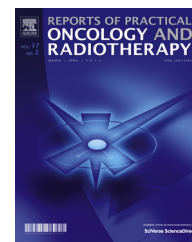


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Case report

Radiotherapy alone as a method of treatment for sinonasal mucosal melanoma: A report based on six cases and a review of current opinion



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ABSTRACT

Objectives: Radiotherapy in patients with sinonasal mucosal melanoma (SNMM) was given as alternative treatment to surgery in cases with advanced, inoperable tumors or those not eligible for surgery. We presented the outcomes for patients with SNMM treated with radiotherapy alone.

Material and methods: The retrospective review of 6 consecutive SNMM (nasal cavity – 4 pts. and paranasal sinus – 2 pts.) patients (3 males and 3 females at mean age 64 years) treated between 2008 and 2016 was presented. The stage of disease was: T3 (1 pt.), T4a (3 pts.), T4b (2 pts.); with N0 and M0 in all patients. All patients underwent definitive primary photon radiotherapy (IMRT) alone; dose 66–72 Gy was delivered in 22–24 fractions given in 5 fractions (3 Gy) a week.

Results: The complete remission was observed in all our patients but only one patient survived 5 years without disease. Five patients died due to multiple distant metastases; two of those patients developed associated local recurrence 7–8 months after radiotherapy.

Conclusion: SNMM has a poor prognosis due to its high metastatic potential. Based on our numerically small report and data from literature we concluded that primary radiotherapy alone assured complete remission and even 5-year disease-free survival in only a few individual patients.

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1. Introduction

Sinonasal mucosal melanoma (SNMM) is a rare tumor that accounts for 0.7–1% of all malignant melanomas, approximately 4% of all sinonasal tumors and 8–10% of melanomas occurring in the head and neck (HNMM).^{1–6}

The prognosis for patients with HNMM is currently poor; the 5-year overall survival rate ranges between 8 and 45% of cases, and is usually less than 30%.^{2,3,7–11} HNMM is characterized by relatively frequent local recurrences (26–85%) and distant metastases (18–68%).^{2,9,11–14} Primary surgery, aimed at removing the tumor within the margin of healthy tissue, is the treatment of choice for such patients.^{4–7,9,13,15} Unfortunately, radical procedures are often difficult, mainly due to the dissemination of HNMM, its frequent multi-focal character and complex anatomy in the surgical field associated with the close proximity of numerous critical structures with important functions.^{4,5,10,13,16} If the procedure is not micro- or macroscopically radical, the widely accepted approach is the use of postoperative radiotherapy.^{4,5,7,14,17,18} In patients who are not eligible for primary surgical treatment, primary definitive or palliative radiotherapy is applied.^{4,5,14,17–22}

The objective of our study was to present the outcomes of SNMM patients treated with primary radiotherapy alone, and analyse current views on the role of external radiotherapy as a definitive treatment modality for HNMM.

2. Methods

The study focused solely on SNMM patients who had undergone definitive primary radiotherapy at the Maria Skłodowska-Curie Institute – Oncology Center in Krakow between 2008 and 2016. Patients were referred to our Department of Radiotherapy from Otorhinolaryngology Clinics, either because their cancer was inoperable or they had refused surgery. The extent of the disease was evaluated on the basis of local, thoraco-abdominal and brain CT and head and neck MRIs in all patients, scintigraphy in 2 patients and PET-scan in 4 patients. TNM staging was based on the 7th edition of the AJCC (American Joint Committee on Cancer 2010) classification of SNMM.²³ The radiotherapy toxicities were graded using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. Weekly follow-ups continued until acute toxicity was easily manageable. To confirm local control, MRI and/or PET-CT was performed every 3–6 months following the end of radiotherapy, and distant metastases were assessed by CT and for PET-CT. The overall survival time was calculated from the start of the treatment to the date of death or last confirmed date of survival.

3. Results

3.1. Patients

We presented six consecutive SNMM patients treated with primary radiotherapy alone; their characteristics are listed in [Table 1](#).

Three males and 3 females were treated. The mean age was 64 years (range, 56–72 years). One patient was diagnosed as stage T3, 3 patients T4a, and 2 patients T4b, according to the 7th edition of the AJCC classification. No cervical lymph node or distant metastases were observed in the initial radiotherapy (N0, M0). Four patients were diagnosed with nasal cavity melanomas (2-T4a NOM0 inferior turbinate, and 2-T4bNOM0 nasal cavity without further anatomic details, because of the advanced state of the disease), one patient had ethmoid sinus melanoma and another sphenoidal sinus melanoma. All the patients reported nasal obstruction and/or epistaxis; one patient reported visual impairment. In four patients the tumour was inoperable, while the other two refused surgery.

Five patients had 3 positive melanocyte markers (S100 protein, HMB-45, and Melan-A); one patient had two positive markers (S100 and HMB 45). Ulceration was observed in 2 patients, and necrosis in one.

3.2. Treatment

All patients were treated with definitive primary photon radiotherapy alone. Doses varying between 66 Gy and 72 Gy were delivered in 22–24 fractions (3 Gy), 5 fractions a week. Intensity modulated radiation therapy (IMRT) was applied. The gross tumor volume (GTV) was determined with CT, MR, and PET-CT. The clinical target volume (CTV) was defined as GTV + 5 mm margins, and the planning target volume (PTV) as CTV with the addition of 3–5 mm. The dose constraint for organs at risk (brain stem and optic nerves/chiasma) was 45 Gy.

3.3. Toxicity

The most common acute toxicities were dermatitis and mucositis, which were observed in all 6 of our patients, ranging from grades 1–2 in 5 patients and grade 3 grade in 1 patient. Conjunctivitis grades 1–2 was observed in 2 patients and middle ear inflammation grade 2 in 1 patient.

The most common late adverse event was chronic sinusitis grades 1–2, noted in all our patients. Watery eyes due to lacrimal duct obstruction grade 2 was observed in 2 patients (Nos. 2 and 6), ototoxicity grade 1 in other 2 patients (Nos. 1 and 3). Patient No. 5 had optic nerve toxicity, resulting in decreased visual acuity (grade 2), 23 months after radiotherapy. No late complications were observed in patient No. 4, alive after 5 years disease free.

3.4. Outcomes

Three months after radiotherapy complete remission of the tumor was observed in all our patients. One patient (T3NOM0) survived more than 5 years disease free. Five patients died due to multiple distant metastases; the mean survival time of these patients was 22.2 months (range, 8–52 months). Distant metastases were observed in the liver (4 patients), the lungs (3 patients) and the brain (2 patients); in two patients metastases were also located in the cervical lymph nodes. Two patients with metastases developed associated local recurrence – 7–8 months after radiotherapy. These patients who developed dis-

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