J Laryngol Otol 2011; 125(5): 479−85.
2. *Moreno MA, Roberts DB, Kupferman ME, DeMonte F, El-Naggar AK, Williams M,* et al. Mucosal melanoma of the nose and paranasal sinuses, a contemporary experience from the M. D. Anderson Cancer Center. Cancer 2010; 116(9): 2215−23.
3. *Wagner M, Morris CG, Werning JW, Mendenhall WM*. Mucosal melanoma of the head and neck. Am J Clin Oncol 2008; 31(1): 43−8.
4. *Seetharamu N, Petrick A, Ott PA, Pavlick AC*. Mucosal Melanomas: A Case-Based Review of the Literature. Oncologist 2010; 15(7): 772−8.
5. *Manolidis S, Donald PJ*. Malignant mucosal melanoma of the head and neck: review of the literature and report of 14 patients. Cancer 1997; 80(8): 1373−86.
6. *Dauer EH, Lewis JE, Rohlinger AL, Weaver AL, Olsen KD*. Sinonasal melanoma: a clinicopathologic review of 61 cases. Otolaryngol Head Neck Surg 2008; 138(3): 347−52.
7. *McLean N, Tighiouart M, Muller S*. Primary mucosal melanoma of the head and neck. Comparison of clinical presentation and histopathologic features of oral and sinonasal melanoma. Oral Oncol 2008; 44(11): 1039−46.
8. *Ballantyne AJ*. Malignant melanoma of the skin of the head and neck. An analysis of 405 cases. Am J Surg 1970; 120(4): 425−31.
9. *Mendenhall WM, Amdur RJ, Hinerman RW, Werning JW, Villaret DB, Mendenhall NP*. Head and neck mucosal melanoma. Am J Clin Oncol 2005; 28(6): 626−30.
10. *Medina JE, Ferlito A, Pellitteri PK, Shaha AR, Khafif A, Devaney KO,* et al. Current management of mucosal melanoma of the head and neck. J Surg Oncol 2003; 83(2): 116−22.
11. *Trotti A, Peters LJ*. Role of radiotherapy in the primary management of mucosal melanoma of the head and neck. Semin Surg Oncol 1993; 9(3): 246−50.
12. *Temam S, Mamelle G, Marandas P, Wibault P, Avril M, Janot F,* et al. Postoperative radiotherapy for primary mucosal melanoma of the head and neck. Cancer 2005; 103(2): 313−9.
13. American Joint Committee on Cancer. In: *Greene FL, Page DL, Fleming ID, Fritz AG, Balch CM, Haller DG,* et al, editors. Nasal cavity and paranasal sinuses. 6th ed. New York: Springer- Verlag; 2002. p. 59−67.
14. *Prasad ML, Patel SG, Huvos AG, Shah JP, Busam KJ*. Primary mucosal melanoma of the head and neck: a proposal for microstaging localized, Stage I (lymph node-negative) tumors. Cancer 2004; 100(8): 1657−64.
15. *Shuman AG, Light E, Olsen SH, Pynnonen MA, Taylor JM, Johnson TM,* et al. Mucosal melanoma of the head and neck: predictors of prognosis. Arch Otolaryngol Head Neck Surg 2011; 137(4): 331−7.
16. *Gavriel H, McArthur G, Sizeland A, Henderson M*. Review: mucosal melanoma of the head and neck. Melanoma Res 2011; 21(4): 257−66.
17. *Lund VJ, Howard DJ, Harding L, Wei WI*. Management options and survival in malignant melanoma of the sinonasal mucosa. Laryngoscope 1999; 109(2 Pt 1): 208−11.
18. *Bartell HL, Bedikian AY, Papadopoulos NE, Dett TK, Ballo MT, Myers JN,* et al. Biochemotherapy in patients with advanced head and neck mucosal melanoma. Head Neck 2008; 30(12): 1592−8.
19. *Thompson LD, Wieneke JA, Miettinen M*. Sinonasal tract and nasopharyngeal melanomas: a clinicopathologic study of 115 cases with a proposed staging system. Am J Surg Pathol 2003; 27(5): 594−611.

Received on April 14, 2014.
Revised on August 4, 2014.
Accepted on August 22, 2014.
Online First August, 2015.