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Case Report

Nasopharyngeal carcinoma presenting as proptosis in a child: a diagnostic dilemma

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ABSTRACT

Nasopharyngeal carcinoma (NPC), although rare but does occur in pediatric age group and can present with variable non-specific signs and symptoms. The objective of this report is to emphasize that, because of its rarity, it is not clinically suspected and kept in differential diagnosis of nasopharyngeal mass in children, leading to delayed diagnosis and significant therapeutic implications. We hereby, describe a case of 10 year old boy who presented with bilateral cervical lymphadenopathy and simultaneously developing proptosis of the left eye, which is one of the important rare manifestation of NPC, that creates a diagnostic challenge.

Keywords: Pediatric, Nasopharyngeal carcinoma, Rare, Proptosis, Dilemma

INTRODUCTION

Tumors of pediatric age group are rare.[1] Among them, the spectrum of head and neck tumors continues to be the cause of diverse clinicopathological dilemma. Most of the head and neck masses which occur in childhood are benign in nature. However, neoplasms of the head and neck account for approximately 5% of all childhood malignancies.[2] NPC is a common malignancy in adults but pediatric NPC is uncommon and is distinguishable from the adult form by its close association with Epstein-Barr Virus (EBV) infection, a higher rate of undifferentiated histology, a greater incidence of advanced locoregional disease and metastasis. 95% cases of pediatric NPC present with cervical lymphadenopathy, nasal, aural or neurological symptoms.[3] Ophthalmic presentation as an initial symptom of NPC is unusual and rare.[4] The present case highlights that NPC does occur in children and can mimic other more common pathologies occurring in children. Therefore, the diagnosticians and treating physicians should always keep NPC in the differential diagnosis of all nasal masses in pediatric age group patients.

CASE REPORT

A 10 year old male child presented in outpatient department with chief complaints of gradually developing non-painful protrusion of the left eyeball since last eight months and bilateral cervical swellings with on and off episodes of nasal bleed/discharge since last six months. He also gave history of headache and bilateral ear discharge since last ten days. On inspection of neck, right cervical swelling measured 3x2 cm and left measured 5x4cms in size. On palpation, they were non-tender and the consistency was soft to firm. A clinical diagnosis of lymphoma was entertained. Fine Needle Aspiration Cytology (FNAC) smears of bilateral cervical swellings were highly cellular and showed undifferentiated malignant cells predominantly in clusters and few scattered singly in the background of lymphoid cells and few plasma cells. The individual tumor cells were large round in shape with large vesicular nuclei and prominent

central nucleoli. The cytoplasm was variable in amount, pale and fragile. No evidence of keratinisation was seen. Based on these features a diagnosis of a metastatic poorly differentiated malignant epithelial tumor or a lymphoma was suggested and immunocytochemistry (ICC) was performed. On ICC, the cells were positive for cytokeratin (CK) and negative for leukocyte common antigen (LCA), CD-30, CD-99, Desmin, Vimentin, HMB-45 and S-100. A cell block was also made. Histopathology of cell block revealed features of undifferentiated tumor which showed CK positivity and LCA negativity, on immunohistochemistry (IHC). Based on morphology, ICC and IHC, possibility of metastasis from a malignant poorly differentiated epithelial tumor was kept and of lymphoma was ruled out. Following this, a detail clinical workup was advised to find out the primary.

Ophthalmic examination, revealed moderate proptosis of the left eye but the eye movements in all directions of gaze were full and free for both the eyes. The visual acuity of both the eyes was 6/6. Tonometry and fundoscopy were normal. Bilateral ear examination, revealed central perforation of the tympanic membrane with clear watery discharge. Oral cavity and oropharynx were unremarkable, though there was slight restriction to the movement of mandible on the left side. On examination of the nose, the nasal septum was deviated towards right side and an irregular mass measuring 3x2 cm was seen in the left nasal cavity. It was difficult to pin point its exact origin. Thus, an ultrasound (USG)/Contrast Enhancement Computed Tomography (CECT) Head & Neck was done. USG neck showed multiple heterogeneously enlarged bilateral cervical lymphnodes with evidence of conglomeration in few of them. Thyroid, submandibular and parotid glands were unremarkable. CECT Head & Neck revealed a large destructive heterogeneously enhancing poorly defined mass in the roof of the nasopharynx, more on the left side and extending into both the nasal cavities and upto the anterior nares. The medial wall of left orbit was disrupted and the mass was bulging into the left orbit, resulting in left eye proptosis. Multiple bilateral enlarged nodes were also seen involving multiple nodal chain. A sclerotic lesion was also noted in C6 vertebral body. Based on the above findings, possibility of an epithelial malignancy with nodal and skeletal metastasis or a lymphoma was considered. His haematological and biochemical parameters were within normal limits. As the lesion was deep seated, FNAC was not possible and a excisional biopsy was done from the nasopharyngeal mass. Histological sections showed features of undifferentiated nasopharyngeal carcinoma, which further confirmed our cytological diagnosis. This was further confirmed on IHC. The tumor cells were positive for CK and negative for LCA, CD-30, HMB-45, Desmin, Vimentin, CD-99 and S-100. Based on the morphology, CK positivity and LCA negativity, radiological findings, a final diagnosis of nasopharyngeal carcinoma with bilateral nodal and skeletal metastasis was made.

Despite external radiotherapy and adjuvant chemotherapy, over a period of next three months, his condition deteriorated and he died of respiratory complications.

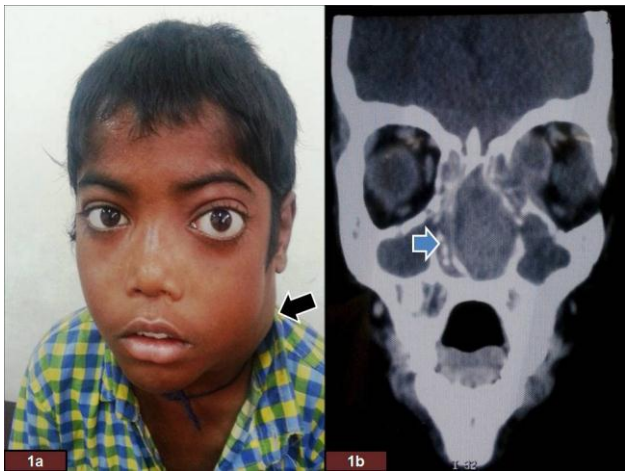

Figure 1: a) Cervical swelling and left eye proptosis on clinical inspection. b) CECT neck revealing heterogeneously enhancing, infiltrating mass arising from the roof of the nasopharynx and disrupting the medial wall of the left orbit.

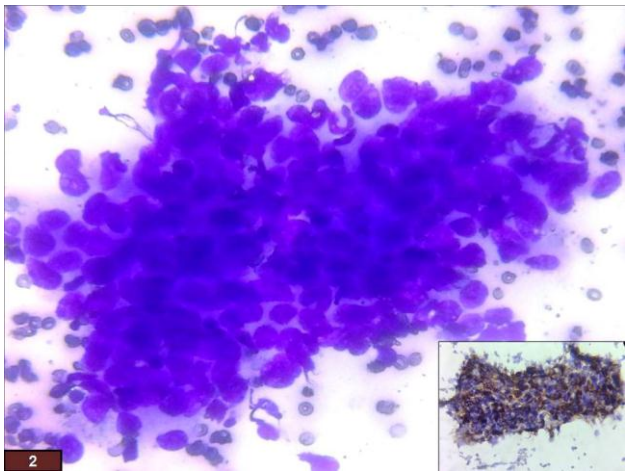

Figure 2: Photomicrograph of cytological smears showing large cells with vesicular nucleus and prominent nucleoli (Giemsa, 40x). Inset: On immunocytochemistry, the cells show cytokeratin positivity (ICC, 10x).

DISCUSSION

NPC is one of the commonest epithelial malignancy of head and neck region, in adults. It varies diversely according to its epidemiology and etiopathological factors, which play an integral part in its occurrence. The incidence of NPC is low in most part of the world (an Age-Adjusted Rate (AAR) of less than 1 per 100000 people). The rates are twice as high in males as in females. However, the incidence of the disease is higher in certain population and geographical regions of the

world. It is more prevalent in South East Asian countries (highest AAR of ~20/100 000 among Cantonese/Zhongshan dialect Chinese), parts of North Africa and the Arctic. In India, NPC has a low incidence (AAR = 0.5/100000 to 2.0/100000), except for the Hill States of Northeast India (Nagaland, Manipur, and Mizoram) where the AAR is19.4/100000.[5] There are also various etiological factors which play an important role in NPC like Epstein-Barr Virus (EBV) infection, genetic susceptibility, exposure to environmental carcinogens.[6]

Benign adenoidal hypertrophy is the most common cause of a mass in the posterior nasopharynx in children. Malignant tumors of the nasopharynx are rare in this age group and the histology generally varies with the age of the patient at presentation. Sarcomas and lymphomas are more common in younger children, whereas pediatric NPC, is an extremely rare malignancy, accounting for 1-3% of all pediatric malignancies and constitutes 20-50% of all NPC. It is very uncommon in children younger than 10 years but increases in incidence to 0.8 and 1.3 per 1 million per year in children aged 10 to 14 years and in children aged 15 to 19 years, respectively.[8]

Since NPC is so rare in pediatric population and there is paucity of data on it in India, therefore the exact incidence of pediatric NPC in India, has still not been estabilished or known. Therefore, high index of suspicion is required by all diagnosticians in detecting this malignancy which can present with varied signs and symptoms.[9]

The diagnosis of pediatric NPC often produces clinicopathological dilemma since it is more aggressive biologically and often presents at an advanced stage. Late diagnosis in the NPC is because of ignoring or misdiagnosing the unspecific symptoms mimicking upper respiratory tract infection during early stages.[6]

NPC usually originates in the lateral wall of the nasopharynx, which includes the fossa of Rosenmuller. It has a great propensity to spread and infiltrate into adjacent tissues. It can extend to the other lateral wall and/or posterosuperiorly to the base of the skull or the palate, nasal cavity, paranasal sinuses, oropharynx, pterygopalatine fossa and apex of orbit. Then, it can typically spreads to cervical lymph nodes, owing to the rich lymphatic drainage of nasopharynx. Distant metastases may occur in bone, lung, mediastinum and, more rarely, the liver.[10]

Cervical lymphadenopathy, especially at posterior triangle of neck, in most of the cases is its initial clinical manifestation. Other symptoms related to it are trismus, pain, otitis media, nasal regurgitation, hearing loss and cranial nerve palsies. Larger growths may produce nasal obstruction or bleeding and a “nasal twang”. Metastatic spread may result in bone pain or organ dysfunction. Ocular and/or orbital manifestations of NPC include ocular motility problems (cranial nerve involvement), blurred vision, proptosis, diplopia, orbital pain, chemosis, eyelid swelling and optic disc oedema. Most cases presented with nasal and/or aural symptoms prior to ocular or orbital manifestations.[11] NPC presenting with proptosis as a major symptom is a uncommon presentation in children and should raise a suspicion.[11,12]

NPC with orbital invasion, however, is rarely reported in the literature. NPC is a highly infiltrative tumor and can invade the orbit via several routes. The pterygopalatine fossa and inferior orbital fissure are the most common routes of invasion, followed by invasion via the paranasal sinuses. The inferior orbital fissure represents a direct communication between the orbit and infratemporal fossa. Its most posterior part also meets the most superior extension of the pterygopalatine fossa, thus forming direct communication between the pterygopalatine fossa and the apex of the orbit. NPC involving the pterygopalatine fossa and infratemporal fossa may thus infiltrate directly into the orbit through the inferior orbital fissure. On the other hand, tumors in the ethmoid and/or sphenoid sinuses may erode the lamina papyracia to reach the medial orbital wall and retrobulbar region. On rare occasions, NPC involving the maxillary sinus may invade the inferior orbit via the floor of the orbit. As the lamina papyracia and the orbital floor are thin, they are relatively weak barriers for protecting against tumor infiltration.[13] Direct invasion of the orbit, however, is relatively rare in NPC patients. Orbital involvement from NPC is seen in 3.2% of cases.[12]

Diagnostic evaluation of NPC is done by multidisciplinary team approach which is done by various methods which not only determine the extent of primary tumor but also the presence of metastasis. The most important is the clinical evaluation of the size and location of cervical lymph nodes. Others are indirect nasopharyngoscopy to assess the primary tumor, FNAC of the nodes, ICC, cell block , neurological examination of cranial nerves, CT)/MRI scan of the head and neck to below clavicles to assess base of skull erosion, chest radiotherapy (anteroposterior and lateral), bone scintigraphy by Tc99 diphosphonate to show whether cancer has spread to the bones, full blood count, kidney and liver function tests, detection of plasma levels of EBV viral capsid antigen and EBV DNA followed by biopsy of either the lymph nodes or primary tumor for histological examination and IHC.

NPC must be distinguished from other cancers that can present with enlarged lymph nodes or can present in the head and neck area. These include conditions like thyroid cancer, rhabdomyosarcoma, Non-Hodgkin lymphoma, Hodgkin lymphoma, and Burkitt’s lymphoma, benign conditions such as benign hypertrophy of adenoids, nasal angiofibroma, which usually presents with epistaxis in adolescent males, and infectious lymphadenitis.[8]

Standard therapy for NPC in children has generally followed the guidelines established for adults,

irrespective of orbital involvement or distant metastasis, which consists of combined modality therapy with high-dose radiation to nasopharynx and involved cervical node areas as well as moderate doses to uninvolved cervical node sites along with chemotherapy. Although high-dose radiotherapy in children can be curative it has been associated with rare but significant morbidity among long term survivors like late endocrine effects manifested by stunted growth, thyroid dysfunction, and soft tissue fibrosis, bone, dental problems and secondary malignancies.[14] Few studies utilizing preradiation chemotherapy with different combinations of methotrexate, cisplatin, 5-fluorouracil, and leucovorin with or without recombinant interferon-beta have been reported, which showed a good response rate.[15] Surgery has a limited role in its management because the disease is usually considered unresectable due to extensive local spread. Now a days, the use of EBV-specific cytotoxic T-lymphocytes has shown to be a very promising approach with minimal toxicity and evidence of significant antitumor activity in patients with relapsed or refractory nasopharyngeal carcinoma.[16] Distant metastasis remains the major pattern of failure in NPC. Poor prognostic factors for NPC are skull base involvement, extent of the primary tumor and cranial nerve involvement.[10] Though, the presentation with lymphadenopathy implies that the disease has spread beyond the primary site. However, in childhood the presence of metastatic disease in cervical lymph nodes at diagnosis does not adversely affect prognosis. In our case, the child died within three months despite of extensive chemoradiation.

CONCLUSION

Pediatric NPC, though uncommon, should always be kept as a differential diagnosis in a case of cervical swellings and proptosis in a child. A prompt careful evaluation should be carried out in all the children presenting with these symptoms so as to hasten the treatment and prolong their survival.

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