

TREATMENT OF NASOPHARYNGEAL CARCINOMA IN SINGAPORE

A STUDY OF 545 CASES TREATED BETWEEN 1960-1964

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SYNOPSIS

The lack of information about the treatment results of nasopharyngeal carcinoma in Singapore has been due largely to the poor follow-up of patients in the past. This study of patients treated with radiotherapy between 1960 and 1964 showed the disease to be especially prevalent in Chinese between the 4th and 6th decades of life. Only 10% had disease limited to the nasopharynx. 80% presented with lymph node metastases and 30% with cranial nerve lesions. In planning treatment with radiotherapy it is important to deliver adequate dosage to the primary lesion, the base of skull and the cervical lymph nodes. Of the 545 patients referred for treatment during this period, only 412 completed their full course of radiotherapy, and the crude 5 year survival rate for this group was 23.5%. Where the growth was confined to the nasopharynx, the survival rate was 50%. Females showed a better prognosis than males. Radiation myelitis as a complication of treatment was rare and was seen only in cases receiving repeated treatment. With early detection of cases and the use of supervoltage irradiation treatment results could be expected to improve.

INTRODUCTION

Mekie and Lawley (1954) collected 120 cases of nasopharyngeal carcinoma seen at the General Hospital, Singapore between 1947 and 1953 and observed their longest survival from earliest symptoms as 3 years with an average survival of 13½ months.

There were no large scale local clinical studies of these cases and their survival since then until 1964 when Chia reported some preliminary results of treatment in a paper presented at the UICC Symposium on Nasopharyngeal Carcinoma in Singapore (Chia, 1964). This lack of information has been largely due to the inadequate follow up of treated patients.

However, since 1960 increased efforts were made to trace patients treated at the Radiotherapy Department in Singapore within the limitations of the facilities available. Although the follow up was far from complete some interesting facts on the results of treatment have been elucidated from the available data.

The difficulty in achieving adequate follow up is due to some of the following factors:

1. Patients' failure to appreciate the need for continued surveillance when they were free from symptoms;
2. Unreliability of some of the old records of addresses;
3. Lack of personnel to trace out and call up defaulters;
4. The inclusion of patients in the series from neighbouring Malaysia, Brunei and Indonesia who could not be expected to make regular visits to Singapore.

Presently, some of these difficulties are being overcome and we hope to get better information for future studies.

TREATMENT METHODS

One of the earliest reports from Singapore on treatment of nasopharyngeal carcinoma is Mekie's article on "Lymphoepithelioma" (1949) in which he commented on the poor results of deep X-ray therapy with the facilities then available. He remarked, "While it is to the radiologist that apparently we must look for a curative method of treatment the question of the relief of suffering amongst those who are incurable is pressing". He advocated the use of prefrontal leucotomy as a method of relieving the intense headache and suffering associated with the late stages of the disease. Fortunately, today with better understanding of the disease and improved radiotherapeutic methods we do

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not have to resort to such drastic surgical methods. Surgery's role is primarily to obtain biopsy confirmation of the primary growth and, on occasion, to deal with radio-resistant lymph nodes.

Chemotherapy has been used from time to time but the results have proved disappointing and its role is confined to palliation of wide-spread disease where radiotherapy is not technically feasible.

RADIOTHERAPEUTIC MANAGEMENT

The mode of spread of the disease constitutes a problem in the planning of radiotherapy for this condition.

1. The growth may extend from the post nasal space to the nasal fossae, orbits, palate, oropharynx, tonsils and to the parapharyngeal space;
2. It may invade the sinuses and base of skull and also spread intracranially through the foramen lacerum or other foramina, including the foramen magnum, thus often giving rise to cranial nerve lesions;
3. The tumour more often than not spreads to the lymph nodes. The lymph nodes generally involved are the lateral parapharyngeal nodes (which are not palpable clinically), the jugulo-digastric group and the deep nodes of the posterior triangle.

Lymph node metastases are so common that an adult Chinese presenting with a metastatic node under the upper posterior aspect of the sternomastoid is considered a case of carcinoma of the nasopharynx until proved otherwise; intensive investigations must then be carried out to demonstrate the primary e.g. contrast studies of the nasopharynx (Khoo, Chia and Nalpon; 1967) examination under anaesthesia, transpalatal strip biopsy of the post nasal space and so on.

TECHNIQUES OF TREATMENT

2 Field Treatment

The earliest method of treatment in Singapore involved the use of 2 large opposing cervico-facial fields with conventional X-rays covering the base of skull including the basisphenoid above and the supraclavicular region below.

The average field size was 15×20 cm. and an incident dose of 3,500-4,000 rads was given. Estimated midline dose was in the region of 4,000-4,500 rads given in 5½-6 weeks. This dose was thought to be adequate for what was then referred to as lymphoepithelioma, an entity believed to be highly radio-sensitive. It soon became apparent, however, that despite the appreciable regression of the cervical nodes, the primary in the nasopharynx was seldom eradicated and this method has been abandoned for more radical treatment. However, it is still used in the palliative treatment of massive cervical node metastases.

To increase the dose to the nasopharynx 2 small anterior oblique fields were added to the lateral cervico-facial fields.

The oblique fields each measuring 4×4 cm. were placed in the anterior maxillary regions just below the orbits and inclined towards the nasopharynx. The lateral fields were reduced to 10×20 cms. By this method a dose of 5,500 rads could be given to the nasopharynx in 6-7 weeks. Although many lasting cures were obtained by this technique, there were some recurrences in the choana, orbits and ethmoids. The technique is inherently difficult to set up accurately and errors in beam direction probably played a part in the treatment failures.

3 Field Technique

To achieve better accuracy the use of a direct anterior field was introduced. This field extended from just above the glabella to the columella, with both eyes protected by lead shielding. This field was used together with the 10×20 cm. lateral cervico-facial fields.

The incident dose to each field is about 4,000 rads and the dose to the post nasal space is in the region of 5,500-6,000 rads delivered in about 7 weeks. This method was used continuously from 1960 until the advent of cobalt therapy in Singapore in 1969.

CLINICAL MATERIAL

In a study of 545 cases of nasopharyngeal carcinoma treated between 1960 and 1964 at the Radiotherapy Department, we found the following clinical features:

Ethnic Group

The Chinese who make up 74.4% of the population in Singapore account for most of these cases, as shown in Table I.

TABLE I
CASES TREATED BETWEEN 1960 TO 1964
ACCORDING TO ETHNIC GROUPS

Chinese	521	95.6%
Malays	18	3.3%
Indians	3	0.6%
Others	3	0.6%
Total	545	

Age

Most of the cases occurred between the 4th and 6th decades of life and the peak incidence was in the 40-49 age group.

TABLE II
CASES TREATED BETWEEN 1960 AND
1964 ACCORDING TO AGE GROUPS

10-19	20-29	30-39	40-49	50-59	60-69	70+
12	34	103	170	155	61	9

Histology

All the cases mentioned in this paper were histologically proven squamous cell carcinomata, almost all poorly differentiated and referred in the past as lymphoepithelioma.

Cranial Nerves and Lymph Nodes

The frequency of cervical node and cranial nerve involvement is shown in the following table:

TABLE III
CERVICAL NODE AND CRANIAL NERVE
INVOLVEMENT (1960-1964)

Total Number irradiated	545	
Number with cervical nodes	445	82%
Number with cranial nerve involvement	163	30%

Results of Treatment

An assessment of the results of treatment using the 3 field conventional X-ray therapy is given below:

It must be pointed out that:

1. All cases of nasopharyngeal carcinoma referred to the Radiotherapy Department

- between 1960 and 1964, and histologically proven are included in this study;
2. All cases were treated irrespective of stage of disease unless actually moribund;
3. All cases lost to follow up are presumed dead from the disease.

TABLE IV
CASES TREATED BETWEEN 1960
AND 1964

Total No. treated	545
No. alive over 5 years	97
Crude 5 year survival	17.8%

Inadequate Treatment

However, not all the above cases completed their treatment. 133 or about 24% either did not have any irradiation to the nasopharynx or received doses below the minimum 4,500 rads. These inadequately treated cases can be divided into the following categories:

1. Those who defaulted in favour of treatment by herbalists, acupuncturists and pedlars of native medicine. These constitute about 40% of the inadequately treated group;
2. 24% presented with widespread metastases when first seen and were treated only palliatively;
3. 20% could not tolerate their treatment after receiving about 2 weeks or so of treatment;
4. 16% had had treatment elsewhere with radiation or chemotherapy and could not therefore be given a full course of radiotherapy.

TABLE V
CASES INADEQUATELY TREATED

1. Deliberately defaulted treatment	40%
2. Widespread metastases	24%
3. Unable to tolerate	20%
4. Previous radiation or chemotherapy elsewhere	16%

Excluding these incompletely treated cases, the results are as follows:

TABLE VI

No. adequately treated	412
No. alive over 5 years	97
Crude 5 year survival	23.5%

Results according to Stage of Disease

As with other cancers the stage at which the patient is treated has an important bearing on the prognosis.

TABLE VII

CASES GIVEN ADEQUATE RADIATION

1. Growth confined to Nasopharynx No. survived 5 years Crude 5 year survival	56 cases 28 cases 50%
2. With cervical nodes No. survived 5 years Crude 5 year survival	339 cases 67 cases 19.8%
3. With cranial nerve lesions No. survived 5 years Crude 5 year survival	122 cases 9 cases 7.4%

Results according to sex

There appeared to be a slightly better prognosis in females compared with males.

TABLE VIII

No. of Male patients No. survived 5 years Crude 5 year survival	281 63 22.4%
No. of Female patients No. survived 5 years Crude 5 year survival	131 34 26%

SIDE EFFECTS

Radiation sickness seldom occurs with this regime of treatment and patients may continue working while on radiotherapy. However, where sickness occurs it is usually mild and can be controlled with antimetics.

A little more than 2 weeks after commencement of therapy there is usually a mucosal reaction in the pharynx. Normally, this can be treated with antibiotics, analgesics and a good intake of fluids. However, where severe, the patient is rested from treatment for a few days.

Dryness of mouth and loss of taste due to radiation effects on the salivary glands may persist for many months after irradiation. Dental caries also is a problem after treatment; and it is important not to have dental extractions done for some years after radiation.

Some epilation of hair around the neck usually occurs but this is not much of a problem.

The severe skin reactions which followed conventional X-ray therapy are hardly seen now with cobalt and caesium therapy.

COMPLICATIONS OF TREATMENT

Complications following treatment were rare. In this series it is only after a repeat course of radiotherapy for a recurrence that there is a grave risk of radiation myelitis. Out of 22 cases of nasopharyngeal carcinoma who had a repeat full course of treatment, 3 cases developed radiation myelitis (Tan and Khor, 1969). This is surprising because we do not shield the brainstem. One unusual case of pituitary dwarfism was documented in a girl of 12 who had received 2 courses of treatment (Tan and Kunaratnam; 1966).

COMMENTS

Lederman (1961) summarised the world literature on the results of treatment of nasopharyngeal carcinoma from 1944-1958, and showed that the 5 year survival rate varied from 5.5% to 30% with an average of 15.7%. Our figure, for those who completed radiotherapy, of 23.5% is well above this average. More recently in a study of 170 patients of nasopharyngeal carcinoma, Wang (1971) gave an overall 5 years survival rate of 39%. However, this included only those cases treated radically. The histology of these cases according to his classification included "squamous cell carcinoma", "Transitional cell carcinoma", "Lympho-epithelioma" and "undifferentiated carcinoma".

Treatment failures in the past have been due largely to either inadequate dosage to the nasopharynx or failure to cover the possible avenues of spread of the disease. Improved and more accurate techniques with supervoltage radiation, which was introduced in Singapore by the acquisition of Cobalt and Caesium teletherapy units in 1969, gives promise of better results.

As the stage of the disease has an important bearing on prognosis further improvement in results can be achieved by promoting early detection by cancer education programmes and better diagnostic techniques e.g. endoscopy and X-ray contrast study. From the results presented early cases should have at least a 1 in 2 chance of cure. However, improvement of the results in patients with extensive disease would be difficult

in spite of advancement of radiotherapeutic techniques (Wang, 1971).

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