

# Young nasopharyngeal carcinoma: a review of an 8-year experience in the East Coast Malaysia Hospital

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Received 25 September 2016

Accepted 9 December 2016

The Egyptian Journal of Otolaryngology  
2017, 33:490–494

## Introduction

Nasopharyngeal carcinoma (NPC) is among the most common head and neck malignancies seen among adults in Malaysia. It is the third most common cancer in males after colorectal and lung cancers. Even though it has bimodal peak distribution, young NPC is a rare occurrence. It accounts for less than 1% of all paediatric cancers.

## Objective

The objective of this study was to describe the 8-year experience with young NPC in the year 2003 until 2010 in a tertiary centre in East Coast Malaysia Hospital.

## Method

Twenty-four young NPC cases confirmed by histopathology and undergoing treatment in a tertiary centre in East Coast Malaysia Hospital between 2003 and 2010 were retrospectively reviewed. We studied NPC incidence observed during that period, focusing on the age and sex distribution and the ethnic background of patients. We also analysed the most prevalent signs and symptoms and staging of the NPC patients at first presentation, which include neck swelling, ear symptoms, nasal symptoms and other miscellaneous symptoms.

## Results

Presentation was predominant in the Malay population, with age peaking between 16 and 20 years. Most patients were male (70.8%). The main presenting symptoms were neck mass (70.9%), unilateral nasal obstruction (33.3%), epistaxis (29.2%) and other miscellaneous complaints (20.9%), including headache, diplopia and facial paraesthesia. In all, 25% of patients had cranial nerve involvements either isolated or a combination of cranial nerves 2, 3, 4, 5, or 6. Stage I, II, III and IV patients accounted for 0, 4.2, 12.5 and 83.3%, respectively. Majority (91.7%) had WHO type 3 NPC (undifferentiated carcinoma).

## Conclusion

Results from our series are comparable to those reported by other centres. A majority of the patients were diagnosed late and at the advanced stage. The TMN staging was a relevant prognostic factor.

## Keywords:

clinical presentation, Malaysia, nasopharyngeal carcinoma, paediatrics

Egypt J Otolaryngol 33:490–494

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1012-5574

## Introduction

Nasopharyngeal carcinoma (NPC) is a rare malignancy throughout other parts of the world, with prevalence usually less than 1/100 000 [1,2]. It has a high prevalence and is a leading cause of death in some regions in southern China. In Malaysia, there were 900 cases of NPC diagnosed and registered at the National Cancer Registry in 2007, comprising 685 males and 255 females [3]. This placed NPC as the fourth most common cancer among the Malaysian population, and the third common cancer among males in Malaysia. The native Bidayuh people of Sarawak also have a high incidence of NPC [4].

NPC shows a consistent pattern across populations in some areas, with continual increases in NPC risk of age up to a first peak in late adolescence/early adulthood (age: 15–24 years), followed by a second peak later in

life (age: 65–79 years). NPC is a rare paediatric malignancy, which makes up 1–5% of all paediatric cancers and 20–50% of all primary malignant nasopharyngeal tumours in children with infrequent incidence rate. In China, children under 16 years of age make up 1–2% of NPC cases, 10% in USA, 12% in Israel, 13% in Kenya, 14.5% in Tunisia and 18% in Uganda [5].

It also referred to as cavum carcinoma. It is distinguished from the adult form of the disease by its association with Epstein–Barr virus infection, undifferentiated histology and high incidence of advanced locoregional compromise [5].

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The presentation of NPC may be asymptomatic or subtle signs and symptoms. Patients commonly presented with advanced stage of NPC; thus, their prognosis is poor. The delay in seeking medical advice and unusual and confusing nature of the presenting symptoms are among the main reasons for the late presentation and delay in diagnosis. In addition, the occurrence of this tumour in children is biologically more aggressive and most often presents as an advanced locoregional disease.

The disease is linked to aetiological factors including infectious mononucleosis, consumption of food rich in nitrosamines and genetic and epigenetic factors [6].

The aim of the study was to describe the presentation of young NPC as found in the year 2003 until 2010 at a tertiary centre in East Coast Malaysia Hospital.

### Methodology

A retrospective case review of patients with young age at diagnosis of NPC was conducted for the time period between January 2003 and December 2010 at a tertiary centre in East Coast Malaysia Hospital. The entries into hospital's Oncology Registry were used for patient identification and search.

The patient studied in the series includes those who had been investigated, and histologically diagnosed at different hospitals. Details of the patient age, sex, race, duration of presenting complaint and the nature of all the other associated complaints were collected.

All patients had histologically proven squamous cell carcinoma of the nasopharynx, based on the WHO classification.

### Results

Twenty-four patients with the diagnosis of NPC were identified in the 8-year time. The presence of a lesion in the Fossa of Rossemuller was confirmed via nasal endoscopy, and biopsy was taken for histologic grading. None of the patients had any family history of NPC or any other form of malignancy.

All patients had computed tomography scanning to assist in the staging and to assess the extent of spread of the disease. Bone scans also completed investigation for bone metastasis.

Seventeen patients had received concurrent chemo-radiotherapy (CCRT) at the HUSM oncology centre, whereas five patients had received external beam

radiotherapy alone. Two patients had defaulted treatment and never received any treatment. After treatment, nine patients were recorded to be in remission at least for 6 months.

The demographic details, clinical presentation and management of these 24 patients are presented in Table 1.

### Demography

A total of 24 young patients diagnosed as having NPC were included in the study. All (100%) of the patients were Malays. There were 17 male and seven were female patients, with a male to female ratio of 2.4 : 1. The age at diagnosis ranges from 10 to 30 years (Fig. 1). The mean age was 18.3 years.

### Presenting complaint

The most common presenting complaint was neck swelling (62.5%) followed by nasal symptoms (16.7%) (Table 1). The mean duration of the presenting complaint at the time of presentation was 6 months.

### Associated complaints

Table 2 below lists all the complaints in patients with NPC. Among all the complaints in patients with NPC, neck mass (70.9%) was the most common complaint, followed by unilateral nasal obstruction (33.3%) and bleeding from the nose (29.2%).

### Family history

None of the patients had any family history of NPC or any other form of malignancy. There was no documentation for any family members of Chinese origin.

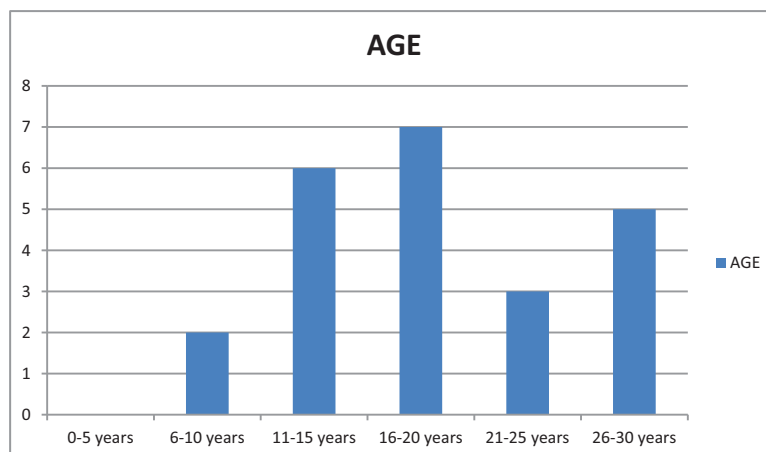
### Cervical lymphadenopathy

Although only 17 (70.8%) patients had complained of neck swelling, almost all of the patients were found to have palpable lymph nodes in the neck. Only one (4.2%) patient had no lymphadenopathy at diagnosis.

**Table 1** The frequency of occurrence of each presenting complaint

Presenting complaint	n (%)
Unilateral neck mass	11 (45.8)
Bilateral neck mass	4 (16.7)
Epistaxis	2 (8.3)
Unilateral nasal obstruction	2 (8.3)
Headache	2 (8.3)
Diplopia	2 (8.3)
Unilateral facial paraesthesia	1 (4.2)

Figure 1



Age distribution of patients with nasopharyngeal carcinoma.

Table 2 Distribution of all complaints

All complaint	n (%)
Neck mass	
Unilateral	13 (54.2)
Bilateral	4 (16.7)
Ear symptom	
Unilateral hearing impairment	5 (20.8)
Tinnitus	2 (8.3)
Otagia	1 (4.2)
Nasal symptom	
Epistaxis	7 (29.2)
Unilateral obstruction	8 (33.3)
Bilateral obstruction	3 (12.5)
Miscellaneous symptoms	
Facial paraesthesia	3 (12.5)
Headache	4 (16.7)
Trismus	2 (8.3)
Diplopia	3 (12.5)
Dysphagia	1 (4.2)
Unilateral blindness and ptosis	1 (4.2)

### Cranial nerve involvement

Cranial nerve involvement is reported in six (25.0%) patients, either isolated or combination of cranial nerves 2, 3, 4, 5 or 6. Among them, three (12.5%) complained of unilateral facial paraesthesia with only involvement of the trigeminal nerve. Another three (12.5%) presented with diplopia (because of abducens nerve involvement) and one (4.2%) of the them presented with blindness with involvement on cranial nerves 2, 3, 4 and 6 in combination.

### Distant metastasis

Two (8.3%) of the patients had evidence of distant metastasis at diagnosis, which involves bony metastasis. One (8.3%) patient had defaulted treatment and had not completed full metastasis workup. The most common site of metastasis was bone (five patients).

Table 3 Distribution of patients with nasopharyngeal carcinoma by stage

Stage of disease	n (%)
Stage I	0 (0)
Stage II	1 (4.2)
Stage III	3 (12.5)
Stage IV	
IVA	7 (29.2)
IVB	11 (45.8)
IVC	2 (8.3)

None of the patients had metastasis to liver or lungs.

### Tumour staging

It was found that twenty (83.3%) patients had presented with advanced disease, tumour staging of T4 disease including T4 a, b and c. Three (12.5%) had T3 staging of tumour. One (4.2%) patient presented with T2 disease, and no patients presented with T1 disease. In one of the cases, the patients initially presented solely with parapharyngeal mass that delayed the diagnosis of NPC (Table 3).

### Histopathology

The majority of the patients (91.7%) with NPC belonged to WHO type 3 (undifferentiated carcinoma), and two (8.3%) of the patients had NPC type 2 (nonkeratinizing carcinoma). None of the patients had NPC WHO type 1 (differentiated squamous cell carcinoma).

### Discussion

NPC has a consistent pattern across populations, with continual increase in NPC risk by age up to a first peak in late adolescence/early adulthood (age: 15–24 years)

followed by a second peak later in life (age: 65–79 years) [7]. Chan *et al.* [8] proposed that the first ‘hit’ in individuals diagnosed with NPC in late adolescence/early adulthood is most likely a germline alteration (major gene transmission) according to the current model for the development of NPC.

Our study is an institutional review of young NPC seen in a tertiary centre in East Coast Malaysia Hospital. We found that our patients with young NPC have a male to female ratio of 2.4 : 1. The incidence was more than two-fold higher among males when compared with females. This is as reported by others for NPC [9–11]. In a Rare Cancer Network Study conducted on Paediatric Nasopharyngeal Carcinoma, a similar male preponderance was reported, where 66% (109) patients were male and 34% (56) patients were female [12].

In our study, all of our patients with young NPC were Malays. We do not have local data for prevalence of ethnic group in young NPC to compare. In a larger study conducted concerning adult NPC, 73.8% were Malays and 24.6% were Chinese [11]. This result reflects the proportion of the ethnic groups in the state of Kelantan. Overall, the National Cancer Registry 2007 reported a higher incidence rate of NPC in Chinese compared with Malay and Indian [3].

The age presentation of our young NPC ranges from 10 to 30 years with a prominent peak of presentation at the age between 16 and 20 years. The mean age at presentation was 18.3 years. Juvenile NPC in Morocco presented between 15 and 20 years of age [13], whereas in Tunisia the average age for paediatric NPC was 16.2 years of age with presentation between 10 and 20 years of age [14].

All of the patients had no family history of NPC or any other form of malignancy. Besides, there was also no documentation for any family members of Chinese origin.

The most common presenting symptoms of young NPC in our patients was neck swelling (62.5%), with 45.8% unilateral and 16.7% bilateral neck masses. Almost all of the patients presented with neck swelling on clinical examination, although only 70.9% complained of neck swelling. In paediatric patients, the awareness of neck swelling by the parents or carer could be one of the factors that they seek medical advice. In addition, it become the main presenting complaint as it is the exposed and easily noticed area. This presentation is consistent with study findings in adults [15].

In all, 16.6% presented with nasal symptoms such as nasal obstruction (33.3%) and bleeding from the nose (29.2%). Others presented with symptoms as listed under miscellaneous complaints (20.9%), including headache, diplopia and facial paraesthesia. These symptoms are closely related to advanced disease, as erosion into the skull base is common with involvement of cranial nerves.

The mean duration of the presenting complaint at the time of presentation was 6 months. This is similar to the other studies conducted in adult NPC [9].

The incidence of cranial nerve palsy in the study was 25%. The most commonly affected was cranial nerve VI (12.5%) followed by V (12.5%). Commonly, cranial nerve VI was affected followed by III and XII nerves because of extension of tumour into the foramen lacerum and paracavernous sinus tumour invasion. It is the same with adults [16]. The cranial nerve XII was affected when the tumour extended into the poststyloid space. The involvement of cranial nerves is significant as it worsens the NPC staging.

The symptomatic distant metastases were found in two (8.3%) of the patients, which involve bony metastasis. One (8.3%) of the patients had defaulted treatment and not completed full metastasis workup. The most common site of metastasis was bone (five patients). It is the same with adults [17]. The most common bone metastasis was to the spine, involving the thoracic and lumbar vertebrae. Other patients developed multiple bone metastasis. One patient had bone metastasis to the mandible. None of the patients had metastasis to liver or lungs. The frequencies of metastases were as follows: bone (75% of total metastatic patients), lung (46%), liver (38%) and retroperitoneal lymph nodes (10%) [17].

Poor prognosis for patients with NPC is principally because of its advanced stage at the time of diagnosis. Majority of our patients presented with advanced stage and poor histological grade. Twenty-two (91.7%) patients were diagnosed with undifferentiated carcinoma and two (8.3%) of the patients had NPC type 2 (nonkeratinizing carcinoma). Undifferentiated carcinoma is the most common histological variant in childhood similar to a study in South India [18] and Tunisia [19]. It is classically associated with more frequent distant metastases compared with adults. In adults, a majority (41.1%) of NPCs belonged to WHO type 1 in a study conducted in 2003.



Seventeen (70.8%) patients had CCRT, whereas five (20.8%) patients had received external beam radiotherapy alone.

After treatment, 10 (41.7%) patients were recorded to be in remission at least for 6 months, with nine of them completing CCRT and one completing radiotherapy. This suggests that CCRT had better outcome than radiotherapy alone in advanced disease. Present studies have shown that concomitant use of chemotherapy with radiotherapy improves overall survival and reduces recurrence [20]. Three of the patients had defaulted follow-up, with two of them completing treatment. The patients who presented with advanced disease had a higher risk of developing a recurrence or had residual disease after initial treatment. Four of the five patients who received external beam radiotherapy had residual disease and the remaining one later developed recurrence of the disease.

Eleven (45.8%) of the patients later developmental progression of disease with metastases mainly to the spine and bone.

## Conclusion

This study is first to reflect the presentation of young NPC in Malaysia, predominantly in Malay population, with age peaking between 16 and 20 years. The presentations for medical treatment were late and at advanced stage of disease. Majority of the NPC is aggressive in nature with histology finding of undifferentiated carcinoma. Further studies are required to analyse treatment approach and prognostic aspects in treatment of children with NPC.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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