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Original Article

Épidémiologie, clinicopathologie et survie du carcinome nasopharyngé dans un échantillon de l'ouest algérien

Epidemiology, Clinicopathology and survival of nasopharyngeal carcinoma in a sample from Western Algeria

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ABSTRACT

Background : Nasopharyngeal carcinoma (NPC) is the most prevalent head and neck cancer among men in Algeria. The aim of this study is to determine the epidemiology, clinicopathology and survival of nasopharygeal carcinoma in a sample of 120 cases. **Methods** : Patients with nasopharyngeal carcinoma residing in Western Algeria, followed in two centers over a period of 4 years from January 2016 to December 2019, were included in this study. The survival analysis was carried out by the Kaplan-Meïer method. Survival curves were compared using the Logrank test. The level of significance was set at p value ≤0,05. **Results** : 120 cases of nasopharyngeal cancer were diagnosed and then followed up during the study period. A male predominance was observed with a sex ratio of 83/37. The average age of the patients was 45.2 ± 2.5 years old. The most predominant histological type was undifferentiated carcinoma with a frequency of 94.2%. At diagnosis, 86,7% of cases had an advanced stage of NPC. Stage IV represents 60% of cases. The 4-year overall survival of patients was 94.2% with an average survival of 52.3 ± 1.4 months. It represented 85% for advanced stage IVb. **Conclusion** : Nasopharyngeal cancer is frequent in men in Algeria. The advanced stage at diagnosis influences patient survival, it is therefore essential to implement early detection strategies, multidisciplinary approaches and personalized treatments in order to reduce mortality from this cancer and improve the quality of life of patients.

KEYWORDS: Carcinoma, histopathology, nasopharyngeal, prognosis, western Algeria.

RESUME

Introduction : Le cancer du nasopharynx est le plus frequent des cancers de la tête et du cou chez l'homme en Algérie. L'objectif de l'étude est de décrire l'épidémiologie, la clinicopathologie et la survie du carcinome du nasopharynx. **Méthodes** : Etude de survie bicentrique portant sur des cas incidents de cancer du nasopharynx confirmés histologiquement, résidant dans l'ouest algérien et suivis sur une période de 4 ans. L'analyse de la survie a été faite par la méthode de Kaplan-Meïer. La comparaison des courbes de survie a été réalisée par l'exécution du test de Logrank. Le seuil de signification α a été fixé à 5%. **Résultats** : 120 cas de cancer du nasopharynx ont été diagnostiqués puis suivis durant la période de l'étude. Une prédominance masculine a été observée avec un *ratio homme sur femme de 83/37*. L'âge moyen des patients était de 45,2 ± 2,5 ans. Le type histologique prédominant était le carcinome indifférencié avec une fréquence de 94,2%. Au moment du diagnostic, 86,7% des cas appartenaient aux stades avancés, avec une prédominance du stade IV dans 60% des cas. La survie globale des patients a été estimée à 94,2% à 4 ans avec une moyenne de survie de 52,3 ± 1,4 mois. Elle était de 85% pour les cas diagnostiqués au stade le plus avancé IVb. **Conclusion :** Le cancer du nasopharynx est un cancer fréquent chez l'homme en Algérie. Le stade avancé au diagnostic influence la survie des patients, il est donc essentiel de mettre en place des stratégies de détection précoce, d'approches multidisciplinaires afin de réduire la mortalité par ce cancer et améliorer la qualité de vie des patients.

MOTS CLES : Cancer, histopathologie, nasopharynx, ouest algérien, pronostic.

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Introduction

Nasopharyngeal carcinoma (NPC) stands out from other head and neck cancers due to its high incidence in Southeast Asia and Maghreb countries, while remaining rare in Europe and other developed countries [1, 2]. It is the most prevalent cancer of the upper aerodigestive tract in men in Algeria, with an age-standardized incidence rate of 5,8 per 100 000 [3]. It ranks eleventh in terms of cancer deaths among men [4].

Nasopharyngeal cancer predominates in males with a sex ratio ranging from 2 to 3 men for every woman. In North African countries, the age distribution curve is bimodal, with a first peak of frequency occurring in young individuals aged between 10 and 24 years old, and a second peak after the age of 50 [5, 6]. This distribution differs from that observed in other countries such as China, where this tumor primarily affects older people [7].

Its etiology involves the combination of several environmental and genetic factors. Indeed, a diet rich in Nitrosamine, professional exposure to chemical and toxic substances and certain medicinal plants are implicated in the occurrence of this cancer. Furthermore, the carcinogenesis of NPC is linked to the effect of genetic alteration combined with the carcinogenic effect of the Epstein-Barr virus. EBV infects lymphocytes and oropharyngeal epithelial cells, remaining latent and expressing genes that interfere with the cell cycle. This interaction promotes G1/S phase transition and inhibits apoptosis, facilitating the development of EBV-related malignancies [8].

Nasopharyngeal carcinoma poses a clinical challenge due to its deep anatomical location. Its non-specific symptoms, such as otologic and rhinologic signs, often make diagnosis difficult and delayed [9]. It is usually associated with locoregional lymph node involvement and sometimes distant metastases, most commonly affecting the bones, lungs and liver [10, 11]. Its treatment presents a heavy burden with significant socio-economic impact. Chemoradiotherapy remains the best treatment for this tumor, improving patient survival [12].

The prognosis of NPC depends on several factors to determine, such as TNM stage, histological type, comorbidities, cigarette smoking and alcohol intoxication. Advances in diagnostic and therapeutic approaches over time have generated significant interest in enhancing the survival outcomes of patients with nasopharyngeal carcinoma.

However, there is a lack of statistics on cancer mortality and patient outcomes in our country. Only a few studies on survival in nasopharyngeal cancer patients have been published, leaving prognostic factors in our population largely unexplored. This gap underscores the significance of our study.

Our study aims to investigate the epidemiological, clinicopathological characteristics, and the survival of patients with nasopharyngeal carcinoma in western Algeria in order to improve understanding of this tumor and allow us to identify patterns of distribution and potential associations between exposures and disease cases, which can inform public health actions.

Methods

It is a prospective study, carried out in two university hospitals in Oran (Cancer Center and University Hospital Establishment of Oran).

The period of the study : The study was conducted over a 4-year period from January 2016 to December 2019.

Study population and selection criteria : all incident cases of nasopharyngeal carcinoma with histological evidence, diagnosed during the period from January 1, 2016, to January 1, 2018. All patients included in our study provided verbal and written informed consent before their inclusion.

The morphological code of the tumor was identified according to the 4th edition of the World Health Organization classification of head and neck tumours, 2017 [13] .

All malignant nasopharyngeal tumors were categorized based on their topographical location within the range of codes C11.0 to C11.9 in the International Classification of Diseases (ICD-10).

The tumor stage was determined based on the TNM classification (Tumor, Node, metastasis)/UICC (The Union for Internationale Cancer control), 7th edition [14].

Patients with associated cancers and those not residing in western Algeria were not included in the study.

The primary endpoint : The overall survival of patients.

Data collection and recording : data were collected from patients medical records in two centers of oncology. Cases lost to follow up were contacted to inquire about the evolution of their disease.

Statistical analysis

Descriptive analysis of data was carried out by calculating frequencies and percentages for qualitative variables. Quantitative variables were represented by measures of central tendency like the mean (m) and the median (me) and measures of dispersion such as variance (σ^2) and standard deviation (σ). The association between categorical variable was examined using Chi square χ^2 test with determination of the significance threshold.

The survival analysis was performed using Kaplan–Meier method. The status of patients as either alive or deceased was recorded. Overall survival (OS) was determined from the date of diagnosis histological confirmation until the date of death or the date of last follow-up. Survival curves of age, sex and stage were afterward compared using the Log Rank test. The level of significance was set at p value of 0,05.

Ethical aspects

All patients included in our study provided verbal and written informed consent before their inclusion. The information gathered was kept anonymous and confidential.

Results

1. General patient Characteristics

Considering the eligibility criteria, a total of 120 cases of nasopharyngeal cancer was recorded during the period of the study

Among all patients, 40,8% resided in Oran, 14,2% in Mostaganem, 10,8% in Mascara. The other patients lived in other cities in western Algeria.

A male predominance was observed with a *sex ratio (male/Female)* of 2,2. The average age of patients was 45,2 ± 2,5 years old. The majority of cases (70%) occurred in individuals aged over 40 years old. However, young subjects aged between 16 and 39 years were also affected.

2. Pathological characteristics

In our study population, the histopathological examination of the tumor shows that the vast majority of cases were carcinomas (99,2%). The predominant histological type was undifferentiated carcinoma with a frequency of 94,2%. Only one case of adenocarcinoma was reported (**Table 1**).

3. Tumor Stage and TNM Classification

Among patients classified according to tumor extension and lymph node involvement, more than half of the tumors (T) have locoregional extension and are classified as T4. Lymphadenopathy is present in 77.5% of patients (**Table 1**).

Using the UICC staging classification, we found that patients were diagnosed at different stages. However, over 80% of the cases were in advanced stages. Stage IV was the most common, accounting for 60.9% of the cases (**Table 1**).

4. Clinical progression

Three-quarters of the cases (73.3%) showed a good clinical progression after treatment (remission or stabilization (**Table I**). Nonetheless, 22,5% of them or 27 cases experienced a relapse either locally or at distant sites. Local relapse occurred in 10 patients (37%), lymph node relapse in 5 cases (19%), and distant recurrence in 12 cases (44%). The bone and brain were the most frequent metastatic site, each with a percentage of 33% (4 cases each), followed by the liver and lung 17% (2 cases each). Among all patients, only 4,2% died (**Table I**).

Table 1 : Clinicopathological Characteristics of nasopharyngeal carcinoma cases

Histological type	**N**	**%**
Undifferentiated carcinoma (UCNT)	113	94,2
Moderately Undifferentiated carcinoma	5	4,2
Well-differentiated carcinoma	1	0,8
Adenocarcinoma	1	0,8
TNM classification		
Tumor		
T_1	23	19,2
T_2	18	15,0
T_3	17	14,2
T_4	62	51,6
Node		
N_0	27	22,5
N_1	29	24,2
N_2	45	37,5
N_3	19	15,8
Metastasis (M)	00	00,0
Tumor stage		
Stage I	3	2,5
Stage II	13	10,8
Stage III	31	25,8
Stage IV a and b	73	60,9
Clinical progression		
Remission	88	73,3
Relapse	27	22,5
Death	5	4,2

5. Overall Survival

The vital status of all patients was documented, with no loss to follow up recorded. The median survival was not reached in our series. The average survival rate was 52,3±1,4 months. The overall survival rate was estimated at 98,3% and 94,2% respectively at 12 et 48 months (**Figure 1**).

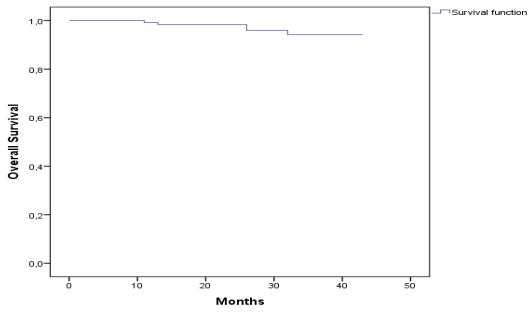

Figure 1: Overall Survival (OS) of NCP patients

The average survival was better in woman. The mean of follow up was 42,4±1,2 months for female and 41,6±0,7

months for males. The 4-year overall survival rates were 95,8% for men and 96,6% for women, respectively. The Kaplan-Meier survival curves for both genders did not show a statistically significant difference as determined by the Log-Rank test (p=0,54) (**Figure 2-a**).

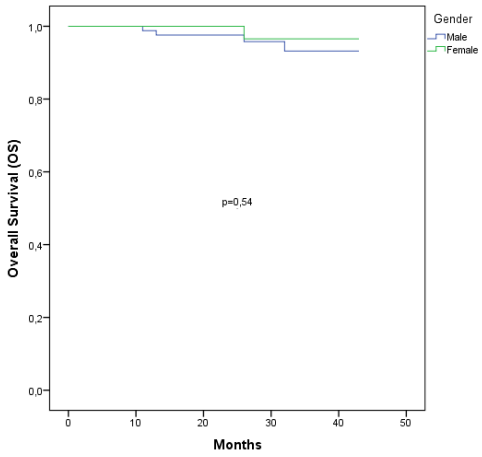

Figure 2-a : Overall Survival (OS) of NCP between male and female patients

Regarding the age, the highest survival rate (100%) was observed in young patients aged between 16 and 19 years, followed by patients aged 30-39 years (92,9%). The survival probability for individuals aged 70 years and older was the lowest (80,0%) (**Figure 2-b**).
The 4-year overall survival in patients younger than 50 years was 96,7%, with a mean of follow up 42,3±1,1 month. In patients aged 50 years and older, OS was 90,3%. However, the difference between the age groups was not statistically significant (p =0,25) (**Figure 2-b**).

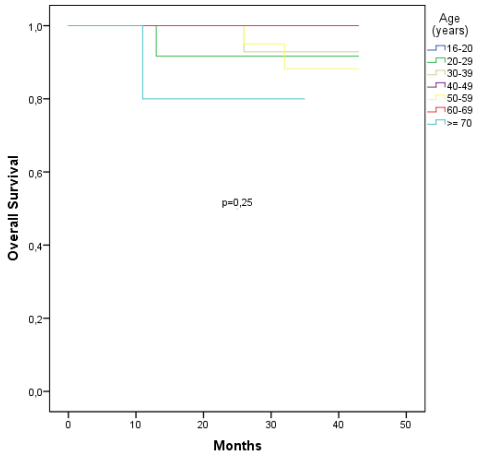

Figure 2-b: Overall Survival (OS) of NCP according to age

The 4-year survival probability was 95% for cases diagnosed at stages III and IVa, and it was lower for the most advanced stage, IVb (85%). Survival curves did not differ significantly among the several tumor stages (p=0,30) (**Figure 3**).

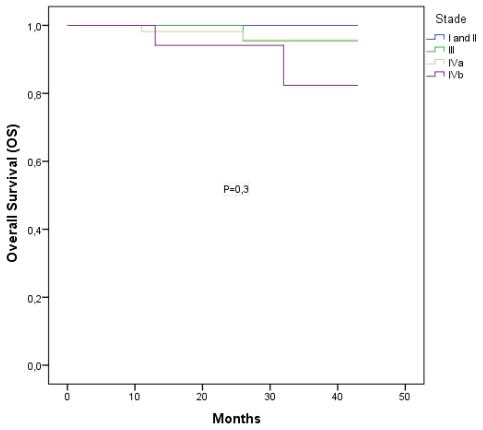

Figure 3 : Overall Survival (OS) of NCP according to the tumor stage

Discussion

Among all patients with nasopharyngeal carcinoma recorded over a two-year period, 120 cases were included in our study according to the eligibility criteria.
Nasopharyngeal carcinoma is the first cancer of the ENT sphere in Algeria. It occupies a significant place among countries with high incidence such as southern China and Asia, while it remains rare in developed countries [15]. This high incidence in our countries is similar to that of other Maghreb countries such as Tunisia and Morrocco, due to exposure to dietary and environmental factors specific to these region [16].
Nord Africa represents 9% of all cases reported worldwide [17]. Intermediate rates of 3 to 7 cases per 100,000 hbts are observed in the three Maghreb countries. Algeria is in the lead with a standardized incidence of 5,4/100 000hbts in men and 1,7 in women, followed by Tunisia then Morocco [16].
Nasopharyngeal carcinoma remains one of the most common cancers in Morocco with a prevalence of 5% during the period 2017-2019 [18]. It ranks seven among head and neck cancers and 10th among all cancers. Its incidence is 3,1/100 000 in men and 2,3/100 000 in women [19].
In Tunisia, NPC ranks first among ENT cancers and occupies ninth place among all cancers with a percentage of 3,3%. Its incidence varies between 3,1 and 3,9/100 000 hbts [20].
The incidence in China increases geographically from north to south reaching very high rates in Guangdong province et Hong Kong [21, 22]. The incidence of NPC is also elevated in Singapore (6,7), Indonesia (6,6), Malaysia (6,3), and Vietnam (5,7); as well as in other parts of Southeast Asia, including Myanmar (3,7), the Philippines (3,2), and Thailand (2,2) (Globocan 2018).
NPC is rare in most parts of the world with an incidence

less than 1/100 000.
Europe is a region with very low endemicity. According to Globocan data 2018, the incidence is 0,5 in Spain, 0,6 in Italy, and 0,5 in France.
The same applies to the united state with an incidence of 0,7/100 000 [23].

Table 2 : **Comparison of age and gender of cases with the literature**

Authors	Countries	Sex ratio*	Age (years)
Guo X [24]	China	2,6	45
Dan O [25]	France	2,2	49
Hamdi Cherif M[3]	Algeria	2,3	43
Zenab A [26]	Morocco	1,7	46
Mnejja [27]	Tunisia	2,2	42
Boumansour N [This study]	Algeria	2,2	45

* Male/Female

In our study population, a male predominance is observed with a sex ratio of 2,2. This is consistent with literature were the sex-ratio varies between 2 et 3 in the world (**Table 2**). This dissimilarity between men and women may be due to smoking which remains common in men and to professional exposure to certain toxic substances such as wood and cement dust, vehicle emissions and factories fume[28].
The average age of patients is 45,2±2,5 years old. It's a relatively young population. This is similar to the results obtained in other North African countries (**Table 2**). EBV infections are more common in childhood and adolescence, which may contribute to the early development of this cancer in infected individuals. Furthermore, exposure to carcinogens early in life could influence the age of onset of this cancer [29, 30]. These results can also be explained by the genetic predisposition. Certain genetic variants are more prevalent in specific ethnic groups, thereby elevating the risk of developing this type of cancer at a younger age.

Histology

According to the latest World Health Organization (WHO) classification of head and neck tumors published in 2017 (4th edition), Nasopharyngeal carcinomas are classified into two histological categories (keratinizing or non-keratinizing squamous cell carcinomas). non-keratinizing squamous cell carcinomas can be differentiated or undifferentiated (Undifferentiated Carcinoma of Nasopharyngeal Type "UCNT") [13]. The most common histological type in endemic areas is UCNT found in more than 90% of cases [31].
In our study, the predominant histological type is UCNT (94,2%). This confirms the results of studies carried out in endemic areas [32, 33].
Undifferentiated Carcinoma of Nasopharyngeal Type (UCNT) is the most prevalent histological type in Morocco. It represents 96,12% of cases. Differentiated non-keratinizing squamous cells and keratinizing squamous cells are rare [18].
In Tunisia Undifferentiated Carcinomas account for 54,4 % of cases while Poorly Differentiated Carcinomas represent 45,6% of cases [34].
The histological type found in almost all cases of endemic areas of south China is non-keratinizing carcinoma (99% of cases). This type is commonly associated with Epstein Barr Virus (EBV) infection [35]. Additionally, NPC carcinogenesis is associated with genetic alterations and the carcinogenic effects of Epstein-Barr virus (EBV). EBV infects lymphocytes and oropharyngeal epithelial cells, where it remains latent and expresses genes that disrupt the cell cycle. This disruption promotes the G1/S phase transition and inhibits apoptosis, supporting the development of EBV-associated malignancies [8].

TNM Classification and tumor Stage

The TNM classification finds respective frequencies of 51,6%, 19,2%, 15,0% et 14,2% for T4, T1, T2, T3 Tumors. Among all the patients in our series, 77,5% presented adenopathy. *N Bouaouina and al* in Tunisia found similar results reporting that 47% of patients had a T4 tumor and 74,2% of cases presented adenopathy [34]. Liu and al. in Taiwan found that 23% of cases had a T4 tumor and 77% had adenopathy [36].
NPC is characterized by a late diagnosis in our population, 86,7% were diagnosed at stage III and IV. *Reffai A and al* et *Marnouche et al* found high proportion of cases diagnosed at advanced (respectively 82,2% and 85,5%) [18, 37]. Indeed, nasopharyngeal cancer can take several decades to develop before symptoms appear. Also, the deep location of this cancer means that it is often diagnosed late and therefore notified at an advanced stage.
The use of serological markers of the Epstein-Barr virus and molecular tests for the detection of viral DNA would enable early screening of this tumor.

Relapse

Among all the cases in our study, 22,5% experienced a recurrence of NPC. *Zeng Z et al et Sun Y* found a similar result [38, 39]. The relapse of patients could be due to resistance to treatment of certain tumors. Alternatively, sometimes, even after successful initial treatment, residual cancer cells may remain in the body, which can eventually multiply and lead to a relapse.

Survival

Survival serves as an indicator of effective management within specialized healthcare facilities, particularly through chemotherapy and radiotherapy, which simplifies the process of diagnosis and treatment.
The 1-year and 4-year Overall Survival probability of our patients was estimated at 98,3% and 94,2% respectively. These rates are nearly similar to the findings of several Chinese studies and those of the study conducted by *Kehili H* in the same Algerian region [40] (**Table 3**).
However, the survival of our patients remains better than those observed in two Tunisian studies of *Toumi N et Frikha M*. This could be explained by the differences in modalities

and patient care times between different countries (**Table 3**).

Table 3 : Comparison of overall patient survival with the literature	
Authors	**3-year Overall Survival Rate**
Sun Y [39]	92,0
Peng H [41]	91,5
Frikha M [42]	86,3
Toumi N [43]	71,6
Boumansour N [This study]	94,2

The 4-year Overall survival was similar in men and women in our study population with respective rates of 95,8% et 96,6%. Literature show better survival in female, this could be explained by hormonal differences between the two sexes [44]. Furthermore, it is possible that there are biological differences between nasopharyngeal tumors in men and women, which could influence treatment response and survival. Studies suggest that nasopharyngeal tumors in women may be less aggressive or respond better to treatments.

The four-year Overall Survival rate of patients was 95% for cases diagnosed at stages III and IVa. It was less for the most advanced stage IVb (85%). This means that the stage of NPC could influence patient survival. These results are consistent with those of various studies which have shown that NPC stage is an important prognostic factor [45].

Limitation

Due to the limited number of deaths, the Logrank test may lack statistical power to detect significant differences between survival curves, even if such differences actually exist. This remains a limitation of the study. Additionally, the generalizability of findings may be limited by the specific characteristics of the study population, limited sample size and geographical homogeneity (centered on western Algeria).

Conclusion

Nasopharyngeal cancer poses a significant concern among head and neck cancers in men in western Algeria, underscoring the need for special attention and a deeper understanding of its epidemiology and prognosis. This study contributed to the understanding of CNP and its evolution. It is a cancer that particularly affects males aged over 40. Survival of patients with NPC is better when the cancer is diagnosed early and when treatment is appropriate. The advanced stage at diagnosis influences patient survival, emphasizing the necessity of implementing early detection strategies, multidisciplinary approaches, and personalized treatments, to reduce mortality from this cancer and improve patients' quality of life. It is also crucial to underscore the importance of knowledge of risk factors, awareness and screening in the fight against nasopharyngeal cancer, particularly in populations at high risk.

Conflicting interests

The author(s) declared no conflicts of interest.

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