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Therapy of sinonasal malignancies invading the orbit-orbital exenteration versus preservation of the orbit plus radiotherapy☆,☆☆

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ABSTRACT

Introduction: Orbital invasion is a strong independent prognostic factor for sinonasal malignancies. While there is consent about preservation of the orbit for tumors limited to the orbital periosteum there is controversy about the optimal management of sinonasal malignancies transgressing this barrier. Therefore the aim of our study was to compare exenteration versus preservation of the orbit.
Material and methods: 52 patients with sinonasal malignancies invading the orbit beyond the orbital periosteum with involvement of the orbital soft tissues were included in the retrospective study. Prognostic factors were identified through univariate analysis.
Results: Univariate analysis revealed a significant impact of N-classification ($p = 0.017$), and treatment strategy ($p = 0.016$). Exenteration of the orbit was associated with a significantly better 5-year overall survival rate (65.5%) than preservation of the orbit (14%).
Conclusions: For patients with invasion of the structures beyond the orbital periosteum, exenteration yields better survival results than preservation of the orbital structures in combination with radiotherapy. In cases where both eyes are affected from the tumor or if only one dysfunctional eye would be left over after therapy, we do not recommend orbital exenteration because life quality would be critically deteriorated.

1. Introduction

Sinonasal malignancies are rare and account for only 3% of all head and neck tumors (Maghami and Kraus, 2004; Turri-Zanoni et al., 2015). The majority are classified as squamous cell carcinoma (60–70%) and adenocarcinoma (10–20%) (Maghami and Kraus, 2004; Dulguerov et al., 2001). The 5-year overall survival rate and local control range from 30 to 40% (Waldron and Witterick, 2003). Sinonasal malignancies are often detected in advanced stages mainly due to their growth in air filled space, which leads to unspecific symptoms until the tumor reaches a considerable volume or infiltrates close proximity structures such as skull base, central nervous system or the orbit (Waldron and Witterick, 2003; Katz et al., 2002). Surgical treatment and radiation is often compromised by infiltration of the adjacent structures (Maghami and Kraus, 2004). Particularly the therapy of orbital invasion, which is a highly significant and independent parameter for poor prognosis of patients with sinonasal malignancies, remains controversial (Suarez et al., 2008). Main reasons are the small amount of available data, especially prospective studies addressing management options and outcomes and the lack of an official classification, which hampers comparison of existing reports (Suarez et al., 2008; Waldron and Witterick, 2003; Guntinas-

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Lichius et al., 2007). Present studies often categorize the orbital invasion into erosion of the bony orbital wall (grade I), involvement of the orbital periosteum (grade II) and penetration beyond the orbital periosteum and involvement of the orbital soft tissues (grade III) (Suarez et al., 2008). Several studies indicated that prognosis is negatively affected when tumor invasion is beyond the orbital periosteum and therefore observed a clear decrease for the 5-year overall survival rate from 49% for grade I and II to 17% for grade III orbital invasion (Nazar et al., 2004). The treatment strategy for sinonasal malignancies affecting the orbit is based upon oncological safety and the functional outcome of preserved eyes (Suarez et al., 2008; Maghami and Kraus, 2004). For low and middle grade orbital involvement most authors recommend preservation of the orbit plus radiotherapy (Nazar et al., 2004; Nishino et al., 2003; Howard et al., 2006). An exenteration of the orbit, defined as removal of the orbital contents within the bony sockets, is a critical procedure as it goes along with a significant functional defect, esthetic deformity and emotional hardship (Hill and Rinker, 2011; Nassab et al., 2007; Spiegel and Varvares, 2007). Therefore indication needs to be thoroughly evaluated and less radical therapy options need to be considered for patients with sinonasal malignancies invading the orbit beyond the orbital periosteum. To the best of our knowledge there is no published study comparing exenteration of the orbit with preservation of the orbit plus radiotherapy for grade III orbital invasion of sinonasal malignancies. Therefore in this retrospective study we examined histopathological and prognostic parameters of patients with sinonasal malignancies invading the orbit beyond the orbital periosteum and compared the prognostic outcome of exenteration of the orbit versus orbit preserving surgery plus radiotherapy.

2. Material and methods

2.1. Patients and data collection

Our retrospective study included 52 patients who were diagnosed with a T4a sinonasal malignancy invading the orbit beyond the orbital periosteum (grade III) between 1967 and 2003 without distant metastasis. Mean follow up time was 62 months (standard deviation 24.7 months) and 139 months (standard deviation 105.7 months) for patients alive. Median follow up time was 24.7 months and 110.1 months for patients alive. All patients were treated at the University Hospital of Cologne.

Clinicopathologic data were collected from medical records as well as pathological and surgical reports. Parameters were carefully reviewed and included age, sex, therapy of tumor infiltration of the orbit, N-Classification, UICC Stage and histopathologic tumor type. Tumors were staged according to the 7th edition of the UICC. Orbital infiltration was defined as transgression of the orbital periosteum with involvement of the orbital soft tissue. The patients' clinical characteristics and survival data are listed in Table 1.

2.2. Treatment strategies

Treatment included radical surgery and neck dissection as well as orbital exenteration or preservation of the orbit and postoperative radiation.

Postoperative radiotherapy included daily doses of 1.8–2.0 Gy 5 days per week for a total dose of 60–65 Gy.

2.3. Statistical analysis

Overall survival (OS, time interval from beginning of primary therapy until death; patients who did not die were censored at their last date of follow-up) was calculated using the Kaplan–Meier method (Kaplan and Meier, 1958). Prognostic factors were identified through univariate analysis using the log-rank-test. P-values of <0.05 were considered as significant. All statistical analyses were performed using SPSS Statistics 22.0.

Table 1
Patient characteristics and univariate analysis of prognostic factors (OS = overall survival).

	N (%)	5-year OS	*p*-Value
Age			0.263
Younger half of median	26 (50%)	54.2%	
Older half of median	26 (50%)	37%	
Sex			0.507
Male	37 (71.2%)	41.8%	
Female	15 (28.8%)	53.3%	
N-classification			**0.017**
N0	42 (80.7%)	50%	
N1	3 (5.8%)	0	
N2	3 (5.8%)	0	
N3	4 (7.7%)	50%	
UICC Stage			0.929
IV a	48 (92.3%)	44.8%	
IV b	4 (7.7%)	50%	
Histopathology			0.437
Squamous cell carcinoma	30 (57.7%)	45.4%	
Sarcoma	7 (13.5%)	20.0%	
Anaplastic carcinoma	8 (15.4%)	28.6%%	
Adenocarcinoma	2 (3.8%)	50%	
Adenoidcystic carcinoma	2 (3.8%)	50%	
Others	3 (5.8%)	66.7%	
Treatment			**0.016**
Orbital exenteration	29 (55.8%)	65.5%	
Preservation of the orbit	23 (44.2%)	14%	

Values in bold are defined as significant values, determined through univariate analysis.

3. Results

3.1. Patient characteristics and prognostic factors in univariate analysis

At the time of diagnosis, patients had an average age of 58.9 years (standard deviation 15.7 years) and a median age of 63.9 years. A significant impact in univariate analysis was found for N-Classification ($p = 0.017$) and treatment of orbital infiltration ($p = 0.016$). Exenteration of the orbit led to a significant higher 5-year overall survival rate (65.5%) than preservation of the orbit (14%) (Fig. 1).

4. Discussion

Orbital invasion is one of the most important independent prognostic factors in patients with sinonasal malignancies (Suarez et al., 2008). The orbit is often involved due to the silent growth pattern of malignant tumors of the nasal cavity and paranasal sinuses (Porceddu et al., 2004; Waldron and Witterick, 2003; Katz et al., 2002). Mostly these tumors are diagnosed in advanced stages and therefore go along with a higher risk of infiltration of surrounding structures, for example, skull base, brain or the orbit (Maghami and Kraus, 2004; Waldron and Witterick, 2003; Katz et al., 2002; Purohit et al., 2013). The therapeutic procedure of sinonasal malignancies invading the orbit remains controversial, on the one hand because of the few published studies, which furthermore mainly have small numbers of patients, and on the other hand due to the lack of an officially recognized classification of the depth of orbital involvement, which makes comparison difficult (Waldron and Witterick, 2003; Re et al., 2013; Perry et al., 1988; Suarez et al.,