ONCOLOGY

Non-Hodgkin's lymphoma of nasal cavity and paranasal sinuses. A clinicopathological and immunohistochemical study

Linfoma non-Hodgkin delle cavità nasali e dei seni paranasali. Studio clinico, patologico e immunoistochimico

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SUMMARY

Aim of this study was to investigate the clinical characteristics, management and prognosis of non-Hodgkin lymphomas of the nasal cavity and paranasal sinuses. Overall 12 patients with non-Hodgkin malignant lymphoma, at our Institute, were studied over an eight-year period from 1997 to 2005. Patients' data collected were age, sex, presenting signs and symptoms, histology, treatment, complications, and outcome. Also available were computerised tomography findings, and paraffin-embedded tissue bocks. Mean age was 62 years (range: 42-81), with a male dominance (male to female ratio: 7:5). Most patients had not presented any specific symptoms, such as nasal obstruction, headaches, epistaxis and facial swelling. Using immunocytochemistry on paraffin-embedded tissue sections, the predominance of large B-cell subtype was detected. Treatment administered: only radiotherapy (stage IEA) or in combination with chemotherapy (IIE-IVE). Of these patients, 5 died from the disease, 4 survived without disease, 2 survived with the disease, and one died of non-related causes. Non-Hodgkin's lymphomas are relatively rare. Early diagnosis, based mainly on tissue biopsy and computerised tomography, is essential in the management of non-Hodgkin lymphoma.

KEY WORDS: Nose • Paranasal sinuses • Lymphoma • Non-Hodgkin's lymphoma • B-cell lymphoma

RIASSUNTO

Lo scopo della presente ricerca era di studiare le caratteristiche cliniche, il trattamento e la prognosi del linfoma non-Hodgkin (NHL) della cavità nasale e dei seni paranasali. Sono stati studiati 12 pazienti con NHL, che si sono ricoverati presso il nostro ospedale, durante un periodo di 8 anni dal 1997 al 2005. I dati raccolti comprendono l'età, il sesso, i segni e i sintomi di esordio, l'esame istologico, il trattamento, le complicazioni e l'esito finale. L'età media dei pazienti è di 62 anni (range: 42-81 anni) con il sesso maschile dominante (maschi/femmine ratio: 7/5). La maggior parte dei pazienti presentava sintomi non specifici come epistassi, cefalea, senso di tensione nasale ed edema facciale. Dal punto di vista immunoistochimico c'era la predominanza delle cellule B. In tutti i casi è stata eseguita la radioterapia, come monoterapia (stadio IEA), o in combinazione con la chemioterapia (IIE-IVE). Cinque pazienti sono deceduti, quattro sono sopravvissuti liberi da malattia, due sono sopravvissuti con la malattia e uno è deceduto per altre cause. Il linfoma non-Hodgkin del naso e dei seni paranasali è relativamente raro. La diagnosi precoce, che si basa soprattutto sulla biopsia tissutale e la tomografia computerizzata, è essenziale per il trattamento dei NHL.

PAROLE CHIAVE: *Naso • Seni paranasali • Linfomi • Linfoma non-Hodgkin • Linfoma a cellule B*

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Introduction

Lymphomas represent a group of malignant neoplasms of lympho-reticular origin which are divided into Hodgkin's disease and non-Hodgkin's lymphomas (NHL) [1]. A systematic attempt to determine the histological and immunological category of the lymphoma is necessary, since new modalities of treatment are now available that are neoplasm specific. According to REAL (Revised European-American Lymphoma) classification, NHL is a heterogeneous group of diseases with peculiar, morphological, phenotypic and molecular features (B-cell neoplasms, T-cell and putative natural killer (NK)-cell neoplasms) [2]. Unlike other classifications, the REAL classification does not distinguish these tumours as being high or low grade, since it is recognized that each entity has its own characteristic pattern of behaviour [3 4]. The nasal cavities and paranasal sinuses are rarely affected by primary NHL. Common primary extra-nodal sites of lymphomas include liver, soft tissue, *dura*, bone, stomach, intestine, bone marrow, and others [5]. Geographic factors play a role in the frequency and histological subtype of NHL of the sinonasal tract. In Asian populations and in

Peru, nasal lymphomas are more common and are predominantly T-cell lymphomas, whereas B-cell subtypes are typically more common among the sinonasal lymphomas observed in Western populations [6]. The aim of this study was to investigate the clinical characteristics, stage, histological type, treatment modalities, and the prognosis of 12 cases of sinonasal NHL observed at the Hippokration Hospital, Athens, Greece.

Patients and methods

A review of medical records at the Hippokration Hospital revealed that, from 1997-2005, 12 patients were diagnosed with NHL of the nasal cavity and the paranasal sinuses.

Clinical examination, with nasal endoscopy, showed masses in the nasal cavities of all the patients, which sometimes extended behind the nasopharynx. In 6 patients, inspection of the oral cavity and the oropharynx revealed swelling of the soft palate, and the mucosa of the hard palatal was granular.

Tissue biopsy was performed under general anaesthesia. Tissue specimens were fixed in 10% formalin solution, embedded in paraffin, sectioned at 5 μm, and stained with haematoxylin-eosin. Immunohistochemical staining was performed on formalin-fixed, paraffin-embedded tissue sections using the following primary antigens: anti-CD2, anti-CD3, anti-CD5, anti-CD10, anti-CD19, anti-CD20, anti-CD22, anti-CD79a. Specimens of all the patients were evaluated according to the REAL classification system proposed by the International Lymphoma Study Group [2].

Staging was completed with additional computed tomography (CT) scans of the chest and abdomen and with bone marrow biopsies. The clinical features, histological type, treatment modality, and outcome were determined.

Results

The mean age of the patients was 62 years (range 42-81) while the male-to-female ratio was 7:5 (Table I). The major symptoms reported by the patients were: nasal obstruction (12 patients), epistaxis (7 patients), headaches that did not subside with analgesia (6 patients), facial swelling (6 patients) palatal lesion (5 patients), and visual disturbances (2 patients) (Table II).

Histological examination revealed that the most common type was diffuse large B-cell lymphoma (58.3%), followed by angiocentric lymphoma (16.67%), lymphoplasmacytoid lymphoma (8.33%), follicle centre lymphoma (provisional cytologic grade III) (8.33%), and adult T cell lymphoma (8.33%) (Table I).

CT of the head and neck demonstrated pathological masses in the nasal cavities with bone destruction which extended to the nasopharynx and paranasal sinuses. Soft palate masses were observed in 4 patients. Lymph node involvement of the neck was not determined in all patients, and no pathological findings were detected in the anterior and the middle skull base (Figs. 1, 2). No evidence of lymphomatous involvement was identified outside the nasal cavity in any of the patients. The Ann Arbor classification system was used for staging (Table I).

The patients were treated either with radiotherapy alone or in combination with chemotherapy. Patients with stage IEA disease were treated only with radiotherapy. Doses ranged from 45 to 55 Gy, with most patients receiving 50 Gy. Chemotherapy with radiotherapy was used in patients with stage IIE-IVE. The most common chemotherapy regimen

Table I. Patient characteristics.

Characteristic	No. patients
Sex	
Male	7
Female	5
Age (yrs)	
Range	42-81
Median	62
Ann Arbor Stage	
IE	2
IIE	6
IIIE	3
IVE	1
Histologic type	
Diffuse large B-cell lymphoma	7
Angiocentric lymphoma	2
Lymphoplasmacytoid lymphoma	1
Follicle centre lymphoma (grade III)	1
Adult T cell lymphoma	1

Table II. Patient symptoms.

Symptom	No. patients
Nasal obstruction	12
Epistaxis	7
Headache	6
Facial swelling	6
Palatal lesion	5
Diplopia	2

Fig. 1. Coronal computer tomography scan shows mass occupying ethmoid and maxillary sinuses together with nasal cavities.

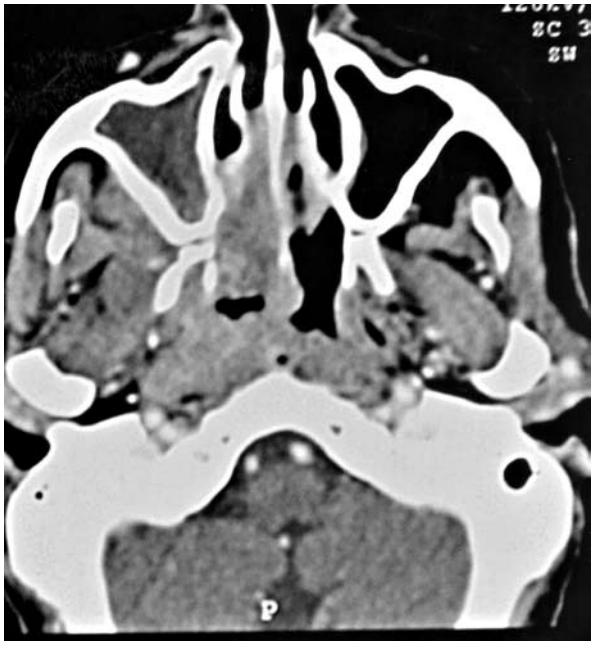

Fig. 2. Axial computer tomography scan shows mass occupying ethmoid and maxillary sinuses, which extends to adjacent nasal cavity.

used was CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisolone). At least four courses of chemotherapy were completed.

The follow-up period ranged from 1 to 72 months (mean 52). Five patients died from the disease in a period of 8 to 22 months. Four patients survived free of disease, two survived with the disease and one died 44 months after the diagnosis from an unrelated cause.

Discussion

NHLs of the sinonasal tract are uncommon malignancies representing 3% to 5% of all malignancies, with NHL accounting for 60% of all lymphomas. In the present study, the most frequent histological type was B-cell lymphoma. In Western populations, predominance of the histological type is unclear, with some finding B-cell lesions more common [9], whereas others noted a greater frequency of T-cell lesions [10 11]. On the contrary, according to Hatta et al. [12], the most common histological type, in Japan, is angiocentric lymphoma (35.9%), followed by B-cell lymphoma (22.6%), peripheral T-cell lymphoma types (15.1%), and other lymphomas and non-specific types.

B-cell lymphoma is predominant in paranasal sinuses. Tumour cells with positive T-cell markers (angiocentric lymphoma and peripheral T-cell lymphoma) are predominant in nasal cavities. Patients are usually elderly males with locally advanced tumours. Children present with a higher proportion of extra-nodal NHL of the head and neck, and an early diagnosis of NHL of nasal cavity and paranasal sinuses is necessary for adequate and successful management [7 13].

In Western populations, lymphomas of the maxillary sinus are more common (9 patients in our study) than in the nasal cavity. On the contrary, in Asian patients the nasal cavity is more common as a primary site than the maxillary sinus [6 14 15].

More than 60% of NHLs of the head and neck occur in extra nodal sites, such as the paranasal sinuses, nasal cavity, oral cavity, salivary glands, and laryngopharynx [7].

Lymphomas are usually submucosal and on gross appearance differ from squamous cell carcinomas, which are usually ulcerative. Early diagnosis of primary NHL of the nasal cavity and paranasal sinuses was difficult in our patients, because this lesion develops in an anatomic space and expands toward the sinus, nasal cavity or nasopharynx, not usually causing symptoms in the early stages. Only after reaching a considerable size and involvement do the symptoms appear, and these may simulate other nasal or head and neck diseases. The most common presenting symptoms of sinonasal lymphomas are nasal obstruction, epistaxis, headache, and unilateral facial, cheek, or nasal swelling [1 7 16 17]. Other infrequent symptoms are diplopia or blurred vision, and nasal or cheek pain.

In our study, the 5 year survival rate for sinonasal lymphomas was 50%. The prognosis of patients with lymphoma of the sinonasal region, according to Longsdon et al. [6], is better than in those with Waldayer's lymphomas of similar histological grades in Western populations. Based on this study, between 1947 and 1993, 70 patients with lymphoma of the nasal cavity and paranasal sinuses were treated at the M.D. Anderson Cancer Center (University of Texas, Houston, USA) with the following results: 5 years free of progression 57% and 5 year overall survival for all types 52%.

Treatment, in our study, was radiotherapy combined with chemotherapy (exception stage IE). In the past, these lymphomas were treated only with local radiotherapy having a good response, but a high percentage of local and distant recurrence was observed. With the combined treatment of chemotherapy and local radiation, patients with lymphoma of the nasal cavity and paranasal sinuses had a better prognosis [1 6 16].

Specific diagnosis, in these cases, in order to begin treatment as soon as possible was difficult. Correct diagnosis results from tissue biopsy, which should be performed in patients with any unilateral intranasal lesion. Early diagnosis and staging are essential for effective treatment, and lymphomas must always be included in the differential diagnosis of lesions of the nasal cavity and paranasal sinuses.

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