

FAMILIAL NASOPHARYNGEAL CARCINOMA: A CASE REPORT

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ABSTRACT

Background: The main risk factor for the development of nasopharyngeal carcinoma (NPC) is Epstein-Barr virus (EBV) infection. NPC is rare among Yemeni people while it is common among people of Chinese or some Middle Eastern ethnicity. Of the three histological types, the most globally diffused is the type III or undifferentiated carcinoma. We present a three cases of NPC which occurred in Yemeni brother and sister and cousin aunt's daughter. **Case presentation and clinical discussion:** We present the three cases report with NPC. The significant features are diagnosed in the same period with identical histology; therefore, the prognoses may be similar. Environmental factors could not be addressed in these cases because they shared the same background, and at the same time, they had no potential known contributing factors. Individuals with FH+ of NPC who had undergone EBV-directed investigations, with no restriction in the testing methods or analytic techniques. **Conclusions:** Even if it is rare, NPC can occur among Yemeni patients. EBV-DNA test is useful for diagnosis and post-treatment follow-up.

KEYWORDS: Nasopharyngeal carcinoma, Epstein-Barr virus, Yemen, Lymph nodes.

INTRODUCTION

Nasopharyngeal carcinoma (NPC) is the seventh most common type of cancer in Yemen. The poor outcome most commonly affects patients in the economically active age groups, with 50% of patients being between 41 and 60 years of age.^[1] Most patients with NPC have stage III or IV disease.^[2] Radiation, the key to disease-free survival rates, is early detection. The results and studies show a good correlation between disease stage and 5-year survival rates.^[3,4] The result is that an improvement in 5-year survival rates would be expected if more patients were diagnosed with the disease at an early stage would.

Epstein-Barr virus (EBV) infection is considered the most important risk factor for the development of nasopharyngeal carcinoma (NPC), which is a malignant neoplasm diffused mostly in some geographical areas (mainly among Greenland natives, Middle-Eastern and Eastern Asian people). Of the three different types of NPC recognized by WHO, the most globally diffused (around 95% of all diagnosis) is the type III or undifferentiated non-keratinizing cell carcinoma (type III)^[5]. We report a case of three nasopharyngeal carcinoma cases occurred in one family.

This study was performed to characterize our NPC patients who have affected first-degree relatives.

CASE REPORT

Case 1: In July 2020, 38 years old female was admitted to National Oncology Center, Aden. She was non-smoker and complain of severe headache since six months and deteriorated with cervical lymphadenopathy and gradual deterioration of vision which complicated with atrophy of right eye and complete blindness. At the same period started similar complains with her brother and cousin. The worthy of attention was family history of death of her father and father of cousin with similar manifestations.

EBV-VCA IgG and EBV-DNA were positive in all 3 cases

Brain and neck CT scan in 11/7/2020 showed large enhanced soft tissue mass rarified the overlying skull bone with intracranial extension (10x5x4cm) in dimensions. It infiltrates the right temporal lobe, right cavernous sinus and right optic nerve and abuts the brain stem, it results in right temporo-parietal deep white matter vasognial oedema, intracranial mass effect and increased intracranial pressure. Multiple bilateral markedly enhanced deep cervical enlarged LNs.

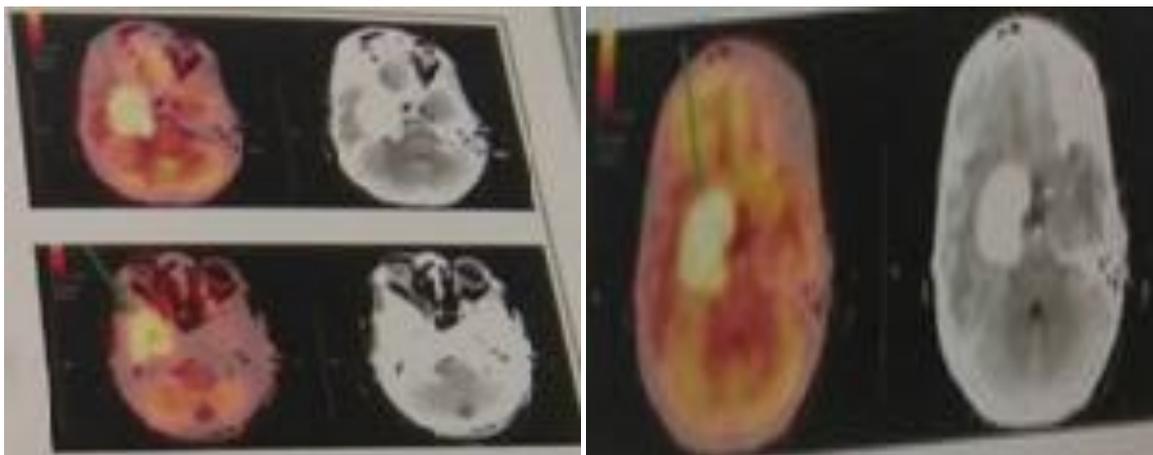


Figure 1: Brain and Neck scan.

Histopathology report: Nasopharyngeal mass, Biopsy: Non-keratinizing nasopharyngeal carcinoma, undifferentiated type.

Blood investigations: CEA 3.7, B2M:2.2, EBV-VCA IgG and EBV-DNA were positive.

Chemotherapy started on 16/7/2020 with (TIP) Paclitaxel (220 mg), Ifosfamid (1300mg), cisplatin (70mg).

In evaluation post chemotherapy by CT scan: The process is regressing, evidenced by decreased tumor size as well as decreased size and number of deep cervical, intracranial mass effect and intracranial pressure is evidently decreased. CEA: 3.0 ng/ml, then she continue 3 cycles of the same treatment and followed by radiotherapy.

In evaluation by PET SCAN 25/4/2021: Status follow up regression course of the disease compared to last examination date 27/1/2021

Follow-up by MRI on 28/7/2021: Regressive course regarding the nasopharyngeal mass and right intracranial component.

The second case is the brother male 35 year old confirmed as undifferentiated nasopharyngeal carcinoma. He started chemotherapy and completed 6 cycles of CTH.

In evaluation by PET scan and compared to previous scan 15/12/2020

Excellent response to therapy with near total resolution of the metabolically active neoplastic large ill-defined heterogeneously enhanced soft tissue mass lesion infiltrating nasopharynx with resolution of the previously seen encroachment upon the air column and relieved pressure changes upon right Eustachian tube with resolution of the detected right otomastoiditis as well as resolution of the previously seen obliterated fossa of Rosenmüller, bilaterally. Remarkable resolution of FDG uptake detected by rarefaction of the clivus, also there is resolution of the encroaches upon the right parapharyngeal fat planes. The FDG uptake detected by the rarefaction of the right pterygoid plate.

Marked regression of its creeping component through right posterior nares was noted with residual small sheet measuring about 1.3 cm with SUV max 5.3 compared to SUV max 10.3 in the prior study. The patients die in 8/6/2021 due complication with viral infection.

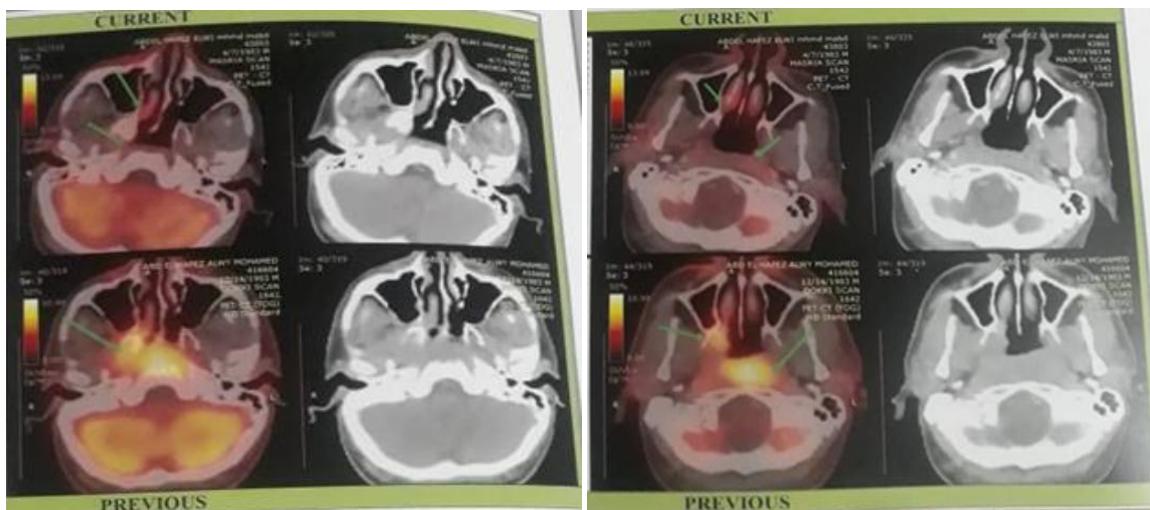


Figure 3: CT scan case 2.

Third case: Cousin 35 year old female complain of nasal obstruction, CT scan of head and neck showing left nasopharyngeal mass 3.5x2.5 cm. Nasopharyngeal biopsy on March 2021 showing undifferentiated carcinoma.

PET scan March 2021: Showing positive study for metabolically active left nasopharyngeal mass lesion 4x4.7 cm with metabolically active UDCLN 3X3 cm. She started radical concurrent chemo radiotherapy. She received radical IMRT a dose 70 Gy/35/7 w to the nasopharyngeal lesion and bilateral neck nodes concurrent with high dose platinum every 3 week for 3 cycles in the period from 20/3/2021 to 11/5/2021. Follow up endoscopy was done on 29/6/2021: showing no evident residual disease.

DISCUSSION

The etiology of NPC is multifactorial. Epstein-Barr virus (EBV) infection, genetic predisposition and environmental factors such as tobacco consumption and high intake of preserved food are suspected in etiology. EBV is thought to be the primary etiologic agent in the pathogenesis of NPC. In endemic areas of NPC EBV screening has been used for population-based screening.^[6]

In this presentation there is associated causative factors include infection with Epstein-Barr virus and an underlying genetic predisposition. This study clearly shows the existence of familial NPC, defined as NPC occurring in at least 3 first-degree relatives. The specific genetic factors that are responsible for the association with NPC remain unanswered. If genetic factors do play a role in NPC, then it would be prudent to maintain surveillance of first-degree relatives of affected patients. First-degree relatives of NPC patients are at a higher risk of developing the disease.

A link between EBV and NPC was first suggested in 1966 when it was reported that NPC patients had a greater antibody response to an antigen later shown to be a product of EBV.^[7] Since then, there has been ample evidence that EBV is a possible cause of NPC, particularly Type III. The hypothesis is considered that very early exposure to EBV and other carcinogens might play a role in the pathogenesis of NPC. Studies of family structure in early childhood can shed light on whether the timing of initial EBV infection is associated with later risk of NPC infection.

There are around 30 copies of the EBV gene in the nucleus of malignant cells. Most copies show the presence of "small circular chromosomes" called loops or episomes. These episomes are in some cases located adjacent to viral DNA releases. Serological and virological tests are recommended for diagnosis and screening of populations at risk. In regions with an increased incidence of nasopharyngeal cancer such as China and Yemen, high levels of IgA antibodies to EBV

capsid antigen and Epstein-Barr antigen are a valuable screening test or new predation model that VCA/IgA and EBNA1/IgA combined and will improve prognosis of NPC can identify populations at high risk for developing NPC.^[8]

According to previous studies, it is known that families with a history of cancer, particularly nasopharyngeal cancer, are 5 to 10 times more likely to develop nasopharyngeal cancer. Some previous studies confirmed that family clusters are stable in areas with high NPC incidence^[9] and in areas with low to moderate incidence.^[10] In southern China, where NPC is endemic, more than 5% reported an NPC with a positive family history for NPC in cases with a first-degree family history.^[11]

It is generally accepted that the treatment of locally advanced squamous cell carcinoma of head and neck cancer (SCCHN) should involve a combined modality approach. Surgery and/or radiotherapy is the main definitive of therapy in patients with locally advanced SCCHN. Induction chemotherapy followed by concurrent chemoradiotherapy is a promising treatment in these cases.

The results of many phase III trials^[12-13] show that adding taxane (T) to the standard cisplatin and 5-FU regimen improved the overall survival rate and led to better organ preservation over a PF regimen. A phase II study combining paclitaxel, ifosfamide and cisplatin (TIP) to treat recurrent and metastatic SCCHN produced a high overall response rates (54%) including prolonged duration of CR and encouraging one-and two-year median survival rates.^[14]

As an induction chemotherapy for locally advanced head and neck cancer, a phase II study combining paclitaxel, ifosfamide and carboplatin resulted in a high overall response rate of approximately 80%.^[15] Based on the demonstrated activity of this triplet regimen in SCCHN and their non-overlapping toxicity profiles, the combination was promising.

Response after concurrent chemoradiotherapy

The two female completed their 6 cycles of induction chemotherapy were treated with concurrent cisplatin and radiotherapy. All of them completed the whole treatment planned. There were achieved a complete clinical response at the tumor

Individuals identified as being at high risk of NPC based on EBV serological markers can be offered fiberoptic endoscopy/biopsy and close medical surveillance to enable early diagnosis of NPC and, ideally, reduced mortality. However, the cost-effectiveness of this labour-intensive strategy has yet not been proven, and new biomarkers are needed to more specifically identify the high-risk population, in order to provide screening for NPC in the general population.

CONCLUSION

NPC is a common health problem in Yemen and should be taken into account further research to determine the risk factors associated with nasopharyngeal cancer.

Conflict of Interests

The Authors declare that they have no conflict of interests.

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