NASOPHARYNGEAL CARCINOMA
A comparative study

JEHORAM TEI ANIM, METHIL KANNAN KUTTY, SALEH SOWAYAN and MOHAMMAD OMER AL-SOHAIBANI

Department of Pathology, King Fahd Hospital of the University, Al-Khobar, Saudi Arabia

Accepted for publication November 19, 1990

Abstract. A comparative study of Ghanaian and Saudi hospital cases of nasopharyngeal carcinoma (NPC) shows a higher occurrence among younger subjects in the Ghanaian group, with the peak age incidence in the Saudi group being similar to those reported from other parts of the world. In view of the known high prevalence of Burkitt's lymphoma among Ghanaian children, it is suggested that the much higher proportion of younger Ghanaian subjects with NPC may be related to early exposure to the Epstein-Barr virus which is known to be associated with both malignancies.

Key words: Nasopharyngeal carcinoma; Epstein-Barr virus; Ghana; Saudi Arabia

Introduction

The highest prevalence of nasopharyngeal carcinoma (NPC) has been reported among Chinese, especially those from Kwantung Province [1-6]. Comparative epidemiological studies have also shown regional differences with its prevalence being moderate among Mongoloid populations of South-East Asia and lowest among Caucasians [6, 7]. Ethnic differences have been reported among Malaysians [6, 7], while the Japanese are among those with the lowest prevalence rates in that region [8]. Reports from Sub-Saharan Africa are scanty in the literature [9, 10], although foci of relatively high prevalence have been reported [5]. In the Middle East, occasional reports are encountered in the literature, largely based on hospital studies or large series collected in a referral center [11, 12].

An association has been demonstrated between NPC and the Epstein-Barr virus (EBV) [1, 8, 13, 14]; and in view also of the known association between Burkitt's lymphoma (BL) and EBV [15], there has been enough grounds to presume a high incidence of NPC in areas of Africa where BL is known to be highly prevalent. In this regard, one of us (JTA) has been impressed by the relative frequency with which NPC presented in young Ghanaians, including children, in contrast to the reported pattern in Chinese populations in which the disease is known to occur most commonly around middle age [6,16].

Impressed by this observation, we have carried out a comparative study of NPC in Ghanaians and Saudi subjects presenting to hospital with the disease, and related our findings with reports on Malaysians and Chinese [1, 6, 17].

Materials and Methods

The study included sections of specimens collected from 16 Ghanaian patients seen at the Korle Bu Teaching Hospital, Accra, Ghana (KBH) and diagnosed as having NPC. In addition, sections from 25 Saudi patients presenting with the disease to the King Fahd Hospital of the University, Al-Khobar (KFHU), were also reviewed. These were all unselected cases. Routine hematoxylin and eosin slides were reviewed and where appropriate, fresh sections were cut and special stains such as Gordon and Sweet's reticulin, Periodic acid-Schiff

and hematoxylin van Gieson were applied to improve interpretation of the sections and to assist in categorising the tumor into the three major types as defined by WHO (WHO-1: Keratinising squamous cell carcinoma; WHO-2: Poorly differentiated or non-keratinising squamous cell carcinoma; WHO-3: Anaplastic or undifferentiated carcinoma including lymphoepithelioma) [18].

Patient particulars such as age, sex and ethnic origin were sought from the request forms.

Results

There were sixteen Ghanaian subjects from KBH (12 males and 4 females) and twenty-five Saudis from KFHU (18 males and 7 females). The age distribution is detailed in *table 1* and shows a higher occurrence of NPC in younger Ghanaian subjects (mean age: 24.5 years) compared to that in Saudis (mean age: 37.5 years). This difference in mean ages between the two groups is statistically significant ($p < 0.05$). Classification of the tumors into the major histological groups revealed no significant differences in the types, anaplastic carcinoma being the most frequently occurring in both groups (*table 2*). The lymphoepithelioma subgroup of anaplastic carcinoma was seen in 3/25 KFHU cases and 2/16 KBH cases respectively. No keratinising form (WHO-1) was seen in the KBH cases.

Table 1. Comparison of age distribution of nasopharyngeal carcinoma between KFHU (25 cases) and KBH (16 cases)

	KFHU Saudi Arabia		*KBH Ghana*	
Age groups (years)	*Number*	*Percent*	*Number*	*Percent*
1-10	0	0	3	18.8
11-20	3	12	6	37.5
21-30	6	24	3	18.8
31-40	6	24	1	6.2
41-50	6	24	1	6.2
51-60	2	8	2	12.5
61-70	2	8	0	0
TOTAL	25	100	16	100.0

Table 2. Comparison of histological types of nasopharyngeal carcinoma between KFHU (25 cases) and KBH (16 cases)

	KFHU Saudi Arabia		*KBH Ghana*	
Type of carcinoma	*Number*	*Percent*	*Number*	*Percent*
Anaplastic and Lympho-epithelioma (WHO-3)	17	68	12	75
Poorly Differentiated Squamous (WHO-2)	7	28	4	25
Keratinising Squamous (WHO-1)	1	4	0	0
TOTAL	25	100	16	100

Discussion

NPC ranks about 9th of all cancers seen in a referral center in Saudi Arabia, accounting for 4.6% of these cancers [19, 20]. In Ghana, it ranks 10th and accounts for 4.3% of cancers in Accra [21]. In Malaysia, the age adjusted incidence of the disease in Chinese has been reported as 17.3 in males and 7.3 in females per 100,000 population; while in Malays the corresponding figures are 2.5 and 0.3 [6]. According to Sawaki [8], the incidence of NPC is 30 times higher in Chinese than in Japanese. The prevalence of NPC in Saudis and Ghanaians in this study cannot be compared to those of Chinese, Malays or Caucasians on the basis of currently available data.

Age distribution has shown some geographical variation. Peak incidences in Chinese have been reported between 40 and 60 years [1, 16]; and in Swedes, between 70 and 74 years [1]. In Japanese, there is a peak in the 6th decade for both sexes [8] and although peak incidences among Caucasians are generally in middle age, NPC has been reported frequently in childhood and adolescence in several Caucasian populations [2]. In Chinese, however, only 1% of all NPC cases occur under the age of 25 years [22]. In our study of unselected cases, the mean age in KFHU was 37.5 years and that for KBH 24.5 years. That for Saudis in KFHU is therefore closer to the peak age groups in Chinese and Malaysians, while the peak incidence among Ghanaians is in a much younger age group. This apparent geographical difference in age incidence is an interesting finding that requires confirmation in a larger population-based study. Yadav [16] has indicated that the overriding factors associated with the development of NPC in the young are still obscure.

Many studies have shown male predominance of the disease: 2.2 in Chinese [1, 6, 16]; 2.1 in Japanese [8] and 2-3 in Malays [6, 7, 16]. The male predominance in our study is 2.6 for KFHU and 3 for KBH respectively. This confirms the worldwide male predominance of the disease reported by many workers [1, 6, 8, 16]. The reasons for this sex predilection are not clear and Ho [1] has indicated that the difference is likely to be related to unknown constitutional differences in the two sexes which are not affected by geographic or ethnic factors.

The preponderance of anaplastic carcinoma in both groups in our study (68% for KFHU and 75% for KBH) is in accord with findings elsewhere [1, 6, 8, 16]. Anaplastic carcinoma has been closely associated with infection by EBV on serologic evidence [1, 8, 14]. The predominance of the anaplastic type in most populations, our two populations included, and the demonstration of a high association between the EBV genome and the less differentiated forms of NPC using DNA hybridisation studies, tend to suggest that the relatively high prevalence in younger Ghanaian subjects is related to early exposure to EBV [23]. Support for this may be forthcoming in the high prevalence of BL (also known to be highly associated with EBV) in Ghana [24-26]. The association between undifferentiated or anaplastic NPC and EBV is thought to be closer than between BL and the virus, and there is also evidence to indicate that EBV seems to act at a late stage of carcinogenesis in NPC in contrast to the situation observed in BL [27, 28].

In conclusion, our study has demonstrated a histological pattern and sex ratio of NPC in the two populations similar to those reported elsewhere, but with greater occurrence of the disease among younger Ghanaian subjects in Accra. We speculate that the close association between EBV and NPC on the one hand and BL on the other could provide a common denominator in explaining the greater prevalence among the young in Ghana. Such an observation requires confirmation using a much larger sample.

We are grateful to our clinical colleagues, both in our hospital and in neighbouring hospitals and clinics, whose cases are included in this study. We also thank our pathology colleagues involved in the initial diagnoses of the cases reviewed.

Correspondence to: Dr. J.T. Anim, Department of Pathology, College of Medicine, King Faisal University, P.O. Box 2114, Dammam-31451, Saudi Arabia.

References

1. Ho HC. Epidemiology of Nasopharyngeal Carcinoma. GANN Monograph on Cancer Reserach 1976; 18: 49-61.
2. Jung PF and Yu C. Nasopharyngeal Carcinoma in China. Postgr Med 1963; 33: A77-82.
3. Clifford P. On the Epidemiology of Nasopharyngeal Carcinoma. Intl J Cancer 1970; 5: 287-309.
4. Yeh S. The relative frequency of Cancer of the Nasopharynx and Accessory Sinuses in Chinese in Taiwan. In: Cancer of the Nasopharynx, UICC Monograph series. Muir CS and Shanmugaratnam K, Copenhagen, Munksgaard 1967; 1: 54-7.
5. Muir CS. Nasopharyngeal Carcinoma in non-Chinese populations with special reference to South-east Asia and Africa. Intl J Cancer 1971; 8: 351-63.
6. Armstrong RW, Kutty MK and Dharmalingam SK. Incidence of Nasopharyngeal Carcinoma in Malaysia with special reference to the state of Selangor. Br J Cancer 1974; 30: 86-94.
7. Armstrong RW, Kutty MK and Armstrong MJ. Self-specific environments associated with Nasopharyngeal Carcinoma in Selangor, Malaysia. Soc Sci Med 1978; 12D: 149-56.
8. Sawaki S, Hirayama T and Sugano H. Studies on Nasophyaryngeal Carcinoma in Japan. GANN Monograph on Cancer Research 1976; 18: 63-74.
9. Clifford P. Carcinoma of the Nasopharynx in Kenya. E Afr Med J 1965; 42: 373.
10. Clifford P. Malignant disease of the nasopharynx and paranasal sinuses in Kenya. In: Muir CS and Shanmugaratnam K, Cancer of the Nasopharynx. Copenhagen, Munksgaard 1967: 82.
11. Cammoun M, Hoerner GV and Mourali N. Tumours of the Nasopharynx in Tunisia, an anatomic and clinical study based on 143 cases. Cancer 1974; 33: 184-92.
12. Parikh SD and El-Ghamarawi KA. Cancer of the Nasopharynx in Kuwait. J Laryngol Otol 1978; 92: 581-91.
13. De The G. Epidemiology of Epstein-Barr virus and associated diseases in man. In: The Herpesviruses. vol. 1. Riozman B (ed). New York, Plenum Press 1982: 25-103.
14. Zeng Y, Gong C, Jan MG, Fun Z, Zhang LG and Li HY. Detection of Epstein-Barr Virus IgA VCA antibody for diagnosis of Nasopharyngeal Carcinoma by Immunoautoradiograph. Int J Cancer 1983; 31: 599-601.
15. De The G, Geser A, Day NE, Tukei PM, Williams EH, Beri DP, Smith PG, Dean AG, Bornkamm GW, Feorino R and Henle W. Epidemiological evidence for causal relationship between Epstein-Barr virus and Burkitt's lymphoma from the Ugandan prospective study. Nature 1978; 274: 756-61.
16. Yadav M, Tan MK, Singh P and Dharmalingam SK. Nasopharyngeal Carcinoma in Malaysians under the age of 20 years. Clin Oncol 1984; 10: 353-51.
17. Kutty MK and Balasengaram M. Malignant Tumours in West Malaysia. J Roy Coll Surg Edinb 1972; 17: 102-7.
18. Shanmugaratnam K and Sobin L. Histological typing of upper respiratory tract tumors. International Histological typing of Tumors. No. 19. Geneva. WHO 1978.
19. El-Akkad SM. Cancer in Saudi Arabia: a comparative study. Saudi Med J 1983; 4: 156-64.
20. El-Akkad SM, Amer MH, Lin GC, Sabbah RS and Godwin JT. Pattern of Cancer in Saudi Arabs referred to King Faisal Specialist Hospital. Cancer 1986; 58: 1172-8.
21. Cancer Registry. Epidemiology Division. Ministry of Health, Ghana 1989.
22. Balakrishnan V and Gangadharan P. Cancer of the nasopharynx in man: younger age peak and related aspects. In: Nasal Tumours in Animals and Man. Reznik G, Stinson SF (eds). Boca Raton, Florida: CRC Press 1983; 1: 188-231.
23. De The G. Is Burkitt's Lymphoma related to perinatal infection by Epstein-Barr virus? Lancet 1977; 1: 335-8.

24. Anim JT, Christian EC and Laing WN. Malignant lymphoma in Ghana - Part 1: Review of surgical material at the Korle Bu Teaching Hospital from 1966 to 1971. Ghana Med J 1973; 12: 176-83.
25. Kovi J and Laing WN. Tumours of the Mandible and Maxilla in Accra, Ghana. Cancer 1966; 19: 1301-5.
26. Nkrumah FK and Perkins IV. Burkitt's lymphoma in Ghana: Clinical features and response to chemotherapy. Intl J Cancer 1973; 11: 19-92.
27. Zeng Y. Anti complementary immunological methods: Epstein-Barr nuclear antigen in Nasopharyngeal Carcinoma cells and normal epithelial cells. Chin Med J 1981; 94: 665-8.
28. Zeng Y, Pi GH, Deng H, Zhang JM, Wang PC, Wolf H and De Thé G. Epstein-Barr seroepidemiology in China. AIDS Res 1986; 87: 15.