European Annals of Otorhinolaryngology, Head and Neck diseases xxx (2017) xxx–xxx

Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en

Original article

Undifferentiated carcinoma of nasopharyngeal type in children: Clinical features and outcome

W.S. Zrafi [a,*], S. Tebra [a], S. Tbessi [a], S. Ouni [a], M. Jebsi [b], N. Bouaouina [a]

[a] Service de cancérologie radiothérapie, hôpital Farhat-Hached, Sousse, Tunisia
[b] Centre médical Ibn Khaldoun, Hammam, Sousse, Tunisia

ARTICLE INFO

Keywords:
Nasopharyngeal carcinoma
Child
Radiotherapy
Chemotherapy

ABSTRACT

Objectives: To describe the epidemiology, clinical features and treatment of undifferentiated carcinoma of nasopharyngeal type in children.
Material and methods: Retrospective study of 40 patients under the age of 17 years managed for undifferentiated carcinoma of nasopharyngeal type in two oncology centres in the central region of Tunisia between 1995 and 2012.
Results: Patients had a median age of 14 years with a sex ratio of 1.3. The mean time to presentation was 5 months. The presenting complaint was cervical lymphadenopathy in 90% of cases. Thirty-seven patients received curative treatment, according to a sequential mode in 85% of cases, starting with chemotherapy followed by radiotherapy to the nasopharynx and cervical lymph nodes. The median dose delivered to the nasopharynx was 70.4 Gy. Two cases of local recurrence and five cases of metastatic relapse (all involving bone), were observed during follow-up. After a mean follow-up of 80.5 months (range: 1 to 180), 29 patients (72.5%) were in complete remission, eight had died and three were lost to follow-up. The 5-year overall survival was 77.7%.
Conclusion: Undifferentiated carcinoma of nasopharyngeal type in children represents 6% of all cases of UCNT managed in our institutions. It is often discovered at an advanced stage. Sequential treatment combining chemotherapy and radiotherapy achieves an excellent local control rate.

1. Introduction

With a standardized incidence of 2.26 per 100,000 inhabitants, Tunisians are at intermediate risk for nasopharyngeal carcinoma. The age distribution of nasopharyngeal carcinoma is bimodal with a first peak between the ages of 15 and 20 years and a second peak between the ages of 50 and 55 years [1,2].

Eleven to 18% of nasopharyngeal carcinomas occur before the age of 20 [3], and the most common histological type is undifferentiated carcinoma of nasopharyngeal type (UCNT), accounting for 93.4% of cases [2].

The treatment of paediatric forms remains a dilemma due to the lack of studies devoted to this population and the absence of guidelines. Consequently, most centres usually apply the guidelines for adult UCNT, despite the very poor representation of this age group in clinical trials.

2. Methods

This retrospective study was conducted on a series of 40 patients under the age of 17 years treated for UCNT in the radiation oncology department of Farhat-Hached hospital and Ibn Khaldoun medical centre in Sousse, Tunisia, over an 18-year period between 1995 and 2012.

3. Results

3.1. Study population

Patients in this series had a median age of 14 years (range: 8 and 16 years) and a sex ratio of 1.3; 2 children had a family history of nasopharyngeal carcinoma and 20 patients (50%) were smokers.

The mean time to presentation was 5 months (range: 1 to 36 months). The most common presenting complaint was neck mass in 36 patients (90%), followed by blocked nose, headache and hearing loss in 35%, 35% and 20% of cases, respectively.

Nasal endoscopy with biopsy was performed in all patients. Histological examination revealed UCNT in all cases (Table 1). Local

* Corresponding author.
E-mail address: zrafiws@gmail.com (W.S. Zrafi).

http://dx.doi.org/10.1016/j.anorl.2017.03.002
1879-7296/

Table 1
Patient characteristics.

	n (%)
Sex	
Male	23 (57.5)
Female	17 (42.5)
Age	
Median	14 years
Presenting complaint	
Neck swelling	36 (90)
Blocked nose	14 (35)
Headache	14 (35)
Hearing loss	8 (20)
Histological type	
UCNT	40
T classification (UCNT)	
T1	7 (17.5)
T2	12 (30)
T3	6 (15)
T4	15 (37.5)
N classification (UCNT)	
N0	5 (12.5)
N1	14 (35)
N2	14 (35)
N3	7 (17.5)
M classification (UCNT)	
M0	39 (97.5)
M1	1

staging comprised CT scan for all patients completed by MRI in only one case. Distant staging, comprising at least chest X-ray, abdominal ultrasound, and bone scan, was performed in all patients.

After this workup, tumours were classified according to the TNM (UICC-AJCC) staging system 2010 edition (Table 1) and the older cases were restaged according to clinical and radiological data in line with the TNM 2010 classification.

Clinically, 15 patients were classified as T4, including 2 patients with impaired visual acuity, 2 patients with oculomotor paralysis, and 2 patients with severe trismus. Eleven patients presented radiological signs of intracranial invasion.

3.2. Radiotherapy

Non-metastatic patients were treated by radiotherapy delivered to the tumour site and bilateral cervical lymph nodes.

The results of radiotherapy concern 37 patients (2 patients were lost to follow-up after 3 and 4 cycles of chemotherapy and one patient presented metastatic disease).

Radiotherapy was performed with a cobalt therapy machine with classical fractionation of 1.8 Gy for 6 patients (20%), 2 Gy for 29 patients (74%), and a bi-fractionated modality of 1.6 Gy, two sessions per day for 2 patients.

Four patients received doses to the nasopharynx less than or equal to 68 Gy, 8 patients received a dose of 70 Gy, and 25 patients received doses higher than 70 Gy, including 17 patients who received a dose of 74 Gy.

Radiotherapy was exclusive in one case, concomitant with chemotherapy in 5 cases (13%) and sequential in most cases (84%).

3.3. Chemotherapy

One patient with bone metastases at the time of diagnosis received 4 cycles of doxorubicin–cisplatin followed by radiotherapy to the nasopharynx at a dose of 44 Gy in 2 Gy fractions. He died 1 month after completion of radiotherapy.

Sequential treatment starting with chemotherapy was administered to 32 patients, with 3 to 4 cycles of EP (epirubicin 80 mg/m^2 and cisplatin 100 mg/m^2 on Day 1) in 27 cases. This cycle was repeated every 21 days.

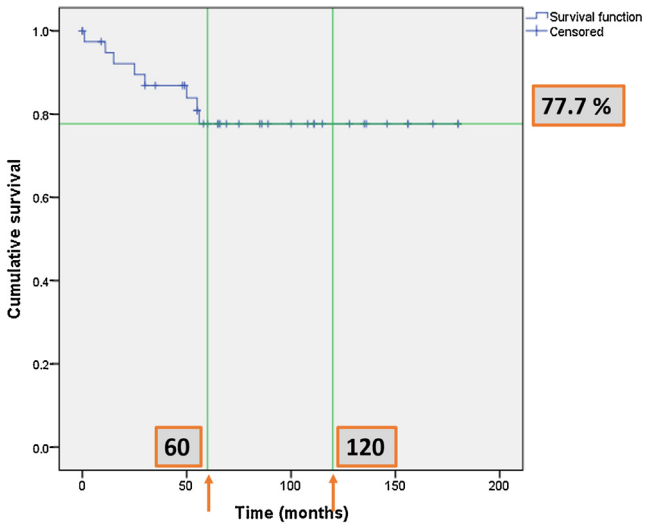

Fig. 1. Cumulative survival curve for the study population. 5-year and 10-year overall survival was 77.7%.

Clinical and radiological evaluation performed after chemotherapy in the context of sequential treatment demonstrated 4 complete responses, 26 partial responses and 2 cases of progressive disease. This evaluation was repeated 2 months after completion of radiotherapy, showing 19 complete responses, 12 partial responses and 1 case of progressive disease.

Treatment failures: One local recurrence occurred at 6 months, 5 cases of metastases (all involving bone) occurred between 1 month and 1 year with a median of 5 months.

3.4. Survival

The median follow-up was 65.5 months (range: 0 to 180 months) with a mean of 80.5 months, calculated from the date of completion of treatment until the date of last follow-up.

Survival rates and survival curves were calculated by the Kaplan-Meier method and were compared by the Log-Rank test (Mantel-Cox). Statistical analysis was performed with IBM SPSS 20.0 software.

Five-year and 10-year overall survival was 77.7% (Fig. 1). Five-year and 10-year disease-free survival was 75%. The Log-Rank test (Mantel-Cox) was used to determine prognostic factors impacting 5-year overall survival. Only T stage and complete response to radiotherapy were significant prognostic factors for survival with *P*-values of 0.03 and 0.001, respectively (Table 2), as 5-year and

Table 2
Prognostic factors.

Prognostic factors for overall survival	*n* (%)	*P*
Sex		0.8
Male	23 (57.5)	
Female	17 (42.5)	
Age		0.7
< 14 years	15 (37.5)	
≥ 14 years	25 (62.5)	
T1 T2 Vs T3 T4		0.03
T1 T2	19 (47.5)	
T3 T4	21 (52.5)	
N0 N1 Vs N2 N3		0.3
N0 N1	19 (47.5)	
N2 N3	21 (52.5)	
Complete response after RT		0.001
CR	20 (49)	

Only tumour stage and tumour response after radiotherapy were significant prognostic factors for survival.

Please cite this article in press as: Zrafi WS, et al. Undifferentiated carcinoma of nasopharyngeal type in children: Clinical features and outcome. European Annals of Otorhinolaryngology, Head and Neck diseases (2017), http://dx.doi.org/10.1016/j.anorl.2017.03.002