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Original article

Prognostic value of two tumour staging classifications in patients with sinonasal mucosal melanoma

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ABSTRACT

Introduction: Sinonasal mucosal melanoma is a rare disease associated with a very poor prognosis. The purpose of this study was to assess the prognostic value of the 2 staging systems published in the literature for these tumours: the American Joint Committee on Cancer (AJCC) Cancer Staging Manual for mucosal melanoma of the head and neck published in 2009 (7th edition) and the AJCC Cancer Staging Manual for cancers of the nasal cavity and paranasal sinuses published in 2002 (6th edition) and the prognostic value of tumour site, either limited to the nasal cavities or with paranasal sinus invasion.
Methods: A retrospective study was conducted on 18 patients treated between August 1998 and June 2014. Each lesion was staged according to the AJCC Cancer Staging Manual 2002 and 2009 and the following data were collected: age, sex, tumour site, initial symptoms, treatment modalities, follow-up, recurrences and overall survival. Patient survival, from the date of discovery of the melanoma until death, was analysed by Kaplan-Meier survival curves and between-group comparison of survival was performed with a log rank test.
Results: The mean age at diagnosis was 72 years (range: 54–94) and the cohort comprised 11 women and 7 men. The median overall survival was 80 months, the 1-year overall survival was 82.6% and the 5-year overall survival was 54.5%. The AJCC 2002 staging system presented a statistically significant prognostic value ($P = 0.0476$), while no statistically significant prognostic value was observed for the AJCC 2009 staging system ($P = 0.108$). Paranasal sinus invasion was significantly associated with a poor prognosis ($P = 0.0039$).
Conclusion: This study demonstrates the superiority of the non-specific AJCC 2002 Cancer Staging Manual. Medical and surgical management must take paranasal sinus invasion into account, as it constitutes a major prognostic factor.

1. Introduction

Sinonasal cancers are uncommon, aggressive tumours. Primary mucosal melanoma of the head and neck is a rare entity, accounting for 0.5% of all head and neck tumours [1], and 4% of malignant sinonasal tumours [2,3]. Mucosal melanomas arise from ectodermal (neural crest) melanocytes present in respiratory or stratified squamous epithelium mucosa [1,4]. The most common sites of mucosal melanoma, in increasing order of frequency, are the oesophagus, larynx, pharynx, oral cavity and paranasal sinuses [5]. Clinical features are non-specific and the signs suggestive of melanoma are observed only late during the course of this disease. Mucosal melanoma is associated with high local recurrence and distant metastasis rates [6,7]. Tumour staging is an essential step of management to establish the prognosis and propose the most appropriate treatment. Several classifications of mucosal melanoma have been proposed. The classification proposed by Ballantyne in 1970 described 3 stages: stage I was defined as a tumour confined to the primary site, stage II was defined as a tumour with regional lymph node involvement and stage III was defined as a tumour with systemic metastases [8]. This classification was modified by Prasad et al. in 2004 [2], who added 3 levels of local invasion: in situ, invasion of the lamina propria and invasion of deep tissues. More recently, the non-specific AJCC (American Joint Committee on Cancer) Cancer Staging Manual for cancers of the nasal cavity and paranasal sinuses (6th edition, 2002) [9] was extended to include mucosal melanomas (Table 1). Finally, in 2009, a specific classification for mucosal melanoma of the head and neck was proposed in the 7th edition of the AJCC Cancer Staging Manual ([10,11]; Table 2). It uses histological data based on examination of

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Table 1
AJCC 2009 classification [9].

T3	Mucosal disease
T4a	Moderately advanced disease – tumour involving deep soft tissue, cartilage, bone, or overlying skin
T4b	Very advanced disease – tumour involving dura, skull base, lower cranial nerves (IX, X, XI, XII), masticator space, carotid artery, prevertebral space, or mediastinal structures

cutaneous malignant melanoma and imaging data. Recent studies have analysed the correlation between survival and these various staging classifications. According to some authors, the AJCC 2002 classification is significantly correlated with survival [12], while other authors have reported a significant correlation between the AJCC 2009 staging system and survival, but did not compare the results with AJCC 2002 [13]. The objectives of this study were to assess the prognostic value of the AJCC 2002 and 2009 staging systems and to analyse the prognosis of paranasal sinus invasion.

2. Patients and methods

This was a single-centre retrospective study including 18 cases of histologically confirmed sinonasal mucosal melanoma managed in our department between August 1998 and June 2014. Cases of metastases from cutaneous malignant melanoma were excluded. All patients in this series had primary sinonasal mucosal melanoma and none of them had a previous diagnosis of melanoma in another site. The following data were collected: age, sex, site of the lesion, initial symptoms, treatment modalities, follow-up, recurrences and survival.

The diagnosis of mucosal melanoma was based on histological criteria. Pigmentation of the lesion, the presence or absence of melanin, and bone, perineural, lymph node and vascular invasion were systematically studied. Cytological examination (classification into four cell types: pseudoepithelial, fusiform, undifferentiated or mixed) and immunohistochemical analysis using anti-protein S100, antivimentin, HMB45, melan-A antibodies were systematically performed [14,15].

Assessment of the lesions comprised nasal endoscopy with analysis of tumour characteristics (unilateral or bilateral, colour, site, zone of implantation, and volume) and neck palpation looking for lymphadenopathy. The imaging assessment comprised CT scan, MRI with T1-weighted, gadolinium-enhanced T1-weighted, and T2-weighted sequences and, when appropriate, PET–CT. Regional and distant staging was based on neck and chest CT scan.

Table 2
AJCC 2002 classification [10,11].

T1	Tumour limited to ethmoidal sinus, with or without bony invasion	Tumour limited to maxillary sinus
T2	Tumour involves an adjacent site within the nasoethmoidal complex, with without bony invasion	Tumour causing bone erosion or destruction, including extension into hard palate and/or middle nasal meatus
T3	Tumour extends to invade the medial wall or floor of the orbit, maxillary sinus, palate, or cribriform plate	Tumour invades any of the following: bone of posterior wall of maxillary sinus, subcutaneous tissues, floor or medial wall of orbit, pterygoid fossa, ethmoid sinuses
T4a	Tumour invades any of the following: anterior orbital contents, skin of nose or cheek, minimal extension to anterior cranial fossa, pterygoid plates, sphenoid or frontal sinuses	Tumour invades any of the following: anterior orbital contents, skin of cheek, pterygoid plates, infratemporal fossa, cribriform plate, sphenoid or frontal sinuses
T4b	Tumour invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than V2, nasopharynx, clivus	Tumour invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than maxillary division of trigeminal nerve V2, nasopharynx, clivus

The majority of patients were treated by surgery and radiotherapy.

All tumours were staged and the overall survival and recurrence-free survival of the patients were compared according to the 7th and 6th editions of the AJCC Cancer Staging Manual and according to the presence or absence of paranasal sinus invasion. We only analysed the T tumour criterion of the TNM classification due to the small number of patients with lymph node invasion or metastatic disease at the time of the diagnosis. Paranasal sinus invasion was defined by tumour arising in a paranasal sinus or the presence of paranasal sinus tumour extension (maxillary, frontal or sphenoidal sinuses, excluding the ethmoid sinus) with or without signs of bone erosion or destruction.

Results of statistical analysis were expressed in terms of sample sizes and percentages for qualitative and categorical variables and by mean ± standard deviation for quantitative variables. Patient survival from the date of diagnosis of melanoma until death (or last news) was analysed according to Kaplan-Meier survival curves and survival between groups was compared by a log-rank test. Recurrence-free survival was analysed in a similar way, from the date of diagnosis until the event (death or recurrence). One-year and 5-year overall survival and recurrence-free survival rates are presented with their 95% confidence interval. Median survival was also calculated. All statistical analyses were performed with a two-tailed test and a type I error of 5% with STATA V12 software (Stata Corp, College Station, Texas, USA).

3. Results

Mean age at diagnosis was 72 years (range: 54–94) and the cohort comprised 11 women and 7 men. The most common tumour site was the nasal septum in 7 patients (38%), the inferior turbinate in 5 patients (28%), and the sinus in 5 patients (28%) and the middle turbinate in one case. Initial symptoms were epistaxis in 13 patients (72%) and blocked nose in 9 patients (50%). The other signs were unilateral maxillary pain in 3 patients (18%), deformity of the wing of the nose, a superinfection of the nasal cavity with cacosmia and blindness in one case.

CT scan of the facial bones with 3D reconstruction and staging assessment were performed in all patients. Magnetic resonance imaging (MRI) was performed in 15 patients (83%) and PET–CT scan was performed in 8 patients (44%) at the time of the initial assessment.

According to the AJCC 2009 staging system, 12 patients (66%) were stage T3, 4 patients (22%) were stage T4a and 2 patients (12%) were stage T4b and, according to the AJCC 2002 staging system, 9 patients (49%) were stage T1, 2 patients (12%) were stage T2, 1 patient (6%) was stage T3 and 6 patients (33%) were stage T4. Mean follow-up in this patient series was 40 months and no patients were lost to follow-up. Lesions were classified as strictly intranasal in 72% of cases and arising from the paranasal sinus or with paranasal sinus invasion in 28% of cases.

Treatment consisted of first-line surgery in 15 (83%) patients. Three (18%) patients were not operated because of an anaesthetic contraindication or because surgery was considered to be excessively mutilating. External beam radiotherapy was performed in 2 patients. Palliative chemotherapy adapted to the patient's general state of health was administered to the third patient. Endoscopic endonasal surgery was performed in 8 (44%) patients, including 5 patients with stage T1 tumours according to AJCC Cancer Staging Manual 2002 and transfacial surgery was performed in 7 (38%)

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