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Mucosal Malignant Melanoma of Nasal Cavity Recurring a Year After Radiotherapy

Cem ÇOMUNOĞLU[1], Gamze MOCAN KUZEY[1], Mete İNANÇLI[2], Füsun BABA[1], Hanife ÖZKAYALAR[1]

Department of [1]Pathology and [2]Otolaryngology, Yakın Doğu University, Faculty of Medicine, LEFKOŞA, TURKISH REPUBLIC of NORTHERN CYPRUS

ABSTRACT

Objective: Sinonasal mucosal malignant melanoma is a rare entity. In this report we present a nasal mucosal malignant melanoma case with its histopathological and clinical features.

Case Report: An 88-year-old female patient presented with epistaxis a month ago. Examination revealed a polypoid mass lesion of right nasal cavity originating from the middle concha. Her medical history revealed that she had been found to have a mass lesion in the right nasal cavity 15 months ago. She then underwent a punch biopsy from that lesion. A definitive histopathological diagnosis was not made but it was declared that the lesion had been a malignant epithelial tumor. The patient then had radiotherapy and the lesion showed complete regression. One year after completion of radiotherapy, the lesion recurred. Her last PET-CT showed multiple metastatic foci. Endoscopic excisional biopsy was performed for her recurrent lesion. Fragmented tumoral tissues were measured as 3,6x3x0,5 cm. Macroscopically the tumor was brownish in color. Histopathologically the tumor consisted of spindled and epitheloid cells. Immunohistochemically the tumor cells displayed positivity for S-100, HMB-45 and Melan-A. Findings were consistent with malignant melanoma.

Discussion: Mucosal malignant melanomas have a poor prognosis despite chemotherapy and radiotherapy. Five-year survival for sinonasal melanoma is reported to be lower than 35%. Sinonasal melanomas show a high recurrence rate. The immunohistochemical markers showing high specificity for malignant melanoma such as S-100, HMB-45 and Melan-A are used in order to reach a correct diagnosis. In our case the tumor showed recurrence and multiple metastases 1 year after completion of radiotherapy. For this recurrent tumor, chemotherapy and radiotherapy have been planned.

Key Words: Nasal cavity, Malignant melanoma, Radiotherapy

INTRODUCTION

Sinonasal mucosal malignant melanoma (MM) is a rare entity, representing a small proportion of all malignant melanomas. Mucosal melanoma occurs mainly between the fourth and seventh decades (1-3). These tumors show high local recurrence rate and the majority of recurrences are reported to be observed within 1 to 2 years after treatment. It was suggested that definitive radiotherapy (RT) was curative in a significant subset of patients and yielded similar 5-year survival rates compared with surgery. However, it was also claimed that local–regional control had been more effective after combined surgery and adjuvant RT (4). We herein present a case of nasal MM recurring 1 year after of completion of definitive RT.

CASE REPORT

An 88-year-old female patient presented with epistaxis a month ago. Magnetic resonance imaging (MRI) examination revealed a polypoid mass lesion of right nasal cavity originating from middle concha. The tumor reached the skull base and lamina papyracea but did not invade beyond (Figure 1). Her medical history revealed that she had mass lesion of the right nasal cavity 15 months ago. She then underwent a punch biopsy from that lesion. A definitive histopathological diagnosis was not made but it was declared that the lesion had consisted of malignant epithelial cells. Because of this biopsy report, the tumor might have incorrectly been thought as carcinoma. The patient then had RT and the lesion showed complete regression. A year after completion of her RT, the lesion recurred. Her PET-CT showed multiple metastatic foci in the right and left lung, liver, lymph nodes (neck, mediastinum, abdomen) and bone (right scapula, right femur). Endoscopic excisional biopsy was performed for the nasal mass lesion. Fragmented tumoral tissues were measured as 3,6x3x0,5 cm. Macroscopically the tumor was brownish in color. Histopathologically the tumor consisted of spindle and epitheloid cells. Tumoral cells were proliferating mainly in solid and alveolar pattern under ciliated columnar type respiratory epithelium. Mitotic figures were counted as 14 per 1 mm^2 (Lower than 3 per High Power Field (HPF)).

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Correspondence: Cem ÇOMUNOĞLU
Yakın Doğu Üniversitesi, Tıp Fakültesi, Patoloji Anabilim Dalı,
LEFKOŞA, TURKISH REPUBLIC of NORTHERN CYPRUS
E-mail: cemcomunoglu@gmail.com Phone: +90 536 930 70 89

There was no lymphovascular space or perineural invasion. Intracytoplasmic brown pigment was observed (Figure 2). Coagulative tumor necrosis foci were seen. Tumor borders were infiltrative and there was tumor infiltration in surgical margins. Immunohistochemically the tumor cells displayed positivity for S-100, HMB-45 and Melan-A (Figure 3). Tumor cells were immunonegative for pancytokeratin (PAN-CK), CK 5/6, p63, CD-56, synaptophysin, smooth muscle actin (SMA), desmin and LCA. Histopathological and immunohistochemical findings were consistent with mucosal malignant melanoma. Three months later the tumor showed recurrence as a mass lesion filling the right nasal cavity and metastasized to the thyroid. The tumor located at the nasal cavity was resected completely. Metastatic lesion of the thyroid caused obstruction of respiratory passage. Tracheostomy was therefore performed. The patient is alive with widespread metastatic disease 14 weeks after operation. Chemotherapy and RT have been planned for this recurrent tumor.

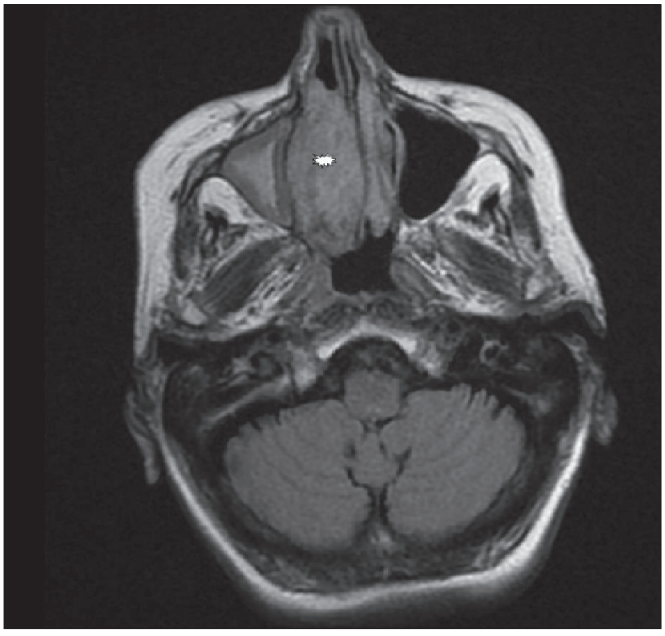

Figure 1: Mass lesion filling the right nasal cavity but not invading beyond (asterix) (MRI).

DISCUSSION

Mucosal MMs of the sinonasal cavity are rare tumors that have a poor prognosis. The five-year survival of sinonasal malignant melanoma was found to be lower than 35% (1). They are thought to originate from melanocytes present in the mucosa of the respiratory tract but they may originate from an area of squamous metaplasia (1). Macroscopically, sinonasal MMs display a polypoid growth pattern (5). Metastasis from another site should be excluded. Presence of junctional activity and Pagetoid spread indicates a primary neoplasm; however these features are usually lost. In addition, it was claimed that sinonasal malignant melanomas were not detected in a pure in situ preinvasive or intraepithelial stage, in contrast to cutaneous and oral melanoma (6).

We could not observe these features in our case but the medical history did not reveal any previous neoplasm. In the differential diagnosis, MMs should be distinguished from non-keratinizing squamous cell carcinomas and neuroendocrine carcinomas. The immunohistochemical markers showing high specificity for malignant melanoma

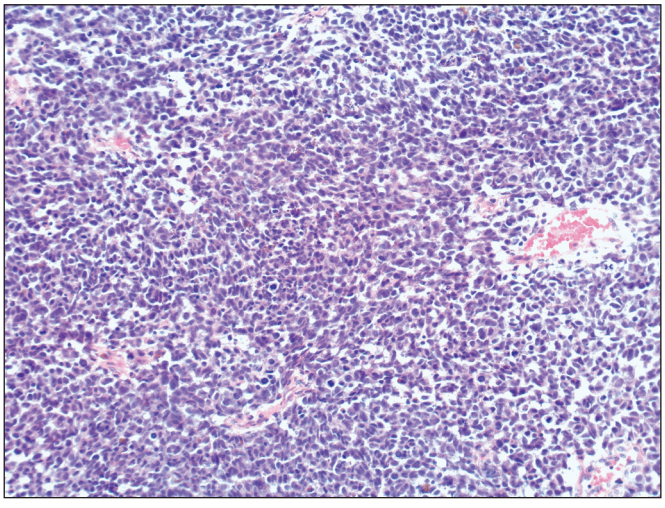

Figure 2: Epitheloid pleomorphic melanoma cells containing intracytoplasmic brown pigment and displaying high mitotic activity (H&E x200).

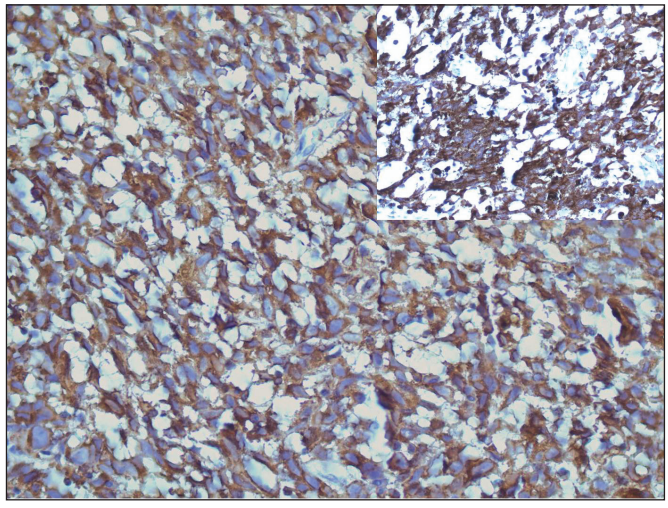

Figure 3: Diffuse and strong immunopositivity for HMB-45 (HMB-45, x400). Inset: Diffuse and strong immunopositivity for Melan-A (Melan-A x400).

such as S-100, HMB-45 and Melan-A, are used in order to reach a correct diagnosis (3,7). MMs are negative for keratins and neuroendocrine markers (3). It has been suggested that tumors composed of small undifferentiated cells should be differentiated from lymphoma and rhabdomyosarcoma (6). Small undifferentiated cells were not observed in our case in spite of repeated sampling. Lymphoid marker LCA and myogenic markers SMA and desmin were also immunonegative, excluding lymphoma and rhabdomyosarcoma.

It was reported that the presence of 10 or more mitosis per HPF suggested a bad prognosis and related with death of disease or locoregional recurrence (2,3). It was stated that the level of melanotic pigmentation was reversely correlated with survival and pseudopapillary architecture was found to be associated with locoregional recurrence (2). In our reported recurrent tumor, mitotic rate was not higher than 10 per HPF (approximately 3 per HPF). A pseudopapillary architecture was not seen but the tumor contained heavy pigmentation. Thompson et al. stated that tumor necrosis and tumor thickness were not mutually related with patient survival. They suggested that the presence of undifferentiated cell morphology was related with poor outcome (3). Tumor necrosis was present in our case but we did not observe undifferentiated cells.

The AJCC staging system (8) has been proposed as the main staging method for sinonasal mucosal MMs (9). According to this system, the tumor size is correlated with 5-year overall survival (OS) (2).

It has been stated that radical surgical resection of the primary tumor with negative margins may ensure the best patient outcome (4). However, it is generally difficult to provide negative margins because the microscopic tumor infiltration is usually more extensive than the impression from the macroscopic lesion (5), as for our case. It was proposed that an endoscopically-assisted procedure provides a higher 2-year OS when compared with those who had an open procedure (2) and also provides lower postoperative complication rates (10). It was suggested that when possible, complete surgical resection and in examples of extensive tumors or where resection margins were limited, postoperative adjuvant radiotherapy should be performed (11,12). However, it was claimed that the optimal RT dose and fractionation schedule for sinonasal mucosal melanomas remained undetermined (2). Although a clear benefit in OS could not be demonstrated with adjuvant radiation therapy it was stated that a total dose of 54 Gy or more provided a lower rate of locoregional recurrence when compared with the results of a total dose 30-50 Gy (2). In some other reports it was also suggested that postoperative RT showed a better local disease control (4,13-15). Kingdom and Kaplan found that postoperative radiotherapy provided increased disease-free intervals and prolonged survival. They also suggested resection of recurrent tumor (16). However Vandenhende et al. claimed that post-operative radiotherapy provided an improved local control only for patients who had stage four tumors and the OS was poor despite post-operative RT (17).

Primary curative RT is proposed in patients with localized inoperable tumors in order to get long-term palliation (4,14). In a retrospective survey of 28 cases of sinonasal MM treated by definitive radiotherapy, it was reported that in 22 out of 28 cases (79%) early complete regression and in 17 out of 28 cases (61%) complete local control was detected. The follow-up was limited by early demise of patients because of metastatic disease; therefore the authors claimed that the statistical 3-year local disease-free survival was 49% (18). In our case, definitive RT was performed 2 years ago, although the primary histopathological diagnosis was not known. The primary pathology report indicated a malignant epithelial neoplasm. It was stated that definitive RT did not differ from other therapeutic modalities in OS (10). Even though complete regression was observed, the tumor displayed recurrence 1 year after completion of radiotherapy.

In conclusion, we have reported a case of mucosal MM originating from the nasal cavity. Our case tumor showed recurrence and multiple metastases 1 year after definitive radiotherapy and a second recurrence 3 months later after endoscopic radical resection, indicating the poor prognosis of these tumors. We now plan to administer chemotherapy and radiotherapy.

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