Nasopharyngeal carcinoma: Imaging features of unusual cancer in children

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Abstract  Background: Nasopharyngeal carcinoma (NPC) is a disease of elderly population while the benign adenoidal hypertrophy is the most common cause of a mass in the nasopharynx in pediatrics. NPC is rare in this age group, unfortunately, these tumors tend to be locally advanced by the time they are diagnosed. Our objective is to emphasize that, although rare, NPC does occur in children and can be diagnosed reliably when certain key radiographic features are recognized.

Material and methods: From January 2008 to May 2014, 50 pediatric patients presented to our hospital with pathologically proven NPC. The initial radiological studies (CT of 35 patients and MRI of all 50 patients) are retrospectively assessed regarding the nasopharyngeal masses and cervical lymph nodes.

Results: All 50 patients had a nasopharyngeal mass. Intracranial extension was detected in 38 cases, 15 of them invaded the central skull base, the other 23 extending along the nerves. The perineural spread along V3 was the commonest in 16 cases followed by V2 in the other 7 cases. Almost all the nasopharyngeal masses showed restricted diffusion with average ADC: $0.7 \times 10^{-3}$ mm$^2$/sec. Enlarged lymph nodes presented in 47/50 of the cases.

Conclusion: Pediatric NPC is generally not suspected clinically until late into the disease process. Awareness that NPC can occur in children should prompt careful evaluation for distinctive radiographic features. Earlier diagnosis may then direct the patient to timely appropriate therapy when these key radiographic features are present and recognized.

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1. Introduction

Nasopharyngeal carcinoma (NPC) is a disease of elderly people while the benign adenoidal hypertrophy is by far the commonest nasopharyngeal mass in pediatrics. Even when the malignancy attacks the nasopharynx in children, the pathological type mostly is lymphoma. NPC is rare in this age group (1). Unfortunately, these tumors tend to be locally advanced by the time they are diagnosed. Because they are rare, they may not be high on the list of differential diagnoses in children who present with a nasopharyngeal mass. The clinical presentation of the nasopharyngeal carcinoma is usually nonspecific. Also the delayed diagnosis reflects on the management and prognosis (2,3).
Early detection and accurate staging are imperative for optimal treatment planning, helping to improve clinical outcome and survival rate (4).

The radiological features of the nasopharyngeal carcinoma in the adults are frequently addressed in many studies, yet to our knowledge the imaging features of the nasopharyngeal carcinoma in the pediatrics were only in few studies (1,5,6). Our objective is to emphasize that, although rare, NPC does occur in children and can be diagnosed reliably when certain key radiographic features are recognized.

According to WHO classification, NPC is pathologically divided into three categories: keratinizing squamous cell carcinoma (WHO type I), nonkeratinizing squamous cell carcinoma (WHO type II), and undifferentiated carcinoma (WHO type III). Most of the cases are undifferentiated carcinoma (WHO type 3) in the advanced stage (7).

NPC is caused by the interaction of genetic susceptibility, environmental factors (e.g., exposure to chemical carcinogens), and infection with Epstein–Barr virus. High antibody titers to Epstein–Barr virus antigens are useful diagnostic markers, and there are many tests to detect both IgG and IgA titers (8).

Children with NPC generally present with neck mass and/or nasal symptoms such as obstruction, bleeding and discharge or fever of unknown origin (1).

CT has been used for staging NPC for long time, especially for better visualization of skull base invasion and tumor involvement with lytic or sclerotic lesions, but it has now largely been replaced by MRI for primary and nodal staging. However, CT is still used for radiotherapy planning and with PET using 18F-FDG. PET/CT is of value in NPC staging. However, CT is still used for radiotherapy planning, helping to improve clinical outcome and survival rate (4).

Each case was assessed regarding the following:

- The size, signal behavior (compared to the muscles), enhancement pattern of the nasopharyngeal mass.
- The skull base of invasion, the intracranial extension and perineural spread.
- The behavior on the DWI and the ADC values.
- The presence of the cervical lymph nodes enlargement, their side, levels, size of the largest and ADC value.

Staging of NPC was done depending on the 7th edition of American Joint Committee for Cancer (AJCC); International Union against Cancer (UICC) (11,12) which is as follows:

### 2.2. MR imaging technique

Conventional MR imaging was performed on 1.5T MR Unit (Siemens MRI Magnetom Espree) with a protocol that included coronal, sagittal & axial non-contrast T1WI, axial T2WI, coronal T2WI, as well as post contrast enhanced axial, coronal, and sagittal T1WI. DWI was acquired by using b values of 0, 500, and 1000 s/mm² applied in the X, Y, and Z directions. Processing of ADC maps was performed automatically on the MR scanners. The ADC was measured by manually placing ROIs 50–100 mm² in size within the tumor regions on the ADC map.

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- The behavior on the DWI and the ADC values.
- The presence of the cervical lymph nodes enlargement, their side, levels, size of the largest and ADC value.

### 2.3. T-classification

- T1: nasopharynx, oropharynx or nasal cavity.
- T2: parapharyngeal extension.
- T3: bony structures and/or paranasal sinuses.
- T4: intracranial extension and/or cranial nerves, hypopharynx, orbit or infratemporal fossa/masticator space.

### 2.4. N-classification

- N0: none.
- N1: unilateral cervical and/or unilateral or bilateral retropharyngeal node(s), ≤6 cm in greatest dimension, above the supraclavicular fossa.
- N2: bilateral cervical node(s), ≤6 cm in greatest dimension, above the supraclavicular fossa.
- N3a: > 6 cm.
- N3b: in supraclavicular fossa.

### 2.5. M-classification

- M0: no distant metastasis.
- M1: distant metastasis.

### 3. Results

#### 3.1. Regarding the nasopharyngeal masses

The lesions include the entire nasopharynx in 30/50 cases, the lateral wall in 15/50 cases and posterior superior wall in 5/50...
cases. Almost all cases show the same signal behavior: hypo intense on T1WI and isointense on T2WI compared to the muscle signals. These masses also usually showed significant enhancement on post Gd series. The masses usually showed restricted diffusion, the average ADC value for undifferentiated carcinoma was $0.65 \times 10^{-3} \text{mm}^2/\text{sec}$ and for squamous cell carcinoma was $0.8 \times 10^{-3} \text{mm}^2/\text{sec}$. Skull base invasion was detected in 38/50 cases either by direct skull base destruction in 15/38 cases or by extension through the foramina in 23/38 cases along the nerves. This perineural spread was detected along the V3 (mandibular branch of the trigeminal nerve) in 16/23 cases while the other 7/23 cases showed extension through V2 (maxillary branch of the trigeminal nerve).

3.2. Regarding the cervical lymph nodes

Presence of enlarged lymph nodes was seen in 47/50 cases, usually located at levels 2 & 3. Parotid lymph nodes enlargement was seen at 5 cases. Lateral retropharyngeal lymphadenopathy that measured greater than 1 cm in maximal transverse dimension was present in 10 patients. Bilateralism was seen at 10 cases. These lymph nodes showed restricted diffusion with cystic degeneration showed in 13 cases.

Distant metastasis was detected in 5/50 cases, bone deposits in 3 cases and lung deposits in the other 2 cases.

3.3. Regarding TNM staging of our cases

- 23/50 cases were T4, 15/50 cases were T3, 8/50 cases were T2 and 4/50 cases were T1.
- 20/50 cases were N3, 17/50 were N2, 10/50 were N1 and no lymph nodes were detected in 3/50 cases.
- 5/50 cases were M1 and 45/50 cases were M0.

3.4. Prognosis and patient outcome

All patients were treated by radiotherapy with overall good prognosis: complete remission was reported in 37/50 cases, recurrent lesion in 6/50 cases, mortality reported only in 4/50 cases and the other 3 patients lost their follow-up.

4. Discussion

When evaluating significant nasopharyngeal masses in children, benign adenoidal hypertrophy is by far the most common. On the other hand, the rhabdomyosarcoma and lymphoma are the commonest malignancy (13). The nasopharyngeal carcinoma is less common and therefore usually, it is not considered in the differential diagnosis. In addition, children with nasopharyngeal carcinoma generally present with neck mass and/or nasal symptoms such as obstruction, bleeding and discharge or fever of unknown origin, and these clinical presentations overlapped with many other benign conditions. In light of these facts, the clinical and radiological experience in diagnosis and treatment of the nasopharyngeal carcinoma in pediatrics is limited (14).

Some radiographic features of the primary tumor may help in differentiating nasopharyngeal carcinoma from benign adenoidal tissue. In contrast to benign masses, the configuration of NPC is almost always asymmetric and extension into the adjacent space and skull base invasion as well as the presence of malignant looking lymph nodes (15).

On other side, it is hard to differentiate the nasopharyngeal carcinoma from the rhabdomyosarcoma and lymphoma on radiological basis. But rhabdomyosarcoma doesn’t associate with enlarged lymph nodes. Our results go in the same way of that of Stambuk et al. (6) who described the radiological

![Fig. 1](image) 7 year old male patient with nasopharyngeal mass spreading along the V2 nerve as demonstrated at the coronal T1 post contrast images with bilateral cervical lymph node deposits and multiple pulmonary deposits.
features of eleven children with nasopharyngeal carcinoma (see Figs. 1–3).

Yabuuchi et al. (5) described the radiological appearance of nasopharyngeal carcinoma in 13 pediatric and young adult patients; he demonstrated almost the same feature instead of older age of his patients.

New techniques such as the diffusion MRI which detect the cellularity of the lesions, in our series all fifty cases of nasopharyngeal carcinoma showed restricted diffusion with average ADC about $0.6 \times 10^{-3}$ mm$^2$/sec. Abdel Razek and Kamal (10) reported mean NPC ADC value was $0.99 \pm 0.11 \times 10^{-3}$ mm$^2$/s. We observed lower ADC value
with high grade tumors as well as NPC with metastatic lymphadenopathy. Abdel Razek and Kamal (10) reported a direct inverse correlation between ADC value and histological tumor grade: higher grade showed lower ADC value ($p = 0.001$). This is explained by the increased cellular density of high-grade tumors, with subsequent restricted diffusion and deceased ADC value. Abdel Razek and Kamal (10) also reported that NPC with enlarged metastatic lymph nodes showed lower ADC value ($p = 0.003$) than that in patients without cervical lymphadenopathy. This may be due to patients with metastatic cervical lymph nodes usually having poorly differentiated or undifferentiated malignancy.

We found distant metastasis in 10% of cases. Abdel Razek and King (9) reported frequency of distant metastases (5–41%).

Regarding our study, 46% of cases were T4, 30% of cases were T3, 16% of cases were T2 and 8% of cases were T1. Liu et al. (11) reported (40.5%, 35.4%, 21.5% and 2.5%) for T4, T3, T2 and T1 NPC respectively. We found 40% of cases were N3, 34% were N2, 20% were N1 and 6% of cases were N0. Liu et al. (11) reported (20.9%, 52.5%, 20.3% and 6.3%) for N3, N2, N1 and N0 respectively. 10% of our cases were M1, while it was 24% in the study by Liu et al. (11). The most common site of distant metastasis was bone in the study by Liu et al. (11) and in our study as well (3 of 5 cases with distant metastasis).

MRI is more accurate in detection of the perineural spread and intracranial extension, also more accurate in detection of marrow infiltration, yet cortical destruction of bones is assessed by CT. Both modalities are almost of the same accuracy in assessment of the lymph nodes.

5. Conclusion

Pediatric NPC is generally not suspected clinically until late into the disease process. Awareness that NPC can occur in children should prompt careful evaluation for distinctive radiographic features. Earlier diagnosis may then direct the patient to timely appropriate therapy. Combined CT and MRI are needed to stage the cases of nasopharyngeal carcinoma.

Conflict of interest

The authors declare that there are no conflicts of interest.

References