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Original article

Prognostic factors in metastatic nasopharyngeal carcinoma

Facteurs pronostiques dans le carcinome nasopharyngé métastatique

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Abstract

Background. – The current retrospective study aimed to identify some determinants of survival in metastatic NPC.

Methods. – The study concerned 95 patients with metastatic nasopharyngeal carcinoma treated between 1993 and 2001. Statistical comparison between patients subgroups survival was carried out employing the log-Rank test (statistical significance was defined as $p \leq 0.05$). Multivariable analysis was performed using the Cox model ($p \leq 0.05$ was used as the cut-off value of statistical significance). Factors that were considered included: age group(≤ 45 years or > 45 years and ≤ 25 years or > 25 years), gender, performance status at diagnosis of metastatic disease (PS 0-1 or 2-3), time of metastasis diagnosis(at presentation or later), number of metastatic sites (single or multiple), specific metastatic sites(bone, liver, lung, distant nodes), number of bone metastasis(single or multiple),disease free survival(DFI) (≤ or > 6 months), prior chemotherapy, radiotherapy of metastatic sites.

Results. – Negative prognostic factors in univariate analysis were: poor PS (≥ 1), multiple metastatic sites, multiple bone metastasis, previous chemotherapy, visceral or node metastasis and non irradiated metastasis. Poor PS, multiple metastatic sites, and prior chemotherapy were independently significant negative prognostic factors in multivariable analysis.

Conclusions. – In this study we identified new prognostic factors in univariate and multivariate analysis. . A regular and careful follow-up of patients treated for NPC is then recommended in order to detect early metastatic dissemination (with minimal localizations) while patients have still a good PS.

Résumé

Objectif. – l'objectif de ce travail rétrospectif était d'identifier certains facteurs pronostiques influençant la survie des patients atteints d'un carcinome nasopharyngé métastatique.

Patients et méthodes. – L'étude a concerné 95 patients atteints d'un carcinome nasopharyngé métastatique traités entre 1993 et 2001. L'analyse de la survie selon les différents facteurs pronostiques a été faite selon le test de log-rank (*p* significatif si ≤ 0,05) pour l'étude unifactorielle et selon le modèle de Cox (*p* significatif si ≤ 0,05) pour l'étude multifactorielle. Les facteurs étudiés étaient les suivants : âge (≤ 45 ou > 45 ans et ≤ 25 ou > 25 ans), sexe, état général au moment du diagnostic des métastases (PS 0-1 ou 2-3), présentation de la maladie (métastases synchrones ou métachrones), nombre de sites métastatiques (unique ou multiple), nature du site métastatique (os, foie, poumon, ganglions), nombre de métastases osseuses (unique ou multiple), délai de la rechute (≤ ou > 6 mois), le traitement antérieur ou non par chimiothérapie et l'irradiation ou non des métastases.

Résultats. – Les facteurs de pronostic défavorable en analyse unifactorielle étaient : le mauvais état général (indice de performance ≥ 1), les sites métastatiques multiples, les métastases osseuses multiples, le traitement antérieur par chimiothérapie, les métastases viscérales et ganglionnaires et les métastases non irradiées. Les facteurs indépendants à l'étude multifactorielle étaient : le mauvais état général, les sites métastatiques multiples et le traitement antérieur par chimiothérapie.

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Conclusion. – Dans cette étude, nous avons identifié de nouveaux facteurs pronostiques aussi bien en étude monofactorielle que multifactorielle. Un suivi régulier des patients est donc nécessaire afin de détecter précocement la dissémination métastatique (avec le minimum de localisations) alors que les patients sont encore en bon état général.

Keywords: Nasopharynx; Carcinoma; Metastasis; Surviva; Prognosis

Mots clés : Carcinome nasopharyngé ; Métastases ; Survie ; Pronostic

1. Introduction

In contrast to other squamous cell carcinoma of the head and neck, nasopharyngeal carcinoma(NPC) is characterized by a high tendency for metastatic dissemination [3].Thirty to 60% of patients with locally advanced disease will develop distant metastasis within five years of diagnosis, while 5 to 8% present with distant metastasis at diagnosis [3,10]. The high chemoresponsiveness of NPC is well estabilished. High objective response rates and a substantial proportion of durable complete responses and long-term-disease-free survival have been attained in metastatic disease [2,5,8].The predictors of distant metastasis and survival in treated non disseminated NPC have been extensively studied and published [1,4,9,11]. However, there are few reviews that specifically examined the prognostic factors of survival in already metastatic patients. The current study aimed to identify some determinants of survival in metastatic NPC.

2. Patients and methods

This was a retrospective analysis of 95 patients with metastatic histologically proven NPC reffered to our oncolgy departement in the south of Tunisia, between January 1993 and December 2001.The study included patients who were metastatic at first diagnosis or who had presented later metastasis. All the patients underwent a pretherapeutic work-up including clinical history and examination, nasopharyngeal biopsy, head and neck computed tomography scan, chest x-ray, abdominal ultrasound and bone scan. Abdominal and thoracic computed scans were performed when any doubts were raised by routine examinations. Treatment consisted of cisplatin based chemotherapy [BEC regimen (bleomycin, epirubicin and cisplatin) or PBF regimen(bleomycin,5fluorouracil and cisplatin)] and radiotherapy of pauci metastatic (single or double) or threatening metastasis associated with locoregional irradiation for patients with synchronous metastasis who were good responders to chemotherapy. Metastatic survival was defined from the time of diagnosis for patients with synchronous metastasis and from the time of relapse for patients who presented with later metastasis. The survival status was verified as of November 2005. Stastical study was performed using SPSS WIN 11 logiciel. Overall metastatic survival was estimated according the Kaplan-Meier method. Statistical comparison between patients subgroups survival was carried out employing the log-Rank test (statistical significance was defined as $p \leq 0.05$). Multivariable analysis was performed using the Cox model ($p \leq 0.05$ was used as the cut-off value of statistical significance).

Factors that were considered included: age group(≤ 45 years or > 45 years and ≤ 25 years or > 25 years), gender, performance status at diagnosis of metastatic disease (PS 0-1 or 2-3), time of metastasis diagnosis(at presentation or later), number of metastatic sites (single or multiple), specific metastatic sites(bone, liver, lung, distant nodes), number of bone metastasis(single or multiple),disease free survival(DFI) ($\leq$ or $>$ 6 months), prior chemotherapy (yes or no), radiotherapy of metastatic sites(yes or no).

3. Results

3.1. Patient and disease characteristics

There was a male preponderance (sex-ratio: 3.1). The mean age at metastatic disease diagnosis was 47.5 years (ranging from 13 to 73 years). The mean DFI was 21 months (extremes: 1-72 months). Details are shown in Table 1.

Eighty-nine patients were treated with chemotherapy. Seventy patients received PBF protocol and 19 patients received BEC protocol. Twenty-five patients were irradiated on pauci metastatic sites (lymph nodes: 2 cases, bone: 23 cases), they received a dose of 30 Gy over 10 sessions. Nineteen patients who were metastatic at diagnosis received locoregional irradiation(70 Gy to nasopharynx and involved cervical nodes and 50 Gy to remainder neck area).

Table 1
Patient and disease characteristics
Tableau 1
Caractéristiques des patients et de la maladie

	Number	Percentage
Gender female	23	24,2%
Male	72	75,7%
Age (years) ≤ 45 / > 45	50 / 45	52.6% / 47.3%
≤ 25 / > 25	19 / 76	20% / 80%
Performance status(WHO)		
PS 0-1	51	53,6%
PS 2	29	30,5%
PS 3	15	15,7%
Time of metastasis diagnosis		
Metastasis at onset / Later	34 / 61	35,7% / 64,2%
Metastatic localizations		
Bone	79	83%
- Single	19	24%
- Multiple	60	76%
Liver	27	28,4%
Lung	23	24,2%
Nodes	23	24,2%
Brain	2	2%
Bone narrow	5	5%
Number of metastatic sites		
Single / Multiple	51 / 44	53% / 47%