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Nodal recurrence of sinonasal cancer: Does the risk of cervical relapse justify a prophylactic neck treatment?

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SUMMARY

Background: Sinonasal cancers are rare and no high-level evidence exists to determine their optimal management. Prophylactic neck treatment issue remains controversial. The aim of this study was to analyze the pattern of neck failure and to identify any prognostic factors that may influence neck control.
Methods: A retrospective review of 155 consecutive patients treated for sinonasal malignancy, without prophylactic neck treatment, between 1995 and 2005 at tertiary cancer center was performed. Demographic, clinical, morphological and pathological parameters were correlated with oncologic outcomes.
Results: Eight out of 155 patients (5%) presented initially with neck node metastasis. Complete remission was obtained for 133 patients after treatment completion. During follow up, 16 out of 133 patients (12%) were affected with regional recurrence. Neck failure occurred in 8 out of 51 patients with local failure and in 8 out of 82 patients locally controlled. Isolated nodal failure was observed in 5 patients initially cN0 out of 133 (3.8%) representing 7.3% of all recurrences and 3 of them underwent successful salvage therapy. None of the tested factors were significantly associated with neck control ($p > 0.05$). Lymph node at diagnosis time was significantly and independently associated with poor survival ($p = 0.0012$).
Conclusion: Isolated neck relapse, when local control is achieved, is rare and salvage treatment is effective. Routine prophylactic neck treatment has little interest. However, this approach could be profitable to few selected patients, who remain to be defined. Further investigations are needed.

Introduction

Malignant tumors of the paranasal sinuses account for 3% of head and neck cancers and less than 0.5% of all cancers.[1] In consequence, few centers have an extensive experience and no high-level evidence exists to determine the optimal management of these tumors.[2] Local recurrence has been shown to be the main site of relapse[2–5] and thus local control following primary treatment is a central concern, which often leads to consider neck treatment as a secondary issue.[6] Nevertheless, regional metastases are not so rare.[3,7–9] The incidence of primary nodal metastasis at presentation ranges from 3.3% to 26%[3,7] and several authors have reported high rates of neck recurrences in untreated necks, that can reach up to 30%.[8,9] Obviously, patients with clinically positive lymph nodes require treatment of the neck but prophylactic treatment of N0 patients remains controversial.[3,6,10,11] In the current study, we report our experience with 155 consecutive patients, diagnosed with primary malignant neoplasm of the sinonasal tract, over a 10 years period with an evaluation of nodal failures. The incidence and pattern of nodal relapse, its influence on survival and factors that may be associated with neck failures were analyzed.

Patients and methods

Population

A retrospective analysis of 155 consecutive patients with sinonasal cancers treated with curative intent between January 1995 and July 2005 in two collaborative institutions, Lille University Hospital and Lille Comprehensive Cancer Center was conducted. Both teams have similar guidelines for treatment. The initial cohort was composed of 186 patients but 30 patients were excluded

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because they were treated with palliative intent (as a consequence of surgical contra indication ($n = 22$), distant metastases ($n = 6$) or poor medical conditions ($n = 2$)) and 1 patient because of insufficient data. Patients with oral cancer extended to the maxillary sinus or nasal vestibule, skin cancer extended to the nasal cavities or paranasal sinuses, and lymphomas were excluded from this study.

In order to detect the presence of metastatic lymph nodes, initial work up included systematically a radiological assessment of the neck. All patients had a CT scan with contrast of the neck, with the exception of 4 patients with T1 nasal cavity carcinoma who had ultrasound evaluation. FGD positron emission tomography (FDG PET-scan) was not routinely performed.

Collected information included demographic data, histological types, subsites of origin, extension to the infra temporal fossa, oral cavity, cheek, nasopharynx, orbit, cribriform plate, endocranial space, staging, treatment modalities and oncological outcomes.

Tumor stage was defined according to the 2002 American Joint Committee on Cancer classifications. Patients who were not classified at the time of diagnosis were retrospectively restaged by re-evaluating the clinical and radiological details.

Treatment strategies

All cases were discussed in a multidisciplinary tumor board. All patients were treated with curative intent. According to our institutional policy, limited disease (T1T2 N0N1) was treated by surgery or radiotherapy alone. Locally advanced and resectable disease was treated by a combination of surgery followed by adjuvant radiotherapy or chemoradiation (cisplatinum 100 mg/m^2 on days 1, 22, and 43). Unresectable tumors were treated by radiotherapy or concurrent chemoradiation (cisplatinum 100 mg/m^2 on days 1, 22, and 43). In the absence of clinical or radiological evidence of lymph node involvement, prophylactic neck treatment was not performed.

Radiation therapy was delivered using 4–6 MV photons, along with a conventional treatment planning system or three-dimensional conformal radiotherapy. After 2003 patients were treated with intensity-modulated radiotherapy. For patient treated with definitive radiotherapy/chemoradiation, a total dose of 66–70 gy was delivered in daily fractions of 1.8–2 gy. For patients treated with adjuvant radiotherapy/chemoradiation a total dose of 60–64 gy was delivered.

The first post therapeutic assessment was performed 3 month after treatment completion and patients were divided into two groups: those with persistent disease and those in complete remission with no evidence of disease.

Statistical analysis

Overall survival was defined as the time between initial diagnosis and the date of death from any cause or the date of last follow-up contact for patients who were alive and was estimated according to the Kaplan–Meier method. Probabilities of local/nodal failure were estimated using 1-Kaplan–Meier methods, censoring patients without local/nodal failure at the time of last follow-up or death. The 95% confidence intervals (95% CI) of the actuarial rates were calculated using the Rothman method. A prognostic analysis was performed for variables that may influence survival and recurrence in the neck among patients initially staged as N0: histological type, initial location, T and initial N (for survival) stage, extension from sinuses to oral cavity, nasopharynx, infra temporal fossa, orbit and endocranial space. The log-rank test was used for univariate analyses. Variables with a p-value lower than 0.2 in the univariate analysis were studied in multivariate analyses using the Cox model. All statistical tests were two-sided. All analyses were performed using SAS Software, version 9.1.

Results

Population descriptions

One hundred and fifty-five patients (125 men and 30 women) were enrolled. Mean age was 61 years (15–92). Thirty-eight patients worked in the wood industry. Histological types, tumoral locations and TNM staging are summarized in Tables 1 and 2.

Table 2
Distribution of disease stage for nasal cavity, ethmoidal and maxillary carcinomas.

Ethmoid sinus $n = 69$ (44.5%)	Maxillary sinus $n = 44$ (28.4%)	Nasal cavity $n = 34$ (21.9%)
T stage		
T1: 15 (9.7%)	T1: 1 (0.6%)	T1: 9 (5.8%)
T2: 18 (11.6%)	T3: 2 (1.3%)	T2: 14 (9%)
T3: 11 (7%)	T4: 41 (26.4%)	T3: 1 (0.6%)
T4: 25 (16.1%)		T4: 10 (6.4%)
N stage		
N0: 69 (44.5%)	N0: 40 (25.8%)	N0: 30 (19.3%)
	N1: 3 (1.9%)	N1: 4 (2.6%)
	N2b: 1 (0.6%)	
M stage		
M0: 68 (43.9%)	M0: 43 (27.7%)	M0: 33 (21.3%)
M1: 1 (0.6%)	M1: 1 (0.6%)	M1: 1 (0.6%)

Table 1
Distribution of histological types and primary sites.

Total patients	Ethmoid sinus 69 (44.5%)	Maxillary sinus 44 (28.4%)	Nasal cavity 34 (21.9%)	Frontal sinus 3 (1.9%)	Sphenoidal sinus 5 (3.2%)
Histological types					
Epithelial tumors					
– Squamous cell carcinoma	9 (5.8%)	25 (16.1%)	13 (8.4%)	3 (1.9%)	1 (0.6%)
– Adenocarcinoma	43 (27.7%)	2 (1.3%)	5 (3.2%)	–	–
– Adenoid cystic carcinoma	1 (0.6%)	4 (2.6%)	4 (2.6%)	–	1 (0.6%)
– Mucoepidermoid carcinoma	–	2 (1.3%)	–	–	–
– Undifferentiated carcinoma	2 (1.3%)	3 (1.9%)	1 (0.6%)	–	2 (1.3%)
Non epithelial tumors					
– Malignant melanoma	4 (2.6%)	1 (0.6%)	5 (3.2%)	–	–
– Esthesio-neuroblastoma	4 (2.6%)	–	–	–	–
– Sarcoma	1 (0.6%)	3 (1.9%)	1 (0.6%)	–	1 (0.6%)
– Neuro-endocrine carcinoma	3 (1.9%)	–	–	–	–
– Miscellaneous	2 (1.3%)	4 (2.6%)	5 (3.2%)	–	–

Miscellaneous tumors included plasmocytoma, transitional cell carcinoma and neuro ectodermic cancers.