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HISTOPATHOLOGICAL PATTERN OF NASOPHARYNGEAL CARCINOMA IN BENIN CITY

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ABSTRACT

A retrospective analysis of nasopharyngeal tissue biopsies sent to the department of histopathology, University of Benin Teaching Hospital over a ten year period (January 2000 to December 2009) was carried out to define the histopathological pattern of nasopharyngeal carcinoma (NPC) in Nigerian patients in Edo state. Parameters included in the review where histological types of NPC according to the world health organization (WHO) classification, age, gender, and lymph node metastasis. All histological diagnosed cases of nasopharyngeal carcinoma where studied within a 20-year study period. Total number of patients with NPC was 106 with ages ranging from 9 to 63years. The median and mean ages were 33 years and 32.1±16.7years respectively with a male: female ratio of 4:1.The predominant WHO type was type III which accounted for 83% of the cases. WHO type I and II cases cases accounted for 15.1% and 1.9% respectively. Most of the cases had cervical lymph node metastasis (70.2%). The histopathological pattern of NPC in Benin resembles those seen in other parts of Nigeria and non endemic areas of the world. It is how ever characterized by an earlier age of onset, male predominance, a preponderance of undifferentiated (WHO type 3) tumours and late presentation

INTRODUCTION

NPC is a rare tumour with an incidence in the literature of <1/100,000. It shows both racial and geographic variations with high prevalence rates in South East Asia, some parts of Middle East and North Africa. The highest incidence rates of 20-50/100,000 have however been recorded in Southern China[1]. It is a malignant neoplasm arising from the mucosal epithelium of the nesopharynx. The three microscopic subtypes recognized by WHO are: well differentiated squamous cell carcinoma (WHO type 1), moderately differentiated non keratinizing squamous cell carcinoma (WHO type II) and an undifferentiated squamous cell carcinoma (WHO type III) which is further sub typed into the Regaud and Schmincke varients [2].

Epstein-Barr virus (EBV) is consistently reported as an important aetiological factor in the carcinogenesis of NPC. Elevated titres of antibodies against EBV viral capcid antigen, latent viral nuclear antigens 1 and 2 (EBNA-1,EBNA-2) and neutralizing antibodies to EBV-specific DNAse have been seen in virtually all cases of NPC. Interestingly, EBV infects over 90% of the world population with most infectious being latent and subclinical and significantly, only a small percentage of these infected persons develop the cancer. This suggests that other environmental/genetic factors

KEYWORDS: *Nasopharyngeal Carcinoma; Histopathology; Lymph node metastasis.*

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including salt preserved food, smoke from tobacco and other sources of occupational exposure, genetics and racial factors may be critical to the eventual development of NPC. Genetic susceptibility studies have identified alleles including HLA-A2, B14 and B46 as halving positive associations with NPC while HLA-A11, B13 and B22 have consistently shown an inverse association[3-5].

In Nigeria, the exact incidence is unknown. Nasopharyngeal carcinoma was reported to be uncommon in the central part of Nigeria[6]. Nevertheless, reports from various parts of the country suggest that it is the commonest form of head and neck cancer except in Ilorin where it was the third most common[7--]. Statistics on cancer is essential for proper planning and utilization of human and material resources.This will however require a standard cancer registry in Nigeria as a whole. It is noteworthy that University of Benin is a tertiary institution with a well established histopathology laboratory in Edo State and has been the only centre in the region with an ENT surgeon. Nevertheless, there remains a dearth of information on nasopharyngeal carcinoma in this region. This study is thus aimed at defining the frequency and the histopathological pattern of nasopharyngeal carcinoma (NPC) in Edo State. We believe that information generated from this study will be useful in the management of these patients and proper utilization of resources. More so, it should serve as baseline data for research and training.

MATERIALS AND METHODS

We reviewed all histologically diagnosed cases of nasopharyngeal carcinoma in Benin City from April 1991 to April 2010. Clinical information was gotten from the patient. The request cards and case notes retrieved from the Medical Records Department. Cases without adequate information or in which the histology slides and blocks could not be retrieved were not included in this study. New sections were made from the paraffin blocks and stained with Heamatoxylin and Eosin stain when necessary. Histologically these cases were classified according to world health organization classification of nasopharyngeal carcinoma into type I, type II, and type III[2]. Instant statistical software was used for data entry and analysis.

RESULTS

During the 20 years period of study, a total of 132 histologically diagnosed cases of nasopharyngeal carcinoma were seen. Of these, 106 cases fulfilled the inclusion criteria and were analyzed. This represents 80% of the entire nasopharyngeal specimen received. Of the 106 patients with nasopharyngeal carcinoma, 85 (80.2%) were males while 21 (19.85%) were females given a male to female ratio of 4:1. The ages of patients ranged from 9-63years the median age of the patients was 33years with a mean age of 32.1±16.7years.

Table 1 shows the age distribution of patients .the peak age group was 20-39 years accounting for 63 (59.4%) of the cases. This was followed by those in the age group of 40-49 (17.8%, n=19). Those below the age of 20 years made up only 16.2% of cases. In our study nasopharyngeal carcinoma was not common in the elderly as only 2.8% of the cases occurred above the age of 60 years.
The histological types of nasopharyngeal carcinoma are shown in table 2. Most of the cases encountered in this study were undifferentiated squamous cell

TABLE 1: AGE AND SEX DISTRIBUTION OF PATIENTS WITH NASOPHARYNGEAL CARCINOMA

AGE RANGE	MALE	FEMALE	TOTAL (%)
0-9	2	-	2(1.9)
10-19	12	3	15(14.3)
20-29	23	3	26(24.5)
30-39	29	8	37(35.0)
40-49	10	3	19(17.8)
50-59	3	1	4(3.8)
60-69	2	1	3(2.8)
TOTAL	85(80.2%)	21(19.8)	106(100%)

TABLE 2: AGE DISTRIBUTION OF THE HISTOPATHOLOGICAL TYPES OF NASOPHARYNGEAL CARCINOMA

AGE	**NO CASES**				**%**
Age range	TYPE 1	TYPE 2	TYPE 3	TOTAL	TOTAL
0-9	-	-	2	2	1.9
10-19	1	3	11	15	14.3
20-29	1	3	22	26	24.6
30-39	-	22	26	37	35.0
40-49	-	3	16	19	17.8
50-59	-	1	3	4	3.8
60-69	-	-	3	3	2.8
TOTAL	2 (1.9%)	16 (15.1)	88 (83.0%)	106 (100%)	100.0

TABLE 3: SEX DISTRIBUTION OF THE HISTOLOGICAL TYPES OF NASOPHARYNGEAL CARCINOMA.

	MALE (%)	FEMALE (%)	TOTAL (%)
WHO TYPE I	2(1.9)	-	2 (1.9)
WHO TYPE II	11(10.4)	5(4.7)	16(15.1)
WHO TYPE III	72(67.9)	16(15.1)	88(83.0)
TOTAL	85(80.2)	21(19.8)	106(100)

TABLE 4: NASOPHARYNGEAL CARCINOMA AND LYMPH NODE INVOLVEMENT.

LYMPH NODE METASTASES	NO. OF CASES	PERCENTAGE.
POSITIVE CASES	52	70.2
NEGATIVE	22	29.8
TOTAL	74	100

carcinoma (WHO type III) accounting for 88 cases (83%). The moderately differentiated (WHO type II) and well differentiated (WHO type I) NPC constitute 16 (15.1%) and 2(1.9%) cases respectively. Majority of patients with undifferentiated carcinoma NPC [37 cases (35%)] were in the age range of 30-39 years followed by those in the age range of 20 to 29 years 26(24.5%). Only 3 were found in children below 10 years of age.

As shown in table 3, most [72 cases 67.9%] of the undifferentiated NPC (WHO type III) occurred in males. Only 16 (15.1%) of these undifferentiated tumours were seen in females. Fifty seven of 88 cases of undifferentiated carcinoma (WHO type III) were composed of diffuse sheets of epithelial cells intermingled with lymphocytes and thus designated the schmincke-type. The remaining 31 cases diagnosed as Regaud's type showed aggregates of epithelial cells interspersed by dense fibrocollagenous tissue. WHO type II (N=16) cases, were moderately differentiated squamous cell carcinoma composed of sheets of epithelial cells

without evidence of keratinization. WHO type I cases constitute only 2 cases and were well differentiated sqamous cell carcinoma with keratin pearls.
Lymph node enlargement was recorded in 74 cases accounting for 69.8% of all nasopharyngeal carcinoma seen in this study (table 4). Of these cases, 52 (70.2%) cases showed infiltrates of malignant cells and were recorded as positive for metastasis while the remaining 3 (29.8%) cases were negative.

DISCUSSION

In this study, a total of 132 cases of nasopharyngeal carcinoma were seen. This accounted for 3.2% off all malignant tumours reported during the 20 year study period. In plateau and Ilorin, NPC constitute slightly lower figure of 1.7% and 2%[6,9]. Reports indicate that the incidence of NPC in South East China is 25 times higher than that of the rest of the world occurring in 25 per 100,000 persons and accounting for 18% of all cancers[11,12].

In our study, the mean age of patients with NPC was 32.1 ± 16.7 years. This is relatively lower than the age range of 41.1 to 48 years reported from different part of Nigeria and Africa[6-10]. The peak age group of 30 to 39 years is however lower than the peak ages documented in Sudan and Hong Kong were nasopharyngeal carcinoma is endemic[10,12]. The peak age incidence among Nigeria patients is about a decade lower than that of patients from endemic region such as South East Asia[6-9, 12]. The earlier age of occurrence of NPC in our environment may be attributed to the association of NPC with Epstein Barr Virus (EBV). Epidemiological observations suggests that the etiology of NPC includes interplay of both inherited genetic predisposition and environmental factors. Early latent infection by the ubiquitous Epstein –Barr Virus (EBV) and its reactivation has been reported to play an important role in the cancer formation process[3-5]. Significantly, Burkitt's lymphoma which has been reported as showing strong association with Epstein Barr Virus (EBV) is the commonest childhood tumour in Nigeria[13]. These observations suggest infections of patients by EBV at a very early age in our environment.

All the 3 classes of nasopharyngeal carcinoma were represented in this study i.e, WHO types I, II, and III. While most cases of nasopharyngeal carcinoma reported in North America belonged to WHO type I[11], in our study, the predominant type was type III (undifferentiated type) accounting for 83% of the cases. Similar for our finding, in Ilorin, undifferentiated carcinoma was the commonest (70%) followed by well differentiated keratinizing squamous cell carcinoma (20%)[-].

A greater portion of well differentiated squamous cell carcinoma (WHO type I) accounting for 40%of NPC was however reported by obafunwa[6] in central Nigeria. It is note worthy that in endemic areas like China, there is a predominance of type III tumour[12].

The two cases of NPC that presented below the age of 10 years, and 11 of the 15 cases found between the age rage of 10 to 19 were undifferentiated tumours (WHO type III). This findings corroborates the report that most cases of nasopharyngeal carcinoma in children and young adults are undifferentiated WHO type III tumours with a few WHO type II tumours[13,14].

NPC occurred predominantly in males with a M:F ratio of 4:1. This male predominance has been observed in similar studies done in Nigeria[6,8,15,16] and other parts of the world, including endemic and non

endemic zones though with slightly varying ratio[18,19]. Lower M:F ratios ranging from 1.6:1 - 2.8:1 were however reported in previous Nigerian studies[6,8,15,17]. The lowest risk of developing NPC in females of all races remains unexplained and requires further research.

Cervical lymph node metastasis was recorded in almost 70% of the cases. Majority of the NPC patients in Nigeria present with unilateral cervical lymphadenopathy[6-9,15-15]. In Ilorin, 97.6% of patients presented with cervical lymphadenopathy and was the commonest mode of presentation[9]. This finding is similar to the findings in Sudan and India[10,20]. This has diagnostic implications considering the fact that cervical lymphadenopathy has a constellation of causes. Moreso, undifferentiated NPC WHO type III the commonest sub type in this study is composed histologically of undifferentiated cells and may thus mimick histologically the immature lymphoid cells of large cell lymphoma. Incidentally, non-Hodgkin? s lymphoma has been reported by Olu-Eddo at al[21] as the commonest neoplastic cause of cervical lymphadenopathy in Benin. Sections of undifferentiated NPC may show infiltrates of eosinophils simulating Hodgkin? s lymphoma[22]. The differentiation of undifferentiated NPC from the lymphomas may require the use of immunohistochemistry. Sections of NPC may also show areas of granulomatous infiltration and necrosis that may be difficult to distinguish from tuberculous lymphadenitis[22]. These are major diagnostic limitations considering the fact that tuberculous lymphadenitis was overall, the commonest cause of cervical lymphadenopathy in Benin City[21]. in some cases, tumour cells may be masked by lymphoid cells or may develop cystic changes and simulate brachial cleft cyst[22]. There is thus need for caution and a high index of suspicion when accessing a cervical lymph node biopsy. There might be need for special stains (such as Ziehl-Neelson stain for acid fast bacilli) and ancillary investigations.

The high percentage of metastatic lesions encountered in this study is not surprising considering the relative inaccessibility of the nesopharynx. Due to its anatomical position, it is difficult for lesions to be observed and biopsied early. Besides early lesions may not present with symptoms relating to the nasopharynx and where there is any symptom it is usually regarded as sore throat or common cold by the general practitioner of the patient. Nevertheless, the advent of modern imaging technologies and flexible endoscopes has contributed substantially not only to reveal the tumour, but also to locate the most suspicious sites for biopsy and has significantly reduced the mortality rate from NPC[23]. These diagnostic tools should be made available to all tertiary and comprehensive health centres. Moreover there is need for a public awareness campaign. This is particularly important in a society like Nigeria where ignorance and low socio-economic factors affects health seeking behavior.

We conclude that nasopharyngeal carcinoma is relatively common in Edo state. The histopathological distribution resembles that seen in most parts of Nigeria and non endemic areas of the world. It is however characterized by an earlier age of onset, male predominance, a preponderance of undifferentiated (WHO type III) tumours and late presentation with cervical lymph node metastasis.

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