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DISTANT METASTASES FROM NASOPHARYNGEAL CARCINOMA AT KENYATTA NATIONAL HOSPITAL, NAIROBI
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ABSTRACT

Objectives: **To determine the frequency and site of distant infraclavicular metastases of nasopharyngeal carcinoma (NPC), the stage of the primary tumour at presentation of metastasis and the histological trends. To determine if there is a correlation between the follow-up rate and different metastatic sites.**
Design: **A retrospective study.**
Setting: **Ear nose and throat surgical and radiotherapy clinics at Kenyatta National Hospital, Nairobi.**
Subjects: **Case notes, radiotherapeutic and laboratory records of patients presenting with NPC between January 1981 and December 1990.**
Results: **The frequency of distant NPC metastases was 14.6% and 92.3% manifested within 24 months of admission. It was most frequent in the males, a younger age group and early T1 disease. Bilaterality of the neck nodes had no relevance on metastatic rate. The bone (66.7%) was the most common distant metastatic destination followed by the liver (23.2%). Liver metastasis was associated with a shorter follow-up period.**
Conclusion: **Apart from the late presentation of locoregional disease, the findings are similar to studies elsewhere. The preponderance of early primary disease in patients with distant metastasis need further appraisal as it preliminarily suggests existence of specific biological markers that favour metastases. This can only be done after recruiting more cases.**

INTRODUCTION

Nasopharyngeal carcinoma (NPC) is the second most frequent head and neck tumour at the Kenyatta National Hospital (KNH) cancer registry as depicted in Table 1.

The frequency of distant metastases in NPC among various head and neck tumours is known(1,2). The implications of this event on the management approach and survival are clear. The magnitude of this problem had never been clarified in KNH before this study. In the third world, peculiar problems including shortage of medical facilities and expertise, general ignorance by the lay public on disease processes, lack of basic infrastructure and general poverty may be modulators in disease presentation hence the importance of this study. Various studies have shown delayed presentation of major head and neck cancers to the Ear, Nose and Throat - Head and Neck Surgery (ENT-HNS) unit of KNH(3) .

Previous claims that distant head and neck cancer metastases below the clavicle were uncommon have been dispelled over the last century(4-6). Over the last five decades, there has been a notable increase in NPC patients with distant infraclavicular metastases probably due to effective control of the locoregional disease and improved survival(7). In this study, the frequency, sites and other factors affecting distant infraclavicular metastases in a third world environment are determined.

MATERIALS AND METHODS

Case notes of patients admitted between January 1981 and December 1990, in the Ear Nose and Throat-Head and Neck (ENT-HN) Surgery and the Radiotherapy Units of KNH with histologically verified NPC were retrieved and screened for evidence of distant metastasis.

Bone metastasis had to be radiologically qualified while physical signs, ultrasound and/or laboratory results were the criteria accepted for diagnosis of soft tissue involvement. Those with clinical and/or radiological evidence of distant metastasis were reviewed for age, sex, AJC 1978 stage of locoregional disease and sites of distant infraclavicular metastases. This staging system was used because it was the most reliable operational staging system during the period of patient presentation. The time of presentation during the course of the disease, management modalities and follow-up period for different metastatic categories were determined.

RESULTS

A total of 445 patients presented with NPC during the ten-year period. Of these, 333 were males and 112 females. Ninety three point nine per cent had clinically palpable

cervical nodes. There was no distant metastasis at presentation. Sixty-five patients (14.6%) developed distant metastasis during the course treatment.

The following results are derived from the 65 patients with distant NPC metastasis. Males were more likely to develop metastasis than females the cumulative risk being 21.1% and 9.9% respectively giving M:F ratio of 4.9:1. Figure 1 shows the age distribution. The younger age groups had more predisposition to distant NPC metastasis.

Table 1

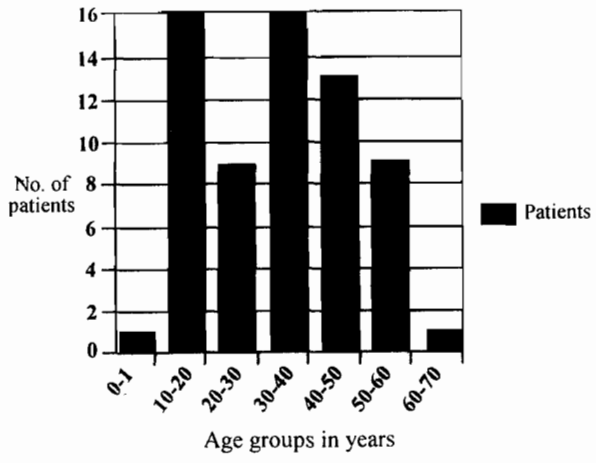
Twenty most frequently occurring cancers in Kenya (1986 - 1990)

Cancer	No. of cases
Cervix	500
Non Hodgkin's lymphoma (including Burkitt's lymphoma)	313
Breast	272
Skin	253
Oesophagus	239
Nasopharynx	234
Kaposi's sarcoma	154
Eye (primary orbital)	134
Connective tissue	130
Mouth and palate	130
Brain and nervous tissue	125
Bones	104
Hodgkin's lymphoma	100
Stomach	100
Larynx	96
Malignant melanoma	95
Liver	73
Prostate	65
Salivary glands	60
Thyroid	44

From the cancer registry, Department of Human Pathology, University of Nairobi

Figure 1

Age distribution in years



The M:F sex ratio was 4.9:1. WHO Type III was the most frequent histological variant accounting for 89.2% of NPC cases. The incidence of distant NPC was similar among the histological types in the 445 general NPC pool. The highest proportion of patients with distant metastasis was in the T1 stage (Table 2).

Table 2

Primary NPC stage vs. distant NPC metastasis

Stage	Frequency	%
T1	28	43.1
T2	18	27.7
T3	8	12.3
T4	11	16.9
Total	65	100

At presentation of distant metastasis the cervical nodes had regressed in 47.7%, persisted in 49.2%, recurred in 3.1% (this has to be compared to 93.3% incidence during the initial presentation of NPC and lack obvious clinically palpable nodes in 6.1%). There was no obvious clinically palpable node. Bilaterality of the neck disease did not increase predisposition to distant metastasis (Table 3). Controlled primary disease seemed to increase the risk of distant NPC metastasis. Sixty per cent of patients with metastasis had complete control of the primary disease.

Table 3

Location of cervical nodes in NPC distant metastasis

Nodes	Frequency	%
Unilateral	31	47.7
Bilateral	30	46.2
Not palpable	4	6.1
Total	65	100.0

The vertebral column at the lumbar level was the most frequent distant metastatic destination for the NPC followed by the liver (Table 4). Metastases were frequently characterised by the relevant organ symptoms and signs.

Table 4

Individual organ involvement by distant NPC metastasis

Site	Frequency	%
Lumbar vertebrae	27	27.3
Liver	23	23.2
Ribs	12	12.1
Pelvis	9	9.1
Femur	7	7.1
Lungs	5	5.1
Thoracic vertebrae	4	4.1
Sternum	3	3.0
Inguinal lymph nodes	2	2.0
Scapula	2	2.0
Sacral vertebrae	1	1.0
Spleen	1	1.0
Stomach	1	1.0
Tibia	1	1.0
Breast	1	1.0
Total metastatic events	99	100

The follow-up period seemed to depend on liver involvement. While the average crude follow-up period was 4.1 months, further analysis revealed that it was 5.2 months in those with multiple organ involvement. Of those patients with multi-organ involvement, follow-up was 6.1 months if the liver was not involved and only 8.8 weeks if the liver was clinically involved. Most patients who did not come back for follow-up were noted to be weak on their last visits while others were discharged to health units nearest to their homes for terminal management.

DISCUSSION

The appearance of distant metastases in any malignant disease has profound consequences on the prognosis of the disease and the economics of patient management. NPC is the most frequent head and neck tumour in Kenya. This study is, therefore, of specific interest to health care providers in third world countries with a similar cancer epidemiology and budgetary constraints like Kenya.

Many studies during the last century dispelled previous claims that distant metastases from head and neck cancer are unusual and NPC has been shown to have the most frequent rate of distant infraclavicular metastasis(9,18). In this study, all distant metastases appeared within 24 months of treatment and the incidence was found to be 14.9%, a figure comparing favourably with those from reported series elsewhere(10). Higher incidences of upto 28.1% have been found in other studies(2,11).

The absence of metastases at presentation is probably a result of the retrospective nature of the study and poor case note documentation. A recent prospective study in the same hospital showed a 5.8% distant metastasis rate at presentation(3). The same study showed that 96.4% of NPC and laryngeal cancers presented at the advanced stage 3 or 4 disease. The higher male predominance in both locoregional and distant metastatic NPC has not been clearly explained.

The low frequency of general NPC patients and those with distant metastases during the fifth and sixth decades is in keeping with the shape of Kenya's population actuarial curves. The high incidence of metastasis in the younger and middle age group, however, needs to be clarified further by well designed larger population studies. The high preponderance of WHO type 1 is in keeping with the general histological prevalence of NPC and is an expected biological behaviour in all high grade malignant disease. T1 tumours were also shown to have had a higher incidence of distant NPC metastasis, probably due to better locoregional disease control leading to longer survival and better chances of development of distant metastasis. However, due to numbers involved in this study, no direct correlation between tumour stage and metastasis rate could be shown. Such findings have been documented elsewhere(7). It is of relevant interest that 60% of patients with NPC metastasis had clinically controlled primary disease and that WHO type 1 are more radiosensitive than the rest of the other types. One would therefore expect a situation of good local control and early distant metastasis. The possibility of existence of a significant population of NPC tumour subtype among the WHO type 1 whose biological activity favour early metastasis should also be considered.

Simple bilaterality of cervical nodes without considering the size and level of the nodes did not affect the prognosis of NPC. This finding is expected and is one of the factors that led to harmonisation of UICC and AJC staging of nasopharyngeal carcinoma(12).

There was lack of consistent policy on which treatment regimes for NPC patients were based. However, treatment of general NPC patients and those with bony metastases was by radiotherapy. Chemotherapy was left at the discretion of the radiotherapist. This state of affairs underlines the various difficulties that frustrate organised treatment of cancer patients. Erratic supply of the generally expensive chemotherapeutic drugs and long waiting periods for the scarce radiotherapy facility obviously have their contribution to this lack of consistent management strategy.

The average follow-up after diagnosis of NPC distant metastases was 4.1 months. As in other cancers, liver involvement was shown to have a negative influence in the duration of follow-up. In third world countries with no mandatory death registries and where terminal and palliative care facilities are non-existent, it is difficult to assess patient survival and management results. Therefore, many cancer management centres have to rely on follow-up duration as a crude indicator of survival. This indicator is in turn influenced by distances from the referral hospital, lack of all weather roads, poverty and the patient's trust in alternative medicine. But crude as this indicator may be it is currently the only available pointer of cancer patient survival in many third world countries.

With the poor prognostic significance of metastasis, one of the current main aims in NPC management is to prevent their appearance in the first place. Various treatment regimes for the primary have been tried and recent evidence suggests that simultaneous radiotherapy and cis-platinum based chemotherapy reduces incidence of distant metastasis and improves survival(13). Neither induction chemotherapy and radiotherapy nor extended irradiation of mediastinum and axilla have any effect on the appearance of metastases(14,15). Elsewhere, investigations are on to determine risk factors and screening techniques for micrometastases in NPC. For example, the rate of expression of cytokeratin 19 on circulating tumour cells have been found to increase with tumour stage, with cured NPC showing negative expression while population of patients with metastatic NPC show 75% expression rate(16). Expression of EBNA 1 DNA by peripheral blood cells is associated with enhanced malignant progression and a higher risk of developing distant metastases(17,18).

CONCLUSION

Apart from the late presentation of locoregional disease, the findings are similar to studies elsewhere. The preponderance of early primary disease in patients with distant metastasis needs further appraisal as it preliminarily suggests existence of specific biological markers that favour metastases. This can only be done after recruiting more cases into this study.

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