

Nasopharyngeal carcinoma: clinical trends

R. INDUDHARAN, DIP.N.B.(ORL), M.S.*; K. A. VALUYEETHAM, M.S.‡, T. KANNAN, M.D., D.M.†,
D. S. SIDEK, M.S.(ORL), M.Sc.*

Abstract

Nasopharyngeal carcinoma (NPC) is one of the most difficult diseases to diagnose at an early stage. The clinical presentation of 122 patients with confirmed NPC is described and the findings analysed. The common modes of presentation and cases where detailed nasopharyngeal examination need to be performed are highlighted. We emphasize the importance of health education and training for primary care physicians for early detection of these cases.

Key words: Nasopharyngeal neoplasms; Carcinoma

Introduction

Nasopharyngeal carcinoma (NPC) is one of the commonest malignancies seen in Malaysia (Prasad *et al.*, 1983). Since patients with NPC commonly present at an advanced stage of the disease their prognosis is poor. The reasons for the late presentation are manifold, viz. 1) delay in seeking medical advice (Skinner and Van Hasselt, 1990), 2) the bizarre and confusing nature of the presenting symptoms misleading the clinician (Neel III and Taylor, 1983), 3) the fact that clinical examination of the nasopharynx is difficult even for experienced clinicians and, 4) the spread of a silent submucosal lesion with a normal appearance of the nasopharynx on examination (Skinner *et al.*, (1991).

We carried out a retrospective study of patients with NPC, admitted to the University Hospital and General Hospital, in Kota Bharu (the two referral centres of the state of Kelantan), from 1986 to 1995, with the aim of detailed analysis of the presentation of NPC with reference to age, sex, race, the stage at presentation and other factors. NPC is of relevance to Malaysia, a country where three ethnic groups of population co-exist and interact biologically. The total population of this state was 125 000 during December 1991, the mid-period of this study, and the proportions of the ethnic groups were 92.9 per cent Malays, 5.4 per cent Chinese, 0.7 per cent Indians and one per cent others. The data from this study are expected to provide the clinical profile of NPC. We also attempted to elucidate the reasons for delay in the diagnosis of NPC and have indicated the necessity for early detection of this disease by appropriate screening methods.

Materials and methods

The case records of patients who were diagnosed as having NPC in the University Hospital and the General Hospital in Kota Bharu, Kelantan over a period of 10 years, from 1986 until 1995, were analysed in this study. All the patients had a confirmed histopathological diagnosis of NPC according to the WHO classification (De Thé and Ito, 1978; Shanmugaratnam and Sobin, 1978; Weiland and Micheau, 1981). We did not attempt a detailed staging of these patients as there is no internationally accepted 'best' staging system (Neel III and Taylor, 1983; Lee *et al.*, 1996). Moreover, the majority of our cases presented at an advanced stage of the disease (59.84 per cent stage IV according to TNM classification); consequently our treatment strategy was combined modality in view of the micrometastasis (Tsao and Shiu, 1990).

Details regarding the age, sex, race, presenting complaints (the main complaint for which the patient sought medical advice), and associated complaints (complaints regarded as unimportant by the patient) of each patient were recorded. The site of the lesion in the nasopharynx: whether on the lateral wall, postero-superior wall, floor, anterior wall or more than one wall, type of lesion; whether it was proliferative, ulcerative or infiltrative, presence of cervical lymphadenopathy, cranial nerve involvement, presence of distant metastasis, and extension of NPC from nasopharynx to adjacent regions were determined for every patient by physical examination. The nasopharynx was examined either using a flexible nasopharyngoscope, a rigid 0° or 30° Hopkins rod telescope or Yankeurs nasal speculum

From the Departments of Otorhinolaryngology*, and Oncology†, School of Medical Sciences, Universiti Sains Malaysia, Kelantan, and the Department of Otorhinolaryngology‡, General Hospital, Kota Bharu, Malaysia.
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TABLE I
RACE AND SEX INCIDENCE IN NPC

Race	Male	Female	Total
Malay	67	23	90
Chinese	23	7	30
Indian	0	0	0
Others	1	1	2
Total	91	31	122

prior to the acquisition of the endoscopes in 1989 by our institute. The imaging methods used were computed tomography (CT) scan, ultrasound, and/or Technetium bone scan. CT scan was performed in all the cases. Ultrasound of the abdomen was performed in those cases where a palpable liver or abnormalities in the liver function test was detected. The criteria for bone scan was any bone pain, low back ache or pathological fractures in any of our patients. Special care was taken in looking for clinical signs of bone metastasis which is the commonest site of metastatic deposit. Ideally ultrasound of the abdomen and bone scan could have been used in all the cases. However, this was a retrospective study and the cost effectiveness of these expensive investigations had limited the use of these tools in every case. The histopathological types of NPC were also analysed.

Statistical analysis was performed using the unpaired Student's *t* test and χ^2 tests. If $p < 0.05$, the results were considered to be statistically significant.

Results

A total of 122 patients were diagnosed as having NPC in the 10-year period of study.

Race and sex

Out of the 122 patients, there were 90 (73.8 per cent) Malays, 30 (24.6 per cent) Chinese. Ninety-one patients were males and 31 were females (Table I).

Age

The patients' ages ranged from 15 to 82 years (Figure 1). The mean age of Malay males was 51 years and that of Malay females was 47.65 years, whereas that of Chinese males was 43.65 years and Chinese females was 44.86 years. The age difference

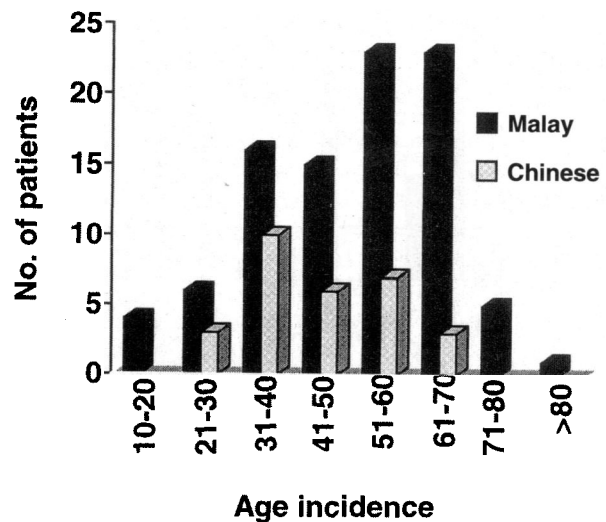


FIG. 1
Age distribution among Malays and Chinese with nasopharyngeal carcinoma.

between males and females in all the races ($p = 0.61$) and among the two main races viz. Malay and Chinese ($p = 0.089$) was not statistically significant. There was no significant sex predilection of NPC among Malays and Chinese.

Presenting complaints

Table II shows the frequency of occurrence of clinical features of NPC either as presenting complaints or associated complaints. The commonest presenting complaint was neck swelling (54.1 per cent) followed by epistaxis (25.4 per cent) and decreased hearing (18.0 per cent).

Associated complaints

Table II lists the associated complaints in patients with NPC. Epistaxis (17.2 per cent) was the commonest associated complaint, followed by decreased hearing (16.4 per cent) and nasal obstruction (9.8 per cent). Other associated complaints included symptoms of pre-senile dementia (Zain *et al.*, 1994) secondary to temporo-parietal metastasis, and jaundice following metastasis to the porta hepatis (Elango and Jayakumar, 1990).

TABLE II
THE FREQUENCY OF OCCURRENCE OF CLINICAL FEATURES IN PATIENTS WITH NPC

Clinical features	Presenting complaint		Associated complaint	
	No. of patients	(%)	No. of patients	(%)
Neck swelling	66	54.1	8	6.6
Epistaxis	31	25.4	21	17.2
Decreased hearing	22	18.0	20	16.4
Ocular symptoms	16	13.1	9	7.4
Tinnitus	15	12.3	6	4.9
Cranial nerve palsy	15	12.3	7	5.7
Headache	14	11.5	7	5.7
Nasal obstruction	12	9.8	12	9.8
Others	14	11.5	7	5.7

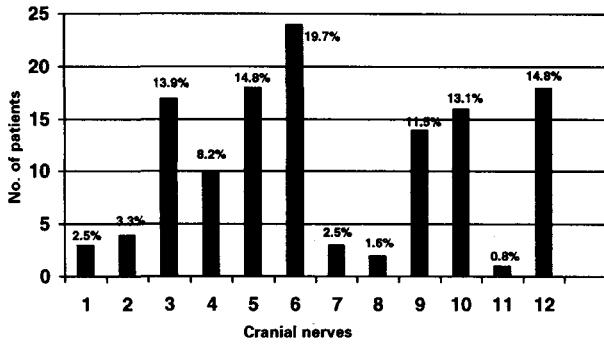


FIG. 2
Distribution of cranial nerve involvement.

Findings in the nasopharynx

It was found that 46 (37.7 per cent) patients had involvement of more than one wall. Forty-four (36.1 per cent) had involvement of the lateral wall only and 27 (22.1 per cent) had involvement of posterior and superior walls. In five patients (4.1 per cent) the site of involvement could not be recorded since the nasopharynx looked normal. However, multiple punch biopsies from various regions in the nasopharynx provided histological diagnosis in these cases where cervical lymph nodes were palpable. In none of the cases was there an extension of the tumour to the soft palate or the choanae. Sixty patients (49.2 per cent) had an ulcerative or infiltrative type of lesion whereas 53 (43.4 per cent) had a large proliferative growth as a space occupying lesion in the nasopharynx. In nine patients (7.4 per cent), the type of lesion was not recorded. The type of lesion, whether it was proliferative, infiltrative or ulcerative had no significant association with lymphadenopathy ($p = 0.28$).

Cervical lymph nodes

Although only 74 (60.7 per cent) patients had complained of neck swelling, 88 (72.1 per cent) patients were found to have palpable lymph nodes in the neck. Among these, 50 (41 per cent) had

TABLE III
SITES OF DISTANT METASTASIS IN 18 PATIENTS WITH NPC

Case no.	Sites of distant metastasis
5	Liver; Inguinal lymph nodes
6	Liver
10	Spine (T4, T5, and L1 vertebrae)
12	Liver
15	Lumbar spine
17	Temporo-parietal region of the brain
18	Bone metastasis (site not specified)
23	Lumbar spine
26	Lung
28	Porta hepatis (Elango and Jayakumar, 1990)
29	Temporal lobe, lung, scapula, humerus
30	Axillary lymph nodes
44	Extradural spinal secondary (Elango <i>et al.</i> , 1991)
50	Brain (left temporal lobe)
53	Lumbar spine
57	Liver
91	Lumbar spine
112	Lung

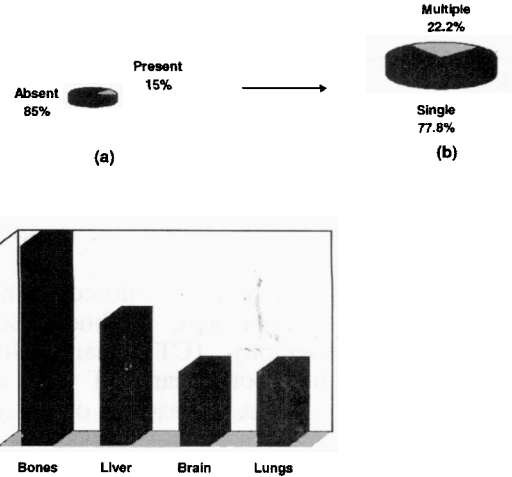


FIG. 3

Distribution of distant metastasis in nasopharyngeal carcinoma.

unilateral and 38 (31.1 per cent) had bilateral cervical lymph nodes. No palpable cervical lymph nodes were found in 34 (27.9 per cent) patients.

Cranial nerve involvement

Figure 2 illustrates the distribution of cranial nerve involvement. Thirty-seven (30.31 per cent) patients had cranial nerve palsy at presentation, of whom 10 (8.2 per cent) had palsy affecting only one cranial nerve, while 27 (22.13 per cent) had multiple cranial nerve palsies. The cranial nerve most commonly affected was the sixth (19.7 per cent), followed by the maxillary division of the fifth nerve and the 12th nerve (14.8 per cent each). In our series a significant number of patients presented with involvement of the 12th cranial nerve.

Distant metastasis

Eighteen patients (15 per cent) had evidence of distant metastasis (Table III), of whom four showed a spread to multiple sites (Figure 3). The commonest site of metastasis was bone, with two patients having two different bone sites, followed by the liver (five patients).

Direct extension into other areas

Fifteen (12.3 per cent) patients had direct intracranial extension of their NPC; six (4.9 per cent) patients had direct extension into the orbit and in six (4.9 per cent) the NPC extended into the nose and paranasal sinuses.

Histopathology

The majority of the patients with NPC belonged to WHO Type III (49.2 per cent), followed by Type II (31.1 per cent) and Type I (13.1 per cent). In eight (6.6 per cent) the type could not be determined.

Discussion

Our patients with NPC, both Malay and Chinese, were found to have a male to female ratio of 2.9 to 1. This is similar to that reported in Chinese patients with NPC from Hong Kong, which is an area of common distribution of NPC (Skinner *et al.*, 1991). This male to female ratio in the incidence of NPC is more or less the same throughout the world and is still unexplained (Dickson and Flores, 1985; Moloy *et al.*, 1985). Most of the female patients in our study had less extensive disease compared to males. While it is not known if this is due to a less aggressive nature of the disease in females or due to their increased awareness of the disease, it could explain the better prognosis of treatment that has been reported in females (Dickson, 1981).

In our study the Chinese were found to be affected at a younger age compared to Malays. NPC was also not seen in any one less than 14 years old. The affected Malays were mainly in the fifth to seventh decades of life which tallies with results of other studies on NPC in non-Chinese (Dickson, 1981; Moloy *et al.*, 1985). Our study also showed that Chinese were six times more at risk than Malays for NPC (odds ratio 5.73).

Among our patients, 54.1 per cent presented with cervical metastasis and 14.75 per cent had metastasis to distant sites. The reasons for this presentation could be poor awareness of this disease, low educational status of the population studied and trivialization of symptoms both by patients and their attending physicians (Skinner and Van Hasselt, 1990). According to our statistics the order of frequency of presenting symptoms were neck swelling followed by epistaxis and decreased hearing. The majority of patients had misconstrued their symptoms as those of an easily treatable disease. An analysis of the frequency of unilateral versus bilateral symptoms would have been useful but could not be carried out as this was a retrospective study.

Although only 54.1 per cent of our patients had neck swelling as presenting complaints, and eight per cent as an associated complaint, on palpation 72.1 per cent were found to have a swelling in the neck. The fact that patients tend to ignore the presence of enlarged neck lymph nodes demonstrates the urgent need of public educational programmes if NPC is to be detected in its early stages.

That decrease in hearing has an association with NPC is confirmed by the fact that 18 per cent of our patients presented with deafness as their main complaint and 16.4 per cent had it as an associated complaint which may include presbycusis also. Due to the retrospective nature of our study, we were not able to distinguish the frequency of the side of deafness or associated presbycusis in our patients in the fifth and sixth decades of their life. In light of the above we feel that all patients with deafness must undergo tympanometry and if middle-ear effusion is suggested then they must undergo a thorough nasopharyngeal examination to exclude NPC.

Patients with involvement of the postero-superior wall of the nasopharynx had a significantly greater incidence of bilateral cervical lymph nodes compared to those with lesions of the lateral wall ($p = 0.03$) where there was only unilateral cervical node metastasis. The type of lesion, whether it was proliferative, infiltrative or ulcerative had no significant association with lymphadenopathy. In our series more females presented with unilateral cervical nodes (48.39 per cent) than males (38.46 per cent). However, bilateral nodes were more common in males (35.16 per cent) than in females (19.36 per cent). Absence of palpable cervical lymph nodes was more common in females (32.26 per cent) than males (26.37 per cent). This probably suggests that females being more conscious of their appearance seek medical attention much earlier than males or that the intra-cranial-spread, or spread through the petrosphenoid route, when cervical nodes may not appear, is more common among females.

On comparing age distribution to the presence of unilateral or bilateral cervical lymph nodes, we found no significant difference.

There was significant absence of cervical lymph node enlargement when Vth (p value = 0.017) or the VIth (p value = 0.001) cranial nerves were involved.

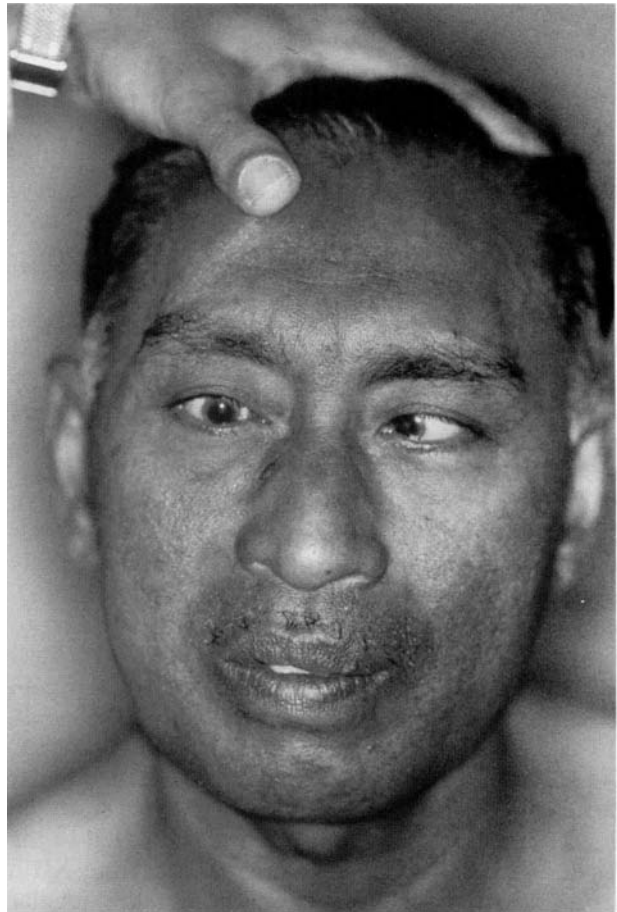


FIG. 4

Ascending type of nasopharyngeal carcinoma with unilateral VIth cranial nerve palsy and no cervical lymph node involvement.



FIG. 5

Descending type of nasopharyngeal carcinoma with massive cervical metastasis.



FIG. 6

Ascending type of nasopharyngeal carcinoma with unilateral VIth and XIIth cranial nerve palsy and ipsilateral conductive hearing loss as evidenced by Weber's test lateralization.

This could be because as the NPC spreads upwards (ascending type) through the foramen lacerum it involves the Vth and VIth cranial nerves early (Figure 4). All the other commonly involved cranial nerves could probably be due to cervical nodes metastasis, when the spread is through the retro-parotidian route (descending type) (Figure 5). Involvement of the first four cranial nerves depends on extension of NPC into the orbit or nasal cavity and in patients in whom such spread occurred, cervical lymph nodes were also palpable. Similar to our series, many previous reports on NPC also have a higher incidence of XII cranial nerve involvement (Neel III and Taylor, 1983; Skinner and Van Hasselt, 1990; Skinner *et al.*, 1991). The explanation that IX, XI and XII cranial nerves are affected at the jugular foramen (Skinner *et al.*, 1991) is disputable since the involvement of XIIth cranial nerve compared to the IXth, Xth and XIth is very high. Further the XIIth cranial nerve does not pass through the jugular foramen and the incidence of XIth cranial nerve involvement which passes through it, is much less. We could not find a reasonable explanation for the high incidence of XIIth cranial nerve involvement (Figure 6).

The mean age of our patients with distant metastasis was significantly lower (39.28 years; SD = 14.07) compared to those without distant metastasis (50.73 years; $p = 0.003$). This probably suggests that the disease is more aggressive in the younger age groups. There was no significant sex predilection for distant metastasis. The fact that bone is the commonest site of secondary deposit suggests that bone scanning should be performed as a routine investigation in all advanced cases of NPC. The two cases of metastasis to porta hepatis and extradural spine from NPC mentioned in Table III have been reported from our centre previously (Elango and Jayakumar, 1990; Elango *et al.*, 1991).

Ours being a retrospective study, screening for distant metastasis was performed only in patients who had clinical evidence of such metastasis. Some of our patients might have had silent metastasis when they presented. Hence the efficacy of these investigations which may seem mandatory, should be weighed against their cost-effectiveness especially in developing countries.

It has been claimed that Eustachian tube dysfunction in NPC is functional in nature and not mechanical (Su and Juan, 1985). One of our patients who presented with deafness, however, was found to

have a growth in the middle ear which on biopsy was reported as NPC. A CT scan showed extension of the growth through the Eustachian tube to the middle ear. We, therefore, feel that in all cases of Eustachian tube dysfunction a thorough search must be made for an organic cause before concluding that the dysfunction is functional in nature.

Conclusion

Nasopharyngeal carcinoma is one of the most difficult diseases to be diagnosed at an early stage. Females present with a less aggressive disease than males. Whether there is any hormonal influence on the disease similar to juvenile nasopharyngeal angiofibroma is yet to be studied. There seems to be two distinct varieties of NPC – the ascending type and descending type.

It is desirable that the primary care physicians be trained to perform a detailed nasopharyngeal examination in all patients in whom they have the slightest doubt of NPC. Cases presenting with cervical lymph nodes where a primary is not detected, nasal symptoms such as epistaxis, hearing loss and unexplained bone pains, pathological fractures and spontaneous weakness or paralysis of lower limbs (as happened in two out of our five cases with spinal secondaries) suggesting bony deposits must undergo meticulous nasopharyngeal examination and biopsy. Cases presenting at an advanced stage of the disease could be reduced if a system for early case detection by primary care physicians could be initiated.

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Address for correspondence:

R. Indudharan,
Department of Otorhinolaryngology,
School of Medical Sciences,
Universiti Sains Malaysia,
16150 Kubang Kerian, Kelantan,
Malaysia.

Fax: 09-7653370
email: dharan@kb.usm.my