

Presentation and epidemiology of nasopharyngeal carcinoma in Jordan

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Abstract

A retrospective study, which highlights some of the aspects of nasopharyngeal carcinoma (NPC) as seen in a large hospital for 20 years in Jordan, was performed. Collected data showed that NPC accounted for one per cent of all malignant tumours during the period. The present series showed an age range from six to 89 years old with a mean of 39.5 years. There was a bimodal peak at presentation at 16 to 20 and 46 to 50 years. A high incidence of childhood NPC was also noticed (two per cent of all childhood malignant tumours). The difficulty in early diagnosis urges for better awareness of the tumour especially among general practitioners. The tumour is still detected at an advanced stage with 34 per cent metastasis most frequently to bone. The study stresses the importance of full ENT examination in cases of persistent middle ear disease, recurrent or persistent nasal symptoms or headache, or neck swelling; and routine bone scanning for all cases with NPC. There is a need for prospective studies of the causal relationship of NPC to environmental factors including Epstein-Barr (EB) virus as well as occupational and domestic hazards.

Key words: Nasopharynx; Carcinoma, squamous cell

Introduction

Nasopharyngeal carcinoma in Jordan presents at an advanced stage when first diagnosed in the vast majority of cases. This is attributed, at least in part, to the delay in seeking medical advice. The tumours are frequently symptomless at the start or they evoke symptoms that are common to other minor clinical conditions that do not draw serious patient attention. Some of these silent tumours have been also overlooked on clinical examination in the early stages. Difficulties arising in early diagnosis might be due to the small size of the tumours, near normal appearance of nasopharyngeal mucosa or the inherent presence of massive lymphoid tissue obscuring the underlying lesions.

While it is one of the most common malignancies in the Far East (Indudharan *et al.*, 1997) nasopharyngeal carcinoma is rarely seen in western countries. In Jordan, as in other Arab countries, a relatively large number of cases of nasopharyngeal carcinoma is seen each year (Jamal, 1991).

In the present retrospective study we report on 91 patients with nasopharyngeal carcinoma admitted to the Jordan University Hospital (JUH) during the period 1977–1996, inclusive.

Materials and methods

A search for biopsies of nasopharyngeal carcinoma was carried out in the files of the Department

of Pathology at Jordan University Hospital (JUH). Ninety one cases of nasopharyngeal carcinoma were retrieved from a total of 9,225 malignancies found in 85,470 surgical biopsies undertaken during the period 1977–1996 inclusive.

The histological preparations were reviewed by at least one staff pathologist. The cases included in the present study were histologically verified in accordance with the WHO classification (Shanmaguratnam *et al.*, 1979). All relevant data available to the Departments of Pathology and Otolaryngology, as well as the medical records at the JUH, were recorded. Special consideration was given to pertinent habits including smoking, heating method, incense, snuff-taking and other similar conditions possibly related to the development of NPC. The site of the lesion in the nasopharynx and whether of monofocal involvement or otherwise were also recorded. The presence and the site of metastasis, submental and cervical lymph-node enlargement as well as any neck swelling or disfigurement were also recorded.

The age, sex, major presenting symptoms, associated other symptoms, previous and family history and site and type of residence were registered. Special attention was given to upper respiratory tract infection, its duration, repetition and associated other symptoms.

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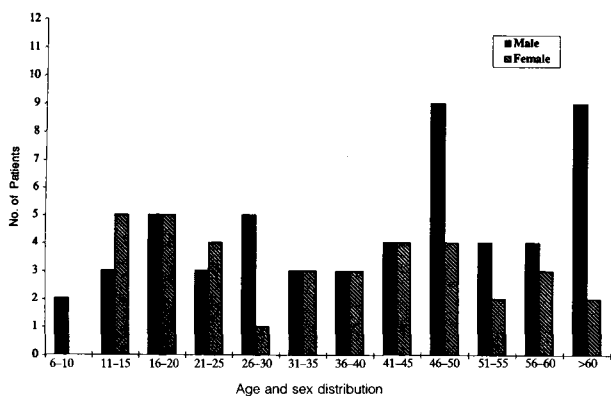


FIG. 1

Nasopharyngeal carcinoma – JUH 1977–1996

Radiological examination of the nasopharynx, blood picture, chest X-rays, bone and computed tomography (CT) scan and other imaging procedures were registered. Audiograms, tympanometry, repeat biopsies following radiotherapy and any other investigations were recorded and tables prepared.

Results

A total of 91 cases of nasopharyngeal carcinoma were diagnosed and managed at the JUH during the period 1977–1996, inclusive. Seventy-seven patients (85 per cent) came from the third socioeconomic

TABLE I
PRESENTATION OF NASOPHARYNGEAL CARCINOMA

Single symptom	No.	%
Neck swelling	32	45.5
Ear symptoms	15	21
Tinnitus	8	
Blockage	5	
Ache	2	
Headache	10	14
Nasal symptoms	6	9
Obstruction	3	
Discharge	2	
Bleeding	1	
Pain	5	7
Ophthalmic	2	3
Multiple symptoms		
Nasal obstruction	11	16
+ Epistaxis	6	
+ Discharge	2	
+ Ear block	2	
+ Neck swelling	1	
Hearing	4	6
+ Tinnitus	2	
+ Neck swelling	1	
+ Ear Ache	1	
Ear blockage	3	4
+ Neck swelling	1	
+ Hearing	1	
+ Fluid sensation	1	
Neck swelling	3	4
+ Dysphagia	1	
+ Ear, nose	2	

TABLE II
NUMBERS AND SITES OF METASTASES IN 31 PATIENTS WITH METASTATIC NPC

	Bone	Lung	CNS	Others
Spine	11	7	7	4
Pelvis	9			
Ribs	4			
Skull	4			
Limbs	4			
Total	32	7	7	4

class judged by their jobs, place of residence, method of health insurance and hospital class upon admission.

Age and sex

The youngest and the oldest patients were both males aged six and 89 years (Figure 1). The mean age was 39.5 years for the whole group and male to female ratio 1.5:1 (the age of one female patient was uncertain and therefore was not included).

Presenting symptoms

Seventy patients (77 per cent) presented with a single complaint and 21 (23 per cent) presented with multiple complaints (Table I). Some of the presenting symptoms were only indirectly related to ENT lesions. The most common single presenting symptom was neck swelling (45.5 per cent).

Associated symptoms

Complaints considered by the patients of secondary importance and therefore not mentioned at the first presentation were diverse, some of which were remotely related to ENT lesions (Table I).

Sites of carcinoma in nasopharynx

In 37 patients (41 per cent) carcinoma affected one site of the nasopharynx most frequently a lateral wall.

Thirty-five patients (38 per cent) had multifocal malignant involvement of the nasopharynx. In 19 patients (21 per cent) the nasopharynx appeared normal and no site of involvement could be seen at the time of first diagnosis.

TABLE III
SITES OF DISTANT METASTASIS IN 13 PATIENTS WITH NPC

Case no.	Sites of metastasis
3	Spine (Lumbo-sacral), inguinal lymph nodes
4	Spine (8th dorsal vertebra)
5	Spine (not specified)
9	Bone marrow
10	Lung
27	Multiple CNS
30	Spine (L3 & L4)
34	Brain (temporal lobe)
40	Both lungs, right humerus, spine (D7 and D8)
54	Chest wall
62	Brain & spinal cord
66	Spine (S2, S3)
75	Brain (right cerebello-pontine angle)

TABLE IV
AGE RANGE OF NPC IN COUNTRIES OF HIGH AND INTERMEDIATE INCIDENCE RATE

Author/Year	NPC incidence	Country/Population	Age range	Childhood peak
Easton <i>et al.</i> (1980)	Intermediate	N. American	10–89	+ (Adolescent)
Jamal (1991)	Intermediate	Jordan	6–69	+
Jenkin <i>et al.</i> (1981)	Intermediate	N. American	1st – 3rd decade	+
Muir <i>et al.</i> (1987)	Intermediate	N. American (White)	15–85	+
		N. American (Black)	10–75	+
		N. American (Chinese)	10–75	+
Present study	Intermediate	Jordan	6–89	+
Indudharan <i>et al.</i> (1997)	High	Malaysia	15–82	–
Muir <i>et al.</i> (1987)	High	Chinese (Shanghai)	10–70	–
		Chinese (Tianjin)	5–75	–
		Chinese (Hong Kong)	5–85	–
Sham <i>et al.</i> (1990)	High	Hong Kong	9–20	–

Histology

Keratinizing squamous cell carcinoma (WHO type I) accounted for 15 per cent of all cases of NPC, 85 per cent were due to non-keratinizing types. The segregation of the latter into squamous and undifferentiated (WHO types II and III respectively) was difficult using light microscopy only.

Distant metastasis

Thirty-one patients (34 per cent) showed metastasis (Table II) of whom 13 cases appear in Table III; the rest (18 cases) have been reported previously (Jamal, 1991).

Discussion

The patients included in this study were of the same ethnic derivation of Arabs (Muslims and Christians) having similar social and dietary habits. The Jordanian diet is only mildly spiced and, generally, is rich in fresh vegetables all year round. Twenty adult males (22 per cent) were smokers or ex-smokers but this habit was not ascertained in any of our female patients. The taking of snuff, is extremely scarce in Jordan and none of the patients in the present series practised such a habit. Incense is rarely used. One male patient was a carpenter, another a painter, a third a mechanic and three others were farmers. In these, a possible role of wood dust, fumes and spray insecticides in the aetiology of NPC, although far from being certain, is worth noticing and following-up in prospective studies. However, all other males were employees, businessmen or students and the vast majority of females were housewives, employees or students.

In the present series NPC accounts for one per cent of all malignant tumours during the period. Similar frequencies have been reported in some Arab countries (Lemaigre *et al.*, 1977; Hidayatallah *et al.*, 1983; Al-Qassab *et al.*, 1987; Mokhtar, 1991; El-Hassani, 1996). NPC in the present study occurs at a frequency nearly half that of laryngeal carcinoma. The proportion affecting males in the latter site (170 of a total of 178 cases) far outnumbers that in NPC. This observation suggests a less dominant role for cigarette smoking (a mainly male habit) in the aetiology of NPC than laryngeal carcinoma.

The age distribution curve was bimodal in the present series with a peak occurring between 16 and 20 years and another between 46 and 50 years. A bimodal age incidence curve, with an older age at the second peak, has been attained previously in European and North American populations (Berry *et al.*, 1980; Easton *et al.*, 1980; Levine *et al.*, 1980; Jenkin *et al.*, 1981; Muir *et al.*, 1987; Singh, 1987). A similar bimodal curve was shown in other populations of intermediate incidence of NPC (Ellouz *et al.*, 1978; Jamal, 1991). In contrast, no such bimodal age incidence curve was noticed in populations with a high incidence rate of NPC including Hong Kong (Sham *et al.*, 1990), Malaysia (Indudharan *et al.*, 1997) and in Chinese populations in China, Singapore and Hong Kong (Muir *et al.*, 1987) (Table IV).

Keratinizing squamous cell carcinoma in our series occurred in an older age group (mean age 54 years) than NPC as a whole (mean age 39.5 years). This type was not seen in the children with NPC in the present study.

NPC was present in 10 children up to 15 years of age among a total of 655 childhood malignancies seen during the period. The relative frequency in childhood NPC in the present series is higher than that reported in several other countries (Marsden and Steward, 1976; Friedmann, 1986; Pao *et al.*, 1989; Fenton *et al.*, 1995; Iyan and Altun, 1996). In a more recent report from Malaysia there was no case of NPC seen in any one less than 14 years old (Indudharan *et al.*, 1997). This observation questions the uniformity of aetiological factors in different geographical places.

EB virus was causally related to all types of NPC except for keratinizing squamous NPC (Tamada *et al.*, 1984; Guffey and Weiss, 1992; Liebowitz, 1994). More recently, it has been indicated that some cases of squamous cell NPC have an association with EB virus with a variability similar to that of Burkitt's lymphoma (Nicholls *et al.*, 1997). Accumulating evidence suggests that the tumour results from the combined action of genetic predisposition, environmental factors and EB virus (Chan *et al.*, 1983; Yu *et al.*, 1986; Kawachi *et al.*, 1989; Guffey and Weiss, 1992; Liebowitz, 1994).

Among several possible factors in the aetiology of NPC the fumes produced from portable paraffin heaters of popular use, especially among the poorer

classes in Jordan, has been suspected (Jamal, 1991). The present study shows that 85 per cent of the patients come from the lowest socioeconomic class living in residences with poor ventilation and generally low hygienic standards.

In the present series, out of a total of 70 patients (77 per cent) presenting with single symptoms and 21 patients with multiple symptoms, neck swelling was the most common presenting symptom followed by ear and nose symptoms in that order of frequency. More cases of neck swelling were detected on clinical examination. The condition, being commonly painless, was overlooked especially by male patients who were less aware of the disfigurement produced and the possibly serious results than the females.

Symptomatic treatment was carried out for short-term headache and nasal symptoms not associated with other complaints. Full ENT examination and relevant investigations were performed for recurrent or persistent nasal symptoms, tinnitus and headache with obscure underlying aetiology. Cases with multiple symptoms as well as neck swelling were taken more seriously in most cases and were investigated and managed accordingly. However, there was delay in seeking medical advice up to several weeks in many cases. Ten cases with headache (14 per cent) presented as single symptoms, in two cases of which the diagnosis was missed and delayed until other symptoms emerged. Therefore, full ENT examination has since been adopted in cases with persistent headache regardless of the absence of other complaints.

The most common site of metastasis involved the bone, notably the spine. Routine bone scan for the cases with NPC has recently been adopted in our department. The mean age of patients with secondary deposits was (38.6 years) lower than that of the whole group (39.5 years). This difference was statistically insignificant suggesting a similar behaviour of the disease in the young as in the old. In agreement with previous observations (Indudharan, 1997) there was no sex predilection in our patients with metastasis. In cases where there are no masses seen in the nasopharynx we adopt, and recommend, taking blind biopsies from the right and left lateral walls (near Eustachian tube openings) and from the posterior wall in order to minimize the chances of missing a small tumour.

Conclusion

Nasopharyngeal carcinoma is found in Jordan especially among the lower socioeconomic classes. The tumour occurs in both sexes with no age exemption. A prospective study is needed to investigate the extent of causal relationship to EB virus and other environmental factors. Blind biopsies from the nasopharynx in cases of unexplained neck swelling or persistent ENT symptoms are recommended. Bone scanning is recommended in each case with NPC especially in the presence of signs and symptoms suggesting involvement of the spine.

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References

- Al-Qassab, K., El-Hassani, M., Al-Zahawi, H., Al-Nasiri, N. (1987) Results of Iraqi Cancer Registry 1976-1985. Iraqi Ministry of Health, pp 9 and 29.
- Berry, M. P., Smith, C. R., Brown, T. C., Jenkin, R. D. K., Rider, W. D. (1980) Nasopharyngeal carcinoma in the young. *International Journal of Oncology Biology and Physics* **6**: 415-421.
- Chan, S. H., Day, N. E., Kunaratnum, N., Chia, K. B., Simon, M. J. (1983) HLA and nasopharyngeal carcinoma in Chinese. A further study. *International Journal of Cancer* **32**: 171-176.
- Children's Tumour Registry in Manchester, 1983 quoted from Friedmann, I. (1986).
- Easton, J. M., Levine, P. H., Hyams, V. J. (1980) Nasopharyngeal carcinoma in the United States. A pathologic study of 177 U.S. and 30 foreign cases. *Archives of Otolaryngology* **106**: 88-91.
- El-Hassani, M. (1996) Results of Iraqi cancer Registry 1992-1994. Iraqi Ministry of Health. pp 23-29.
- Ellouz, R., Cammoun, M., Ben Attia, R., Bahi, J. (1978) Nasopharyngeal carcinoma in children and adolescents in Tunisia. Clinical aspects and the paraneoplastic syndrome. *IARC Scientific Publications* **20**: 115-129.
- Fenton, J., Viani, L., Lang, J., Walsh, M. (1995) Nasopharyngeal carcinoma. The Irish experience. *Irish Medical Journal* **88** (1): 22-23.
- Friedmann, I. (1986) Malignant tumours of the nasopharynx. In *Systemic Pathology: Nose Throat and Ears*. (Symmers, W., ed.) 3rd Edition, Churchill Livingstone, Edinburgh, p 143.
- Guffey, M. J., Weiss, L. M. (1992) Association of Epstein Barr virus with human neoplasia. *Pathology Annual* **27**: 55-74.
- Hidayatallah, A., Malik, M. O., El-Hadi, A. E., Osman, A. A., Hutt, M. S. (1983) Studies on nasopharyngeal carcinoma in the Sudan - I. Epidemiology and aetiology. *European Journal of Cancer and Clinical Oncology* **19** (6): 705-710.
- Iyan, I., Altun, M. (1996) The nasopharyngeal carcinoma in children: retrospective review of 50 patients. *International Journal of Radiation Oncology Biology Physics* **35**(3): 485-492.
- Indudharan, R., Vallyveetham, K. A., Kannan, T., Sidek, D. S. (1997) Nasopharyngeal carcinoma: Clinical trends. *Journal of Laryngology and Otology* **111**: 724-729.
- Jamal, M. N. (1991) Clinical evaluation of nasopharyngeal carcinoma in Jordan. *Journal of Laryngology and Otology* **105**: 432-435.
- Jenkin, R. D. T., Anderson, J. R., Jereb, B., Thompson, J. C., Pyesmany, A., Wara, W. M., Hammond, D. (1981) Nasopharyngeal carcinoma. A retrospective review of patients less than 30 years of age. A report from Children's Cancer Study Group. *Cancer* **47**: 360-366.
- Kawachi, I., Pearce, N., Fraser, J. (1989) A New Zealand cancer registry-based study of cancer in wood workers. *Cancer* **64**: 2609-2613.
- Lemaigre, G., Diebold, J., Temmim, L., Arseniev, L., Lecharpentier, Y., Alouache, A., Delaitre, B., Abelanet, R. (1977) Carcinome du nasopharynx chez le sujet jeune. Etude clinique, anatomique et ultrastructural de 50 cas observe dans l'est algerien. *Nouvelle Presse Medicale* **6**(38): 3509-3513.
- Levine, P. H., Connelly, P. R., Easton, J. M. (1980) Demographic patterns for nasopharyngeal carcinoma in the United States. *International Journal of Cancer* **26**: 741-748.
- Liebowitz, D. (1994) Nasopharyngeal carcinoma. The Epstein-Barr virus association. *Seminars on Oncology* **21**: 382-397.

- Marsden, H. B., Steward, J. K. (1976) Tumours in children. In *Recent Results in Cancer Research*, 2nd Edition, Springer-Verlag, Berlin, Heidelberg, New York. pp 6, 415.
- Mokhtar, N. (1991) Cancer Pathology Registry 1985–1989. National Cancer Institute, Cairo University. Published by the Department of Pathology. pp 3, 41.
- Muir, C., Waterhouse, J., Mack, T., Powell, J., Whelan, S. (1987) In *Cancer Incidence in Five Continents*. Vol. V. IARC Scientific Publications No. 88, pp 284–293, 396–405.
- Nicholls, J. M., Agathangelov, A., Fung, K., Zeng, X., Niedobitek, G. (1997) The association of squamous cell carcinoma of the nasopharynx with Epstein Barr virus shows geographical variation reminiscent of Burkitt's lymphoma. *Journal of Pathology* **183** (2): 164–168.
- Pao, W. J., Hustu, H. O., Douglas, E. C., Beckford, N. S., Kun, L. E. (1989) Pediatric nasopharyngeal carcinoma: long-term follow-up of 29 patients. *International Journal of Radiation Oncology Biology Physics* **17**: 299–305.
- Sham, J. S., Poon, Y. F., Wei, W. I., Choy, D. (1990) Nasopharyngeal carcinoma in young patients. *Cancer* **65**: 2606–2610.
- Shanmugaratnam, K., Chan, S. H., de Thé, G., Goh, J. E., Khor, T. H., Simons, M. J., Tye, C. Y. (1979) Histopathology of nasopharyngeal carcinoma: correlation with epidemiology, survival rates and other biological characteristics. *Cancer* **44**(3): 1029–1044.
- Singh, W. (1987) Nasopharyngeal carcinoma in Caucasian children. A 25-year study. *Journal of Laryngology and Otology* **101**(12): 1248–1253.
- Tamada, A., Makimoto, K., Yamabe, H., Imai, J., Hinuma, Y., Oyagi, A., Araki, T. (1984) Titers of Epstein Barr virus-related antibodies in nasopharyngeal carcinoma in Japan. *Cancer* **53**: 430–440.
- Yu, M. C., Ho, J. H. C., Lai, S. H., Henderson, B. E. (1986) Cantonese-style salted fish as a cause of nasopharyngeal carcinoma. Report of a case control study in Hong Kong. *Cancer Research* **46**: 956–961.

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