# Nasopharyngeal Carcinoma : An Alternative Histological Classification as a Working Formulation

A.N. Kurniawan*, Anida Syafril**, R. Susworo***

**Abstrak**

*Suatu klasifikasi histologik sebagai alternatif klasifikasi WHO, yang diusulkan oleh Hsu dkk (1987), telah diterapkan pada penderita karsinoma nasofaring (KNF) yang diperiksa di R.S. Cipto Mangunkusumo pada tahun 1987-1988. Tumor dibagi atas 3 kelompok, bergantung kepada jenis sel, ukuran inti dan derajat pleomorfi. Klasifikasi KNF sebagai Formulasi Kerja ini terdiri atas : keganasan derajat tinggi (karsinoma sel skuamosa), derajat menengah (karsinoma tipe A) dan derajat rendah (karsinoma tipe B). Hubungan antara gambaran histologik KNF menurut klasifikasi ini dengan hasil pemeriksaan klinik nasofaring dan respons radiasi dipelajari. Jumlah kasus yang diteliti ialah 32 orang. Didapatkan 5 kasus karsinoma sel skuamosa, 7 kasus karsinoma tipe A dan 22 kasus karsinoma tipe B. Semua kasus berada pada stadium 4, kecuali pada 3 kasus. Didapatkan response lengkap ("CR = Complete response") sebagai berikut : 33,3 % pada karsinoma sel skuamosa, 57,1 % pada karsinoma tipe A dan 63,6 % pada karsinoma tipe B. Dari hasil penelitian yang terbatas ini diperoleh kesan bahwa klasifikasi KNF sebagai Formulasi Kerja ini dapat memberikan indikasi prognostik yang bermanfaat bagi pengelolaan penderita KNF.*

**Abstract**

*An alternative classification to the WHO classification, which was proposed by Hsu et al (1987), was applied to NPC patients treated at the Cipto Mangunkusumo Hospital in 1987-1988. The tumour was divided into 3 groups, depending on the type of cells, size of the nuclei and degree of pleomorphism. Thus the working formulation comprised : high grade (KS = Keratinizing squamous carcinoma), intermediate (Type A carcinoma) and low grade malignancy (Type B carcinoma). A study was made on the correlation between the histological picture, ENT findings and radiation response of the tumours. Thirty two cases entered the study. There were 3 KS, 7 Type A and 22 Type B carcinoma. All of the cases were in stage IV clinically, except for 5 cases. The complete response rate (CR) was as follows : KS 33.3 %, Type A 57.1 % and Type B 63.6 %. It appeared from this limited study that this working formulation could provide valuable prognostic indication in the management of NPC patients.*

**Keywords** : *Nasopharyngeal carcinoma, Histological classification*

## INTRODUCTION

Various classifications of nasopharyngeal carcinoma (NPC) have been used to identify and designate a group of tumours arising in the nasopharyngeal wall to facilitate standard nomenclature and comparative studies. An international histological classification was developed by WHO[1] in 1978, comprising squamous cell carcinoma, non-keratinizing carcinoma and undifferentiated carcinoma. This WHO classification was simple and easily reproducible. It had some prognostic value, though limited.

In 1987 Hsu *et al*[2] proposed a new classification, which was a modification of the WHO classification. Out of their cases, they proposed a histological classification, which correlated well with the prognosis; thus it might be used as a working formulation, particularly by the clinicians.

* *Department of Anatomic Pathology, Faculty of Medicine University of Indonesia/Cipto Mangunkusumo Hospital, Jakarta, Indonesia*

** *Department of Ear, Nose and Throat, Faculty of Medicine University of Indonesia/Cipto Mangunkusumo Hospital, Jakarta, Indonesia*

*** *Department of Radiology, Faculty of Medicine University of Indonesia/Cipto Mangunkusumo Hospital, Jakarta, Indonesia*

The purpose of this study was to evaluate the use of Hsu's classification as applied to our cases. The result of this study might be used for the management of our cases in the future.

## MATERIALS AND METHODS

Thirty two cases of NPC treated at Cipto Mangunkusumo Hospital in 1987-1988 were studied. Complete medical data were collected including demographic data, histological diagnosis, clinical findings, radiation dose and response of radiation both at the neck lymph nodes and on the tumour in the nasopharynx.

All the histological specimens were reanalyzed and the Hsu classification was used. The Working Formulation was formulated as :

1. **Keratinizing squamous cell carcinoma (KS)**
   Squamous cell carcinoma with definite evidence of keratinization.
2. **Type A Carcinoma**
   NPC other than KS, with cells showing marked nuclear hyperchromatism, marked variation in nuclear size/pleomorphism and prominent nucleoli.
3. **Type B carcinoma**
   The cells show little or moderate hyperchromatism, smaller/more uniform nuclei, little pleomorphism and fine chromatin.

Clinical staging was done at the E.N.T. Department and/or Department of Radiology, using the UICC-TNM classification.[3] Radiation response as seen at the neck lymph nodes (metastatic lesion) was assessed at the Radiology Department. The responses were either complete response (CR), partial response (PR), no change (NC) or progressive disease (PD). After radiation treatment, the nasopharynx was examined to evaluate whether the tumour was still seen or not.

Eventually, the histological data were compared with the clinical data to assess any possible prognostic association.

## RESULTS

There were 21 male and 11 female cases. The youngest patient in this study was 17 years and the oldest 70 years of age.

Twenty seven cases (84 %) were in stage IV, 4 cases (12 %) were in stage III and only 1 case (3 %) was in stage I.

These histological types were shown in Table 1.

Table 1. Histological types of NPC (working formulation)

| Histological Type | No of cases | % |
|---|---|---|
| KS | 3 | 9.4 |
| Type A Ca | 7 | 21.9 |
| Type B Ca | 22 | 68.7 |
| Total | 32 | 100.0 |

KS = high grade malignancy
Type A = intermediate malignancy
Type B = low grade malignancy

Table 2 showed the radiation response of the tumour types.

Table 2. Radiation response

| Histological Type | CR (%) | PR (%) | PD (%) |
|---|---|---|---|
| KS | 33.3 | 66.7 | 0 |
| Type A Ca | 57.1 | 28.6 | 14.3 |
| Type B Ca | 63.6 | 36.4 | 0 |

KS = high grade malignancy
Type A = intermediate grade malignancy
Type B = low grade malignancy
CR = complete response
PR = partial response
PD = progressive disease

The radiation response showed different results in different clinical stages, as seen in Table 3.

Table 3. Radiation response in clinical stages

| Stage | No of cases | CR (%) |
|---|---|---|
| I | 1 | |
| III | 4 | 100 |
| IV | 27 | 51.9 |

CR = complete response

Clinical examination of the nasopharynx postirradiation showed different results among the histological types (Table 4).

Table 4. Tumour in nasopharynx postirradiation

| Histological Type | % no tumour seen (-) |
|---|---|
| KS | 66.7 |
| Type A Ca | 71.4 |
| Type B Ca | 90.9 |

KS = high grade malignancy
Type A = intermediate grade malignancy
Type B = low grade malignancy

A comprehensive relationship between clinical stage, histological type and radiation response was summarized in Table 5.

## DISCUSSION

Nasopharyngeal carcinoma (NPC) is defined as a malignant tumour of the epithelium lining the surface and crypts of the nasopharynx.[1] By electron microscopy, it has the characteristics of squamous cell carcinoma, hence it may be regarded as such. However, by light microscopy it can show different histological appearances. The classification is based on light microscopic features. The first edition of the WHO classification (1978) put the tumour into 3 groups, namely : squamous cell carcinoma, nonkeratinizing carcinoma and undifferentiated carcinoma.[1] In 1991, the second edition was published,[4] in which NPC is subdivided into 2 main groups according to the presence or absence of a clear evidence of squamous differentiation. The groups are :

1. Keratinizing squamous cell carcinoma
2. Nonkeratinizing carcinomas.
   2.1. Differentiated Non-keratinizing carcinoma
   2.2. Undifferentiated carcinoma.

This classification with its definition and histological description proved to be easy to use by the pathologists. Shanmugaratnam et al[5] studied the relationship of this WHO classification with the epidemiological aspects, survival rate and other biological features and found that 5-year survival rate of squamous cell carcinoma was lower than the other two types combined. However, there were no data which distinguished the survival of the nonkeratinizing carcinoma from the undifferentiated carcinoma, while these 2 types comprised the majority of NPC cases. The number of nonkeratinizing carcinoma and undifferentiated carcinoma was 69.7 % in Singapore,[1] 84,2 % in Taiwan[2] and 97.5 % in Jakarta.[6]

Hsu *et al*[2] in 1987 proposed a modification of the WHO classification, based on the size and shape of tumour cells. They divided NPC into 4 groups, namely Keratinizing squamous cell carcinoma (KS), spindle cell carcinoma (SP), round cell carcinoma (RC) and mixed carcinoma (MIX). They found a clear and significant correlation of the histological types and the

Table 5. Relationship of clinical stage, histological type and radiation response

| Stage | Histological type | No of cases | CR (%) | PR (%) | PD (%) | Metastasis (%) | Period of no tumour in nasopharynx |
|---|---|---|---|---|---|---|---|
| I | B | 1 | 0 | 0 | 0 | | 1 year |
| III | A | 2 | 100 | 0 | 0 | 50 | 2 mo - 1 year |
| | B | 2 | 100 | 0 | 0 | | 2 years |
| IV | KS | 3 | 33.3 | 66.7 | 0 | 33.3 | 1 mo - 1 year |
| | A | 5 | 40 | 40 | 0 | 20 | 1 mo - 1 year |
| | B | 19 | 57.9 | 42.1 | 0 | 15 | 1 1/2 year (longest) |

KS = high grade malignancy
Type A = intermediate grade malignancy
Type B = low grade malignancy

CR = complete response
PR = partial response
PD = progressive disease

prognosis, regardless of the clinical stage. The 5-year survival rates of KS, SP, RC and MIX were 21 %, 41 %, 52 % and 54 %, respectively. However, this classification was not without problem.[7] The not infrequent occurence of cells of different shapes in one tumour might cause difficulties in classifying that tumour in one of the groups. A more workable way of distinguishing the different behaviour of the groups of this tumour was suggested by Hsu *et al* by recommending the use of a Working Formulation, such as high grade malignancy (KS), intermediate grade malignancy (Type A carcinoma) and low grade malignancy (Type B carcinoma). They obtained clear distinction of these groups as reflected by the significantly different 5-year survival rates, which were 21 %, 30-40 % and 60-72 %, respectively. To apply this working formulation to our cases proved to be histologically quite easy and did not cause considerable doubtful questions.

As our study did not have the data of survival of the patients, our attempt was directed towards evaluating the biological behaviour of the tumour, as expressed by the radiation response of the neck metastases and the primary tumour in the nasopharynx.

Data from Table 2 and 4 showed that CR (complete response), which is the aim of radiotherapy, was lowest for KS, highest for Type B carcinoma and in between for Type A carcinoma. This difference was particularly seen in stage IV cases. Although these results are in conformity with Hsu et al's report, it was clearly acknowledged that radiation response of the neck metastatic lesion is not identical to survival, as it was known that about 25 % of NPC cases will show locoregional recurrence after the completion of radiation.[8]

It was not always easy to evaluate the existence of tumour in the nasopharynx postirradiation. Besides technical difficulties in examining the nasopharynx, the compliance of the patients to come for consultation, caused the inaccurate assessments. For cases still showing tumour in the nasopharynx, it was not possible to judge whether the tumour was resistant to irradiation or whether it was a recurrence. Sham *et al*[9] showed that the effect of radiation persisted until 10 weeks after completion of radiation. This means that if after 10 weeks postirradiation, the tumour still persists, then it has to be regarded as residual.

Nevertheless, data from Table 4 showed that the percentage of no tumour in nasopharynx was highest in Type B carcinoma and lowest in Keratinizing carcinoma. Table 5 showed that the period of absence of tumour was longest seen in Type B carcinoma, either in stage IV (1 1/2 years) or stage III (2 years).

Several prognostic factors of NPC have been identified such as size of primary tumour, number of metastatic lesions in the lymph node, gender, age, radiation response of primary tumour, radiation response of neck lymph node, total radiation dose, histological type of tumour, infiltration of eosinophils.[10,11,12,13,14] This study showed that besides the clinical stage, the histological type of tumour showed association with the biological behaviour, hence with prognosis.

## CONCLUSION

The application of the working formulation classification of NPC as proposed by Hsu et al was well adapted histologically. As there were constant differences between KS, Type A carcinoma and Type B carcinoma in the response to radiation, either in the metastatic or the primary tumour, this classification seemed to be useful to provide valuable information to the clinicians as regard to prognosis.

## REFERENCES

1. Shanmugaratnam K, Sobin L. Histological typing of upper respiratory tract tumours. In : International histological classification of tumours. No. 19. Geneva : WHO, 1978: 19-21; 32- 3.
2. Hsu HC, Chen CL, Hsu MW, Lynn TC, Tu SM, Huang SC. Pathology of nasopharyngeal carcinoma. Proposal of a new histologic classification correlated with prognosis. Cancer 1987; 59: 945- 51.
3. Hermanek P, Sobin LH, eds. UICC - TNM classification of Malignant Tumours, 4th ed. Berlin : Springer Verlag, 1987.
4. Shanmugaratnam K, Sobin L. Histological typing of tumours of the upper respiratory tract and ear. In : World Health Organization International histological classification of tumours. 2nd ed. Berlin: Springer Verlag, 1991: 32-3.
5. Shanmugaratnam K, Chan SH, de The G et al. Histopathology of nasopharyngeal carcinoma. Correlation with epidemiology, survival rates and other biological characteristics. Cancer 1979; 44: 1029-44.
6. Kurniawan AN. Patologi tumor telinga, hidung dan tenggorok. In : Himawan S, Tjokronegoro A, eds. Tumor kepala dan leher : diagnosis dan terapi. Jakarta: FKUI, 1983; 47-61.
7. Kurniawan AN, Anida Syafril, R Susworo. Klasifikasi baru karsinoma nasofaring: tinjauan aspek kliniko-patologik. KONAS X IAPI, Surabaya, 5-8 Juli 1990.
8. Hsu MW, Tu SM. Nasopharyngeal carcinoma in Taiwan. Clinical manifestation and results of therapy. Cancer 1983; 52: 362-8.
9. Sham JST, Wei WI, Kwan WH, Chan CW, Kwong WK, Choy D. Nasopharyngeal carcinoma. Pattern of tumor regression after radiotherapy. Cancer 1990; 65: 216-20.

10. Molinari R, Grandi C, Boracchi P, Mezzanotte G, Marubini E. Prognostic factors in nasopharyngeal carcinoma. Uni and multivariate analysis of 410 cases from a multicentric study. In : Wolf GT, Carey TE, eds. Head and neck oncology research. Proc 2nd International Head and Neck Oncology Research Conference, Arlington, VA, USA, 10-12 September 1987. Kugler & Ghedini : Berkeley, 1988: 495-504.
11. Qin D, Hu Y, Yan J et al. Analysis of 1379 patients with nasopharyngeal carcinoma treated by radiation. Cancer 1988; 61: 1117-24.
12. Nomori H, Watanabe S, Nakajima T, Shimosato Y, Kaneya T. Histiocytes in nasopharyngeal carcinoma in relation to prognosis. Cancer 1986; 57: 100-5.
13. Looi LM. Tumor - associated tissue eosinophilia in nasopharyngeal carcinoma. A pathologic study of 422 primary and 138 metastatic tumors. Cancer 1987; 59: 466-70.
14. Iwasaki K, Torisu M., Fujimura T. Malignant tumor and eosinophils. I. Prognostic significance in gastric cancer. Cancer 1986; 58: 1321-7.