Treatment of Nasopharyngeal Carcinoma by Using Deep X-Ray Therapy

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Abstract

Background: Nasopharyngeal carcinoma (NPC) is one of the most challenging tumors because of their relative inaccessibility and that their spread can occur without significant symptoms with few signs, but Radiotherapy (RT) has a role in treatment of it.

Objectives: To show that RT is still the modality of choice in the treatment of NPC, to study modes of presentations, commonest histopathological types and their percentages, to show differences in the sensitivities of these types to RT and to find out a 5 year survival rate(5YSR) and its relation with lymph node involvement.

Methods: This is a retrospective study of 44 patients with NPC who were treated with routine RT from 1988-2007 at the institute of radiology and nuclear medicine. All patients were treated with megavoltage x-ray with a total dose to the primary lesion was 60-70 Grays (1 Gray = 100 Rads) so we gave 6000-7000 Rads in 6-8 weeks and 50 Grays were applied to the cervical lymphatic chain bilaterally.

Results: 10 out of 44 patients treated have survived more than 5 years (with a 5YSR of 22.7%). In this series of cases, the 5- year overall survival rate is: 60% with stage I, 33.3% with stage II, 28.5% with stage III and 13.7% with stage IV. But, it should be noted that most of them were advanced with stages III and IV accounting for 36 patients i.e 81.8%.

Conclusion: Radiotherapy (RT) is the modality of choice in the treatment of NPC and we must irradiate areas of probable spread with the primary lesion because spread can occur without significant signs and symptoms .The most common histopathological type is undifferentiated carcinoma which is more sensitive to RT than squamous cell carcinoma (scc) or other types of carcinoma.

Also we see that stages III and IV NPC (advanced) comprises high number of the total and the 5-YSR decreases as the patient advances from stage I to stage IV, therefore, early detection and diagnosis is very important.

Key Words: Nasopharyngeal Carcinoma (NPC), Radiotherapy (RT).

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Introduction

The nasopharynx is an open cavity and represents the nasal portion of the pharynx situated behind the nasal cavities and above the soft palate. NPC has a tendency for early lymphatic spread and it is often the first sign of the disease (about 60% of all presentations).

The first common palpable lymph node is the jugulodigastric and/or the apical node under the sternomastoid area (1). The lymphadenopathy is most often unilateral, rapidly growing, bulky (6, 8 or 10 cm in diameter), somewhat lobulated and accompanied by smaller nodes in the corresponding chain.

The age-incidence rate is different from other forms of cancers. It begins to rise at the end of the second decade of life and reaches a peak in the fourth decade, then stays at a plateau (this contrasts sharply with the other epithelial cancers of lung andesophagus).This suggests an exposure to carcinogens early in life and/or an interaction of viral or environmental agents with susceptible genes. NPC has a distinctive epidemiological pattern, its incidence among the Chinese and other south-east Asians is about 10-50 times higher than that of other countries.

Methods

This study, which was done at the institute of radiology and nuclear medicine, included 44 patients treated by radiotherapy from 1988-2007, of which, 10 patients have survived for more than 5 years.

The way they were presented had shown that most of them had cervical lymphadenopathy (about 2/3) then otological symptoms then nasal then cranial, … (Table-1)

(Table-1)
Relationship between types of presentation and number of patients

	Type of presentation	No. of patients
1.	Cervical lymphadenopathy	30
2.	Earache, deafness, tinnitus	13
3.	Nasal obstruction	12
4.	Cranial nerve palsies	6
5.	Pain and headache	5
6.	Epistaxis	4
7.	Sore throat	3
8.	Distant metastasis	3

All of them has histologically confirmed NPC (2) and distributed into the following items (table 4):

1. Squamous cell carcinoma (well differentiated) 1
= = = (moderately =) 4
= = = (poorly =) 10

15
2. Non-keratinizing carcinoma 4
3. Undifferentiated carcinoma 25 (of the undifferentiated carcinoma, there were 9 patients of lymphoepithelioma).

Ages ranged from 17-71 years, number of males was 36, number of females was 8 and male : female ratio was 4.5:1 .

All patients were staged clinically by thorough physical examination including neck, cranial nerves examination, anterior rhinoscopy, posterior rhinoscopy, blood biochemistries, chest x-ray, x-ray views for the nasopharyngeal region and base of the skull, CT scanandMRI of the head and neck, transnasal fibroptic naso-pharyngoscopy.

Radiation Therapy (RT):

All patients were treated by RT according to techniques of irradiation and dosage schemes.
Technique of irradiation of NPC:

Irradiation of the primary tumor of post-nasal space, its extension to the base of the skull and cervical lymph nodes, will include large volume, not only of malignant tissue, but of normal surrounding tissues as well (3) like :

1. Lower part of brain, brain stem and cervical spinal cord.
2. Temporomandibular joint and middle ear (4,5,6,7).
3. Eyes specially the lens.
4. Salivary glands.
5. Skin.

Technique (8):
First phase : Using 2 parallel opposed lateral fields from base of the skull down to the clavicle, those fields are of large size e.g 16 to 20 cm X 10 cm X 14 cm and if the cervical lymph nodes are bulky, the spinal cord may have to be involved and if the cranial nerves are involved, then the upper limit of the field, will be few centimeters above the base of the skull.

Dose : 4000 centigray (C.Gy) / 20 fractions / 28 days (5 fractions per week) (9,10), then, there is a rest for 2-4 weeks, to let the acute radiation reaction to settle down, followed by :
Second phase : Using 3 fields tecqnique to the primary tumor, 2 lateral fields and 1 anterior field (the eye should be shielded or outside the radiation field) and the fourth field to the cervical area anteriorly shielding the larynx and the spinal cord anteriorly.

Dose : 2000-2500 C.G / 10-15 fractions / 2-3 weeks.
Note : Following the 2-4 weeks of rest, re-evaluation of the response before starting the second phase of radiotherapy,(11,12) some patients may still have gross residual disease or their general conditions are very poor, then the second phase is either omitted or we use small dose palliative radiotherapy.

Results

10 out of 44 patients treated had survived more than 5 years with a 5-YSR of 22.7%.
The relation between TNM staging and results of treatment is seen in (tables 2 and 3), where the 5-YSR decreased from 60% in stage I to 13.7% in Stage IV.

(Table 2)
Relationship between stage of the disease with the total number of patients involved in the study and number of patients with Successful treatment

Stage	No. of patients	No. of patients with successful treatment
I	5	3
II	3	1
III	7	2
IV	29	4

(Table 3)
Relationship between TNM staging and results of treatment

Stage	No. of patients	5-year survival rate
I	3/5	60 %
II	1/3	33.3 %
III	2/7	28.5 %
IV	4/29	13.7 %
Total	10 / 44	22.7 %

However, we note that most of these patients were advanced with stages III and IV, accounting for 81.8 % (13,14). So it is important to diagnose and treat as early as possible.
Factors affecting the survival:(15,16)
Age: The 5-YSR in the different age groups are similar.
Sex: Of the 44 patients, 36 were males and 8 were females with a male to female ratio of 4.5 : 1 and the 5-YSR was nearly the same in both.

Histological Classification: It seems that the pathological classification did not affect the prognosis too much, but undifferentiated carcinoma and lymphoepithelioma have a better prognosis than squamous cell carcinoma and other types of NPC (table 4), probably because they are more responsive to radiotherapy(1,3,17).

(Table 4)
Relationship between histological types and survival rates

Histopathological types	No. of Patients	No.of patients with successful treatment	5-YSR
1. Sq. c. c. well differentiated Sq. c. c. moderately differentiated Sq. c. c. poorly differentiated	1} 4 } 15 10}	2	13.3 %
2. Non-keratinizing carcinoma	4	1	25 %
3. Undifferentiated carcinoma	25	7	28 %

Clinical stage: Survival rates was markedly higher in stage I and II than in those of stage III and IV (table 3), where there are damages to the cranial nerves, destruction of the base of the skull. Also involvement of more lymph nodes (Table 5):

(Table 5)
Relationship between lymph node involvement and survival rates

Node status	No. of Cases	No. of patients with successful treatment	5-YSR
Upper neck	15	7	46.6%
Upper + lower	6	2	33.3%
Upper + clavicle	4	1	25 %
> 8 cm in diameter	5	1	20 %
Negative	14	9	64.2 %

Discussion

Because of difficulty of resecting the base of the skull or the retropharyngeal spaces, surgery has little role in the primary treatment of NPC, even for stage I cases. Radiotherapy is the modality of choice, as both, the primary tumor and its lymphatic metastases are radiosensitive, even if we need high dose for larger tumors and more resistant ones which may increase risk of normal tissue damage which is acceptable for the eradication of the disease.

In this study, the overall 5-YSR is 22.7 % (table 3), which is slightly lower than that was reported by the Shanghai cancer Hospital in 2000 which is 27.3% (18). Also it is lower than that reported by the Peking Hospital in 1999 with 5-YSR of 25%.

The well-recognized characteristic of extensive tumor infiltration and difficulty of accurately defining the extent of microscopic involvement, dictate that all potential sites must be included within the target volume, even for apparently T1 growths (18).

The retrospective analysis of Hoppe et al. [18] demonstrated that although nearly 1/3 of their patients with local recurrence had initial T1 growths. there had been no such failures in the 7 years following the adaptation of larger treated volumes.

The need for including the whole regional lymphatics in the primary treatment of stage I patients, remains controversial.External Nodal Irradiation (ENI) is advocated by many authors [18, 19] because of:

1. The high incidence of overt lymph node involvement even for T1 tumors.
2. The universal experience of very low regional relapse rates following external node irradiation in node-negative cases.
3. The low morbidity of the treatment.

So, External Nodal Irradiation can at least improve the relapse-free state

Conclusion

1. It is difficult to control lesions of the nasopharynx because of :
   a. their relative inaccessibility.
   b. their failure to produce early symptoms and the patient can neither see nor palpate the primary lesion.
2. Radiotherapy is the modality of choice in the treatment of NPC as both the primary tumor and its lymphatic metastasis are radiosensitive.
3. The fact that any or all of the spread may occur without significant symptoms and with few possitive signs, demands that areas of probable spread be routinely included in the irradiated volume, specially the routes of spread through foramina ovale and lacerum in the base of the skull which are the pathways of least resistance for tumor extension [14,15,20,21,22].
4. Most patients have multiple symptoms which are insidious in onset and the majority develop cervical lymph node without any symptoms referable to a primary lesion in the nasopharynx.
5. The most common histopathological type is undifferentiated carcinoma which is in addition to lymphoepithelioma, are more sensitive to radiotherapy than squamous cell carcinoma or other types.
6. Stages III and IV NPC comprises high number of the total and the 5-YSR decreases as the patient advances from stage I to stage IV.
7. The 5-YSR in patients with no lymphadenopathy is better than patients with adenopathy. Also a patient with upper cervical lymph node has a better 5-YSR than a patient with(upper and lower) neck lymph node or with supraclavicular lymph node or with lymph node more than 8 cm in diameter.
8. The overall 5-YSR in this study is about 22.7 % which is below the results of previous studies done elsewhere(18,19) which gave 25%, 27.3%, this is attributed to the following reasons :
   a. Most our patients come in advanced stages.
   b. Many of them don't complete the cessions of treatment and they disappear after short time of the beginning of treatment.
   c. Lack of the facilities and trained personelle.

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