Nasopharyngeal carcinoma in a Cameroonian girl, a rare tumour in Central Africa: case report and review of literature

Case Report
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Received: November16th, 2011
Accepted for Publication:
December 16th, 2011

ABSTRACT

Nasopharyngeal carcinoma is the most common malignancy of the nasopharynx. It arises from the mucosal epithelium of the nasopharynx, predominantly the Fossa of Rosenmüller. In most parts of the world, it is relatively rare, but in Asian countries where salted smoked fish containing nitrosamines is popularly consumed, it is one of the more common cancers. This work reports a case of nasopharyngeal carcinoma, a rare tumour in Central Africa, in a young Cameroonian girl, and we posit that possibly, an increasing consumption of smoked fish could trigger an increasing incidence of nasopharyngeal carcinoma in Africa as obtainable in Asia.

Keywords: *Carcinoma, magnetic resonance imaging, nasopharynx*

INTRODUCTION

The nasopharynx (NP) is the upper part of the pharynx, a passageway from the nose to the trachea and eventually, to the lungs. The anatomy of the NP is complicated and accurate interpretation has remained a challenge.[1] The advent of magnetic resonance imaging (MRI), with good tissue contrast and multi-planar capability, allows for greater sensitivity and specificity in the study of the NP.[1]

The imaging anatomy of the adult NP consists of a convex forward margin on either side of midline.[2] Directly posterior to the nasopharynx is the retropharyngeal region, longus colli muscles, pre-vertebral space and clivus.[3] Just lateral to each muscle contour is the most postero-lateral recess of the NP (Fossa of Rosenmüller).[2,3] Anterior to each fossa is a soft tissue prominence called *torus tubarius* which contains the cartilaginous portion of the Eustachian tube and *levator veli palatini* muscle. Anterior to the *torus*, between it and the posterior margin of the medial ptyerigoid plate, is the opening of the Eustachian tube. Just lateral to this opening, arising from the pterygoid fossa between the medial and lateral pterygoid plates is the *tensor veli palatini*.[2]

Contrast enhanced computed tomography (CT) or MRI shows the mucosal lining as always intact, and in children and adolescents, hyperplastic adenoidal tissue lies superficial to this mucosa in the roof.[4] In the very young, reactive retropharyngeal lymphadenopathy is also commonly seen.[2]

The NP lies just above the soft palate of the roof of the mouth, posterior to the nasal

fossa and inferior to the sphenoid sinus and base of skull, resting on and protected by the pharyngobasilar fascia.[5] Lateral to it are para-pharyngeal spaces and infra-temporal fossa.

Benign tumours of the NP are usually vascular malformations like angiofibroma, haemangioma and tumours of the salivary glands, whereas malignant tumours include lymphoma and adenoid cystic carcinoma arising from minor salivary glands. Nonetheless, the most common primary malignancy is nasopharyngeal carcinoma (NPC) which arises from the mucosal epithelium and accounts for approximately 70% of all primary NP malignancies.[6,7] The Fossa of Rosenmüller is the most common site of NPC.[3,6,8]

Nasopharyngeal carcinoma was first described as a separate entity by Regaud and Schmincke in 1921.[2] In most parts of the world NPC is relatively rare with an age adjusted incidence rate of 1 per 100,000.[9] However, few pockets of high prevalence are found in certain regions of the world like Asia (Southern China, Taiwan, Hong Kong, Singapore and Malaysia), North Africa, Greenland and Alaska.[5,9,10]

Tumours may invade the anatomical sites surrounding the NP and being a relatively, clinically silent region, patients often do not present until late, when the tumour would have spread into deep tissues or lymph nodes in the neck.[8,3] The NPC is distinct from other malignancies of the head and neck in its subtle clinical presentation, aggressiveness, epidemiology, genetic bias, immuno-histologic behaviour and multi-disciplinary management.[11,12]

AIM/OBJECTIVE

The objective of this publication is to report a case of a young Cameroonian girl, with nasopharyngeal carcinoma, which is a rare and non-endemic tumour in Central Africa.

CASE REPORT

A 24-year old female Cameroonian student presented with a 1-year history of difficulty in breathing through the left nostril, which got worse in the 2weeks prior to presentation. There was a previous history of occasional bilateral epistaxis but there was no similar family history. Physical examination showed bilateral cervical lymphadenopathy with no evidence of cranial nerve deficits. Serological tests were declined by the patient on account of lack of funds.

Brain MRI revealed a 24x29x49mm moderately enhancing nasopharyngeal mass with a left epicentre and obliteration of the Fossa of Rosenmüller (Figures 1 and 4). Axial and coronal MRI (Figures 1 and 3) showed an extension into the left parapharyngeal space and medial left infra-temporal fossa respectively. The T2W images (Figure 4) revealed hyperintense collections in the left posterior choana, left Eustachian tube and left mastoid (mastoiditis). Neck echography revealed bilateral cervical lymphadenopathies measuring 30mm in widest diameter. Skull radiography showed enlarged left inferior turbinate and narrowed nasopharyngeal space, whereas chest radiography and abdomino-pelvic echography revealed nothing contributory.

A clinical diagnosis of stage 4A nasopharyngeal carcinoma was made. The histological diagnosis was Type 111 (undifferentiated) nasopharyngeal carcinoma, stage 4A. Endoscopically-guided biopsy was done and the histology report confirmed the diagnosis of nasopharyngeal carcinoma.

The patient had radiotherapy combined with chemotherapy, yielding a good tumour regression. The adjuvant chemotherapy consisted of vincristine, cyclophosphamide and adriamycin.

Figure 1. Axial post-contrast T1 weighted MRI showing the nasopharyngeal tumour infiltrating the left parapharyngeal space

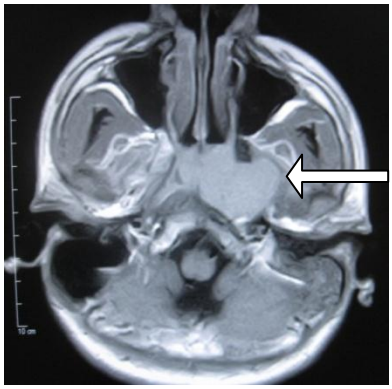


Figure 2. Sagittal T1 weighted MRI showing the nasopharyngeal tumour with inferior extension, crossing the C1/2 level, along the posterior wall into the oropharynx. Note the posterior choanal extension and turbinate enlargement

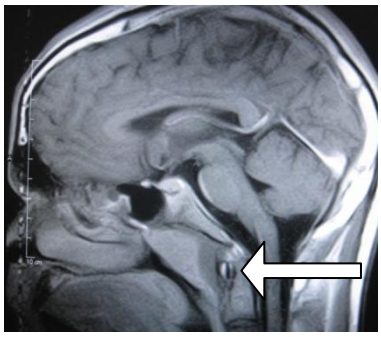


Figure 3. Coronal post-contrast T1 weighted MRI showing the tumour with direct infiltration into the left infratemporal fossa

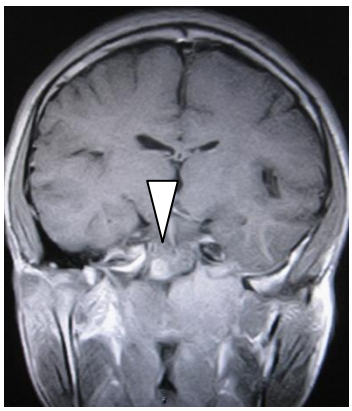
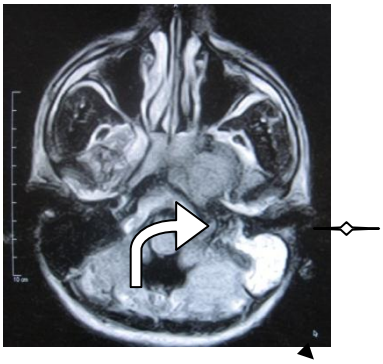


Figure 4. Axial T2 weighted MRI showing the tumour infiltrating the left retro-pharyngeal space with obstructive effusion in the left mastoid sinus



DISCUSSION

Eighty-two percent of NPC arise from the Fossa of Rosenmüller, 12% from the midline; 6% of them have normal NP mucosa on endoscopy.[13] The World Health Organisation (WHO) classified NPC into three histopathological subtypes, namely:

(a) *Type I*: keratinizing squamous cell carcinoma
(b) *Type II*: non-keratinizing squamous cell carcinoma
(c) *Type III*: undifferentiated carcinoma.[2,6,7,14]

Type 1 represents well differentiated keratinised squamous cell carcinoma (SCC); type 11 is moderately differentiated non-keratinising carcinoma; and 111 is the undifferentiated type which typically contains a lot of inflammatory cells like lymphocytes, hence the name lymphoepithelioma. However, more than one histological type could co-exist in 26% of cases.[2] Types II and III can be considered together as undifferentiated carcinoma of the nasopharyngeal type (UCNT).[7]

The histological types may be of prognostic significance with UCNT having a higher local control rate after treatment with radiotherapy than SCC.[7] Risk factors are varied depending on the histologic types. Type I can be thought of as a head and neck squamous cell carcinoma, located in the nasopharynx.[6] Its biological behaviour is similar to that of the latter and it shares the same risk factors, namely smoking and alcoholism.[6]

Types II and III on the other hand are strongly associated with the ubiquitous Epstein-Barr virus (EBV) infection and are seen particularly in Asia.[6] Similar viral associated cancers are seen in the cervix and salivary glands.[15] The immunoglobulin IgA against EBV capsid antigen and the neutralizing immunoglobulin IgG antibody against EBV DNAase are highly specific markers for NPC.[16] For example, the cumulative risk of NPC per 100,000 per year is 11.2 for subjects who tested positive for neither serological markers, whereas it is 45 for those who had one marker, and 371 for those who had both markers.[16]

Additional risk factors for NPC include consumption of salted fish and meat (particularly in childhood), rancid butter and genetic predisposition in family members.[14,17,18,19,29,21,22] In indigenous Chinese populations who reside in Hong Kong, Taiwan and Macau, the tumour type is usually a non-keratinizing undifferentiated carcinoma (Type III) due to the aforementioned risk factors.[14,23,24]

Epidemiological differences in NPC are a multi-factorial interplay of genetics, viral, dietary and environment.[2,7,10,11,17,15] The Chinese that migrated to Western countries have lower NPC incidence rates than those in Asia, but their rates remain higher than those of white populations in Western countries due to genetics.[14] Clusters have been reported with genetic susceptibility with HLA A2, HLA B17, HLA W46 among Asians predisposing them to high risk.[2] In our index patient, a familial link could not be established but smoked fish was a regular component of their family menu.

Nasopharyngeal carcinoma can occur in any age group, but most commonly, it occurs in patients between 40-60years of age with bimodal peaks occurring in the second and sixth decades.[3] It is seen in middle age in Asia but a high proportion of African cases occur in children of 10-19years. Our patient is in her early twenties, not far from the African age range. Male to female ratio of NPC is 2.5-2.9 to 1.[1] In China, NPC is the third most common malignancy amongst men.[7]

Nasopharyngeal carcinoma is locally aggressive, making adjacent structures like the posterior nasal cavity, Eustachian tubes, soft palate, skull base, cavernous sinuses, cranial nerves and paranasal sinuses vulnerable to invasion. Thus, usual clinical presentations are nasal obstruction, anosmia, epistaxis, nasal quality to voice, serous otitis, conductive hearing loss due to Eustachian tube obstruction, middle ear effusion, cranial nerve palsies especially V and V1, headache, tinnitus, diplopia, proptosis and Pseudo-Gradenigo syndrome.[6,11,13,20,21.]

Actual presentation may be delayed until more sinister signs are evident. The most common presenting symptom is cervical lymphadenopathy seen in 75-90% of cases at the time of diagnosis (as in our patient).[2,3,6,7]

The diagnosis of NPC includes clinical evaluations of primary tumour/cervical lymphadenopathy, neurological examination of cranial nerves, immunology, nasopharyngoscopy, radiological evaluations and histopathology. Serological assay is EBV viral capsid antigen (sensitivity 81%–93% and specificity 80%–96%) and EBV DNAase antibody assessment especially for high risk patient.[2,4] The recent widespread use of serological testing in high risk patients with a family history of NPC is leading to early tumour detection.[4,5]

The diagnosis of NPC is initially made by endoscopy and confirmed on endoscopically-guided biopsy (EGB).[3,4] The biopsy is facilitated by direct visualization of the nasopharynx with a fibreoptic nasopharyngoscope. Our patient had endoscopic examination of the nasopharynx along with a biopsy and histology.

Computed tomography or MRI assessment of the NP and the skull base should be undertaken before the biopsy.[7] But MRI is preferable due to its superior soft tissue contrast and potential for detecting submucosal disease despite normal overlying mucosa.[6] Apart from the histological diagnosis, accurate radiological staging of the disease is crucial in pre-treatment planning and prognosis.[1,7]

Defining the exact extent of a primary tumour, skull base erosion, early intracranial spread, regional nodal metastasis and perineural infiltration is best done by MRI, and it also delineates the blood vessels clearly even without the use of intravenous contrast.[7,8] With its excellent soft tissue contrast resolution and multi-planar imaging capability, MRI ensures a direct visualization of smaller nerves and nerve branches, making it a valuable tool in detecting and defining the extent of involvement of the trigeminal, abducent and facial nerves in NPC.[1,3,8] Typically, MRI findings of NPC are isointense to muscle on T1W, and isointense to somewhat hyperintense to muscle on T2W.

Accurate staging is important for treatment planning and long-term survival.[1] Head and neck CT and MRI could be used to stage the primary and nodal NPC, but MRI is preferred because it is superior in terms of delineating small anatomical structures that make up the boundary of the nasopharynx, mapping tumour extent and discriminating between the primary tumour and adjacent retropharyngeal nodes.[5,8] The best MRI combination protocol which provides sufficient information to achieving almost 100% diagnostic accuracy in T-staging of NPC is a combination of contrast enhanced fast saturation axial T1 and non-enhanced axial T1.[1]

This tumour is highly responsive to treatment with a good prognosis when identified at an early stage.[24] It has always been distinguished from cancers of other sites on the head and neck by its relatively higher radio-curability even in patients with advanced disease.[7,12] High loco-regional control for NPC has been achieved with multi-segmental intensity-modulated radiotherapy.[12]

Treatment is the same for all NPC as the presence of lymphocytes in type III (lymphoepithelioma) does not usually affect the choice of treatment options but may be a clue to a new treatment development. Even though undifferentiated NPC is highly radiosensitive, differentiated NPC are known to be less radiosensitive. Adjunctive chemotherapy has shown some promise in improving tumour control and possible survival with advanced NPC.[12] While radiotherapy alone is employed for early stage NPC, radiotherapy and cisplatin-based chemotherapy is the current standard treatment for advanced NPC.[7,12,18] Cisplatin acts both as a cytotoxic agent and radiosensitizer[13,24] Disease-free survival rises from 42% (radiotherapy) to 69% (radiotherapy and chemotherapy) and overall survival rises from 48% to 69%, respectively.[1,2.] Little wonder the favourable response to the combined modality by our patient.

Painfully, though NPC carries an excellent prognosis if treated early, treatment failure occurs due to metastasis.[12,23] Poor prognostic factors are WHO Type II histology, T4 classification, para-pharyngeal extension, clivial involvement, metastasis and lactate dehydrogenase > 4100/L.[7,14,23,14] Circulating EBV-DNA has been shown to improve prognostication and monitoring of NPC patients during radiotherapy and chemotherapy as well as assist in early detection of tumour recurrence.[10] Advanced-stage NPC patients have higher plasma EBV-DNA levels than tumours with early-stage disease.[7] More effective chemotherapy regimens and other systemic agents could decrease the rate of distant metastasis.[12]

CONCLUSION

Nasopharyngeal carcinoma, which origin has interplay of genetic, viral, dietary and environmental factors, is rare in Central Africa. Its prevalence could rise with an increasing consumption of smoked fish and increasing availability of modern imaging tools, the latter serving only to improve the diagnostic yield from the anatomically inaccessible sites.

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