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

Mukozni melanom nosnosinusne sluznice


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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, 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


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. Primary sinonasal mucosal melanoma is a rare entity, which constitutes about 1.5–9% of all malignancies in this site. In an exhaustive review, Manolidis and Donald 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. 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. 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.
One of the difficulties in diagnosing mucosal melanoma relates to its clinical rarity and variable histological presentation. In histopathological sense, especially in case of amelanocytic lesions, differential diagnosis includes other epithelial and mesenchymal tumors. 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. In other words, immunohistochemistry is invaluable in making an accurate diagnosis.

The staging system for mucosal melanoma has not been well established. Therefore, oncologists use different systems to stage mucosal melanoma. 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. 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. According to Ballantyne’s clinical staging system, 76–95% of patients with mucosal melanomas of the sinonasal tract present with stage I disease.

In the recent literature there are numerous controversies concerning treatment of mucosal melanoma. In view of this locally aggressive growth pattern, even seemingly early, localized lesions may require radical surgery with planned resection 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 resected surgical margins. Postoperative radiotherapy is usually considered for the majority of patients with sinonasal mucosal melanoma. Management of disseminated melanoma includes adjuvant and palliative chemotherapy, in an effort to improve systemic disease control and survival. 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.

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. 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.

CT scan also showed enlarged regional lymph nodes. Histopathological findings were as follows: tumor composed of 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 performed: 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 immunohistochemical 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,
advanced stage of the disease (unresectable primary tumor), the presence of regional and distant metastasis, the treatment consisted of radiotherapy. The patient received palliative 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.

Fig. 5 – Mucosal melanoma, histopathological findings with immunohistochemical analysis.

a) HE, x200; b) Cytoplasmic positivity for S-100 (anti-S 100, x 200); c) Cytoplasmic positivity for HMB-45 (anti-HMB 45, x 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 further. At a 3-month follow-up, the patient showed no evidence of local recurrence. 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. 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. 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. 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, 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%. The pathologic diagnosis of melanoma hinges on the identification of intracellular melanin. In histopathological sense, especially in case of amelanotic lesions, differential diagnosis includes other epithelial and mesenchymal tumors. Immunohistochemical staining analysis for S-100, HMB-45, Melan-A, microphthalmic transcription factor, tyrosinase Mart-1 are often required to diagnose malignant melanoma. The pathologic features of this neoplasm 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. Pathologically, fewer mitoses and the absence of ulceration predict better outcomes and should be reported as part of routine histological profiles of mucosal melanoma. Prasad et al. defined microstaging classification based on histological findings on level I as mucosal melanoma in situ (without invasion of the lamina propria) or with 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 chemotherapy and immunotherapy specifically in mucosal melanoma. 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. This likely contributes to the high local recurrence rate, which has been reported to be 50–90%. A study by Dauer et al. 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. In a review of 69 patients with mucosal melanoma, Temamm et al. 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 regions requires new radiographic modalities with better precision.

Chemotherapy/imunotherapy 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. According to Monolidis and Donald, 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. Shuman et al. 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 margins, 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.
REFERENCES


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