

A case series of Nasopharyngeal Carcinoma among Indians, a low risk population, in Perak State, Malaysia

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SUMMARY

Nasopharyngeal carcinoma (NPC) is rare among people of Indian ethnicity. A short retrospective case review of clinical records of Indian patients diagnosed with nasopharyngeal carcinoma in a period of 5 years was conducted. Their slides were further subjected to EBV encoded RNA (EBER) – In-situ Hybridization (ISH). The histologic subtype was non-keratinizing carcinoma in all 4 patients. All were Epstein Barr Virus (EBV) positive. We believe that the crucial factor responsible for nasopharyngeal carcinoma is genetics; either a genetic susceptibility among high risk groups or genetic resistance/immunity in low risk groups. Further genetic studies are required to look for somatic or inherited chromosomal mutations among the various risk populations.

KEY WORDS:

Nasopharyngeal, carcinoma, Indian, Malaysia

INTRODUCTION

Nasopharyngeal carcinoma (NPC) is rare in most parts of the world. However, it shows high rates among Cantonese in the central region of Guangdong Province in Southern China and Hong Kong, and among native people of Sarawak, Borneo¹. Nasopharyngeal carcinoma is the third most common cancer in males in Peninsular Malaysia². The national incidence in Chinese and Malay males is 70% and 28% respectively. Among the Indians, the incidence is 1% of the population², hence the special emphasis on cases diagnosed among Malaysians of Indian background as it is extremely rare. Four cases of nasopharyngeal carcinoma in patients of Indian ethnicity were managed at our centre over a period of five years. The presenting features, histologic subtype as well as management of these patients are discussed.

MATERIALS AND METHODS

A retrospective case review of patients with nasopharyngeal carcinoma was conducted for the time period between January 2005 and December 2009 at Hospital Raja Permaisuri Bainun, Ipoh. The entries into the Malaysian National Cancer Registry database and Hospital Raja Permaisuri Bainun Cancer Registry were used as the foundation of patient identification and search.

Modes of clinical presentation as well as management were studied. Slides and cell blocks of biopsy from the Fossa of

Rossemuller which were available, were stained with Haematoxylin and Eosin and further subjected to epithelial marker testing for cytokeratin presence as well as EBV encoded RNA (EBER) – In-situ Hybridization (ISH). The main objective was to identify any preponderance to a specific histologic type and to establish a linkage with the possible aetiological factors.

RESULTS

Four Indian patients with the diagnosis of NPC were identified in the 5-year time period and their records were scrutinized to obtain relevant details. The presence of a lesion in the Fossa of Rossemuller was confirmed via nasal endoscopy and biopsy taken for histologic grading. None of the patients had any family history of NPC or any other form of malignancy, as well as none of them had any family members of Chinese origin. All the 3 male patients admitted to previous tobacco smoking; however none of these patients had any habitual consumption of salted fish.

All patients had Computed Tomographic (CT) scanning to assist in the staging and to assess the extent of spread of the disease. Immunohistochemistry staining was negative for Leucocyte Common Antigen (LCA), positive for CytokeratinMNF 116 (CKMNF 116).

Three of the patients had received concurrent chemo-radiotherapy at an oncology referral centre whereas one patient had received external beam radiotherapy alone. Post treatment, one patient developed recurrence of the cancer with intracranial extension upstaging his initial presentation of stage III to a stage IV disease. One patient developed spinal metastasis as a complication, and as of the point in time this review was written, 2 patients were in remission. The demographic details, clinical presentation and management of these four Indian patients are presented in Table I.

DISCUSSION

Malaysia is a country with a diverse ethnic background. The three major racial groups are the Malays, Chinese and Indians. Although the region is generally considered a region with intermediate risk for nasopharyngeal carcinoma, the risk actually differs among the different communities. The Chinese, many of whom originate from the Southern Provinces of China are of the highest risk. This is followed by the Malays; intermediate risk, and the Indians; low risk.

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Table I: Details of the four cases in our review

Data	Case 1	Case 2	Case 3	Case 4
Age	46	45	50	16
Sex	male	male	male	female
Clinical presentation	Epistaxis	Epistaxis	Unilateral reduced hearing	Unilateral cervical lymphadenopathy
Stage at presentation	III	IV	II	II
Histologic type	Non-keratinizing differentiated carcinoma	Non-keratinizing differentiated carcinoma	Non-keratinizing differentiated carcinoma	Non-keratinizing undifferentiated carcinoma
Management*	CCRT	CCRT	Radiotherapy	CCRT
Progress/ current condition	Recurrence, in Stage IV	Spinal metastasis	In remission	In remission

*CCRT denotes Concurrent chemoradiotherapy; which is a combination of I/V 5-Fluorouracil + I/V Cisplatin with radiotherapy, or, weekly I/V Cisplatin with radiotherapy.

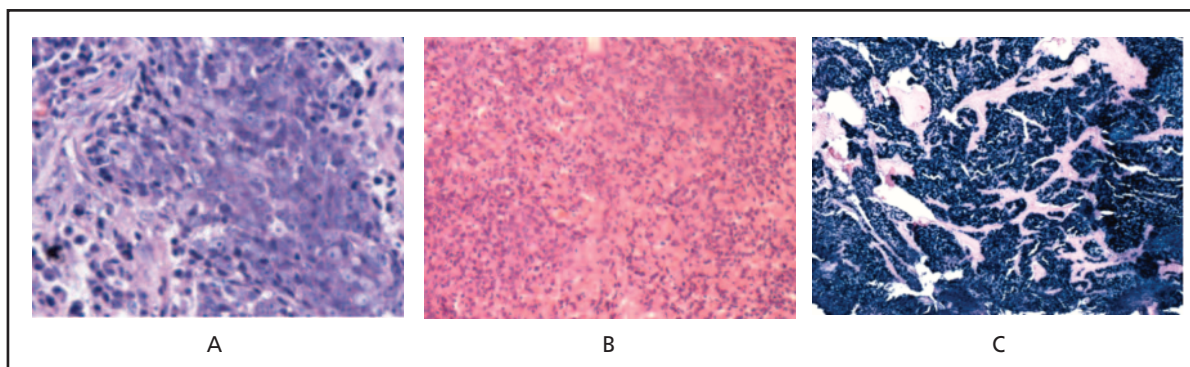


Fig. 1: Histopathological examination of the cases identified in this study: (A) non-keratinizing differentiated carcinoma; (B) non-keratinizing undifferentiated carcinoma and (C) Epstein-Barr virus (EBV) demonstrated by in-situ hybridization for EBV encoded early RNA (EBER) in all the cases.

The pathogenesis of nasopharyngeal carcinoma is indeed thought to be multi-factorial in nature; i.e. an interplay between environmental factors, genetics and Epstein Barr Virus. Risk factors of NPC are the Epstein Barr Virus (EBV), tobacco smoking, and consumption of Chinese-style salted fish. EBV plays a vital role in the pathogenesis of non-keratinizing carcinoma, whereas keratinizing squamous cell carcinoma histological type is the least related to EBV infection among the three different histologies³. In non-endemic areas however, keratinizing squamous cell carcinoma of the nasopharynx has been associated with cigarette smoking and heavy alcohol consumption³.

This short study confirms that all the Indian patients studied had the non-keratinizing type of carcinoma and were consistently associated with a positive presence of Epstein Barr Virus (EBV). The findings are somewhat similar with another study on Indians from South India where NPC is very rare (incidence of less than 1%), in whom Krishna *et al* found EBV infection in sporadic NPC cases of South Indian origin, which confirms the etiological role of EBV in NPC⁴. In this particular study, World Health Organization (WHO) Type III NPC tumour, WHO Type II tumors and WHO I tumors showed 100%, 72.2% and 33% EBV positivity, respectively⁴. Hence it could be extrapolated that the histopathologic typing and EBV association have a similar pattern/incidence among low risk groups and high risk groups.

The combined NPC incidence among Indians in Malaysia in 2003 is 1.2 per 100,000 which is similar to that found in low-risk populations², for example in India it is less than 1 per 100,000 population, except in Nagaland where the incidence is about 4.3 per 100,000 people/year. Compared to India the incidence in Malaysia would have been expected to be higher, if the main cause of NPC was EBV or an environmental factor. The close proximity, shared lifestyle and dietary practices is expected to influence the incidence of NPC among the Indian community if a particular co-factor such as another virus, dietary habit or occupational exposure is responsible for this disease.

Similar observations have been found in other low risk ethnic groups exposed to intermediate and high risk groups. For example; the incidence in Portugal (low risk) is 0.9/100,000, despite the fact that the Portuguese have had a 500 year exposure to intermediate risk North Africans and sporadic exposure to Southeast Asians. Recent dietary habits include high consumption of salted fish and smoked meats, which are all risk factors for NPC. About 6% of the population is involved in occupations (furniture, footwear, textile) exposed to formaldehyde, an oncogenic substance⁵. From the incidence rates among Indians in Malaysia and Portuguese (low risk groups), who have been exposed to high/intermediate risk groups with exposure to common risk factors (diet, formaldehyde etc. and EBV) the incidence is the same as among low risk groups who are not exposed to high/intermediate groups (eg South India, the incidence is less than 1 per 100,000 population).

CONCLUSION

Although, EBV, dietary and occupational factors may be involved in the oncogenesis of NPC, based on the low incidence of NPC observed in Indians in Malaysia, and despite interactions with intermediate and high risk groups, we believe that the crucial factor responsible for NPC is genetics; either a genetic susceptibility among high risk groups or genetic resistance/immunity in low risk groups. Further genetic studies are required to look for somatic or inherited chromosomal mutations among the various risk populations.

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