

Characterization of the Clinical Evolution of Nasopharyngeal Carcinoma in a Portuguese Population

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Objective: Characterization of the clinical evolution of nasopharyngeal cancer (NPC) patients in a Portuguese population during 31 years of follow-up.

Materials and method: Three hundred and twenty patients with epidermoid nasopharyngeal carcinoma were selected for this study. Histological subtypes were analyzed along with survival rates after different treatment schemes and according to AJCC and UICC staging classification systems.

Results: The most frequent histological subtype was undifferentiated nasopharyngeal carcinoma. The AJCC-2001 staging classification was considered the most suitable system for survival prediction. Better survival rates were found in patients treated with adjuvant chemotherapy (cisplatin and 5-fluorouracil) and these findings were similar to other published results.

Conclusions: Although adjuvant chemotherapy may reduce the likelihood of distant metastasis, the latter is still the main cause of death in our study. The distant metastasis rate remains the crucial problem and bringing it down is an ever closer goal and a challenge for the future.

Key words: Nasopharyngeal carcinoma. Histological subtypes. Clinical evolution. Staging systems. Survival. Treatment.

Caracterización de la evolución clínica del carcinoma de la nasofaringe en una población portuguesa

Objetivo: Caracterización de la evolución clínica del carcinoma de la nasofaringe en una población portuguesa en 31 años de seguimiento.

Material y método: Trescientos veinte enfermos portadores de carcinoma epidermoide nasofaríngeo fueron seleccionados para este trabajo. Los siguientes parámetros fueron analizados: variante histológica, tasas de supervivencia después de diferentes modalidades de tratamiento y diferentes estadios (AJCC y UICC).

Resultados: La variante histológica más frecuente fue el carcinoma indiferenciado del tipo nasofaríngeo. La clasificación de la AJCC de 2001 se consideró la más adecuada para el pronóstico de los enfermos. Los enfermos tratados con quimioterapia adyuvante han obtenido mejores tasas de supervivencia, sobre todo los que recibieron tratamiento con cisplatino y 5-fluorouracilo (resultados similares a los obtenidos en otros trabajos).

Conclusiones: Aunque la quimioterapia adyuvante reduzca la probabilidad de metástasis a distancia, continúa siendo la principal causa de muerte constatada en nuestro estudio. La tasa de metástasis a distancia sigue siendo el problema crucial, y disminuirla es una meta cada vez más próxima y un desafío para el futuro.

Palabras clave: Carcinoma de la nasofaringe. Variantes histológicas. Evolución clínica. Métodos de estadificación. Supervivencia. Tratamiento.

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"...a carpenter and a geometer investigate the right angle in different ways; the former does so insofar as the right angle is useful for his work, while the latter inquires what it is or what sort of thing it is; for he is a spectator of the truth."

ARISTOTLE.
(*Nichomachean Ethics*, 1089 to 29)

INTRODUCTION

Nasopharyngeal carcinoma, a disease that was described for the first time little more than a century ago,¹ is the most common malignant neoplasm in this anatomical structure.^{2,3} Although common in South-western Asia⁴ (30-80/100 000 people/year) nasopharyngeal carcinomas are a fairly rare condition in American and European populations (1/100 000 people/year).⁵ It begins in the nasopharyngeal epithelium and, according to the World Health Organization (WHO) in 1978,⁶ 3 subtypes have been described: type I, keratinizing squamous cell carcinoma; type II, non-keratinizing squamous cell carcinoma, and type III, undifferentiated carcinoma.

These neoplasms are currently classified as squamous cells carcinomas and non-keratinizing carcinomas, which are subdivided into differentiated and non-differentiated carcinomas.⁷ The reason for this sub-classification is the association with the Epstein-Barr virus (EBV)⁸⁻¹² of the non-keratinizing carcinomas; that is, WHO types II and III. These carcinomas, called nasopharyngeal-type carcinomas (NTC), have typical epidemiological and pathological characteristics that distinguish them from the majority of epidermoid carcinomas of the airways and digestive tract. These carcinomas were studied at the Instituto Português de Oncologia do Porto (IPO CROP-SA) from the time it was founded in 1974 until August 2005. Thus, in this paper the authors propose to analyze the data systematically collected over this time with the aim of characterizing the debut and clinical evolution and analyzing the survival rates, considering the classification and different treatments for nasopharyngeal carcinoma in a Portuguese population.

MATERIAL AND METHOD

The study began on the final date of the first treatment, in August 1974, and ended in August 2005, bringing to a close a total follow-up time of 31 years.

Three hundred and twenty patients with epidermoid nasopharyngeal carcinoma were studied. Of these, patients presenting the NTC histological subtype were selected and, from the latter, those patients who in the classification system did not present any metastases at the date of diagnosis and, moreover, completed the treatment proposed were included in the final patient group. Of the individuals finally selected, the following parameters were analyzed: form of clinical debut, time elapsed between the first symptom perceived by the patient until diagnosis, gender distribution, age at the time of diagnosis and TNM staging. In the case of this last parameter, local and neck spread were assessed by means of imaging studies using computerized tomography (CT). Distant metastasis was initially analyzed using whole-body bone scintigraphy, abdominal ultrasound, chest x-ray, full blood count, sedimentation rate and liver function test. More recently, chest and abdominal CTs have been incorporated into the study, in lieu of the abdominal ultrasound and the chest x-ray.

All of the patients treated (213) underwent treatment with radiotherapy, performed on the primary tumour at a mean

dose of 70 Gy, as well as on the neck and supraclavicular regions at doses of between 50 and 70 Gy according to the degree of involvement. Treatment techniques have evolved over time, moving away from the cobalt machines and low energy linear accelerators to high energy accelerators. Likewise, imaging evaluation methods have also evolved, as has the radiation therapy approach (the dosimetric approach started off as being 2-dimensional and subsequently became 3-dimensional conformational).

Adjuvant chemotherapy was administered to 134 patients, with the following protocols:

- Thirty-seven patients: bleomycin 25 mg/m² iv; methotrexate 30 mg/m² iv, in weekly cycles up to a total of 5 cycles, then switching to methotrexate alone until reaching a toxic dose
- Twenty-six patients: doxorubicin 25 mg/m² iv; bleomycin 10 mg/m² iv; vinblastine 6 mg/m² iv; dacarbazine 375 mg/m² iv every 15 days for 3 months
- Seventy-one patients: cisplatin (CDDP) 100 mg/m² iv day 1; continuous perfusion of 5-fluorouracil 1000 mg/m² iv from the first to the fifth day, 3 cycles every 21 days

Neck stripping surgery was carried out in all cases in which clinical persistence of adenopathies was verified after completion of radiotherapy alone or in combination with chemotherapy.

The long follow-up period made stage updating mandatory and was particularly relevant with regard to how neck adenopathies were classified. Each process was re-evaluated whenever there were changes in the classification, thereby making it possible to compare the different methodologies used to determine the stages of the disease. After examining the data obtained at the time of patient enrolment, follow-up was carried out depending on the treatment implemented. Thus, all patients were studied on a yearly basis with the same examinations that had been performed "at intake." Finally, total survival rates were analyzed in relation to stages and type of treatment, taking into account, in turn, the possible cause of demise.

Patient evolution was then studied on the basis of treatment performed, and finally, total survival rates were studied per stage and type of treatment. In addition to survival, the cause of death was also considered. The mortality aetiology was classified as: local, regional, or distant.

RESULTS

Of the 320 patients with epidermoid carcinoma located in the nasopharynx, only 20 were squamous cells (keratinizing) carcinomas, while the remaining were non-keratinizing carcinomas.

Three-hundred (300) patients were identified as having NTC and the data concerning clinical debut were analyzed. Of these, the subjects finally selected were those in whom full staging had been possible and showed no distant

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