

Research

Clinicopathological profile of nasopharyngeal carcinoma in 2016-2019 at Dr. Soetomo General Hospital

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ABSTRACT

Background: The number of nasopharyngeal carcinoma (NPC) cases is increasing and causing death, placing this cancer in fifth place as the cause of death in Indonesia. The initial clinical symptoms that are less specific often cause patients coming with advanced stage conditions. Therefore, the study of clinical and pathological profiles of NPC patients are required. **Objective:** To find out the clinicopathological profile of NPC patients in Dr. Soetomo General Hospital in 2016-2019. **Methods:** This study was descriptive research with a retrospective study using medical records of NPC patients in Dr. Soetomo General Hospital from 2016 to 2019. **Results:** 192 NPC patients that meet the criteria were divided according to their age, gender, histopathological classification, stage, and post-therapy response. Out of 192 patients, 22 patients had post-therapy response based on histopathological data. **Conclusion:** NPC patients in Dr. Soetomo General Hospital in 2016-2019 were found in the range of 14-77 years old, most patients were in the age group 41-≤50 years old (66 patients, 34%). There were more male than female patients (73%). The most common clinical symptoms experienced by patients were a lump on the neck (82%), local ear complaints (79%), and local nasal complaints (75%). The most common histopathological subtype was non-keratinizing squamous cell carcinoma undifferentiated in 181 patients (94%). The highest stage of patients was IV A in 122 patients (64%). In 18 (82%) from 22 patients, based on histopathology examination had good criteria on therapy response.

Keywords: neurogenic dysphagia, non-neurogenic dysphagia, fiberoptic endoscopic examination of swallowing (FEES)

ABSTRAK

Latar belakang: Angka kasus karsinoma nasofaring yang (KNF) kian meningkat dan dapat menyebabkan kematian, menempatkan kanker ini pada urutan ke lima di Indonesia. Gejala klinis awalnya yang kurang spesifik seringkali menyebabkan penderita datang dengan kondisi stadium lanjut. Oleh karena itu, profil penderita KNF secara klinis dan gambaran histopatologinya perlu diteliti lebih lanjut. **Tujuan:** Mengetahui profil klinikopatologi penderita KNF di RSUD Dr. Soetomo tahun 2016-2019. **Metode:** Penelitian secara deskriptif dengan studi retrospektif menggunakan rekam medis penderita KNF di RSUD Dr. Soetomo tahun 2016-2019. **Hasil:** Sebanyak 192 penderita KNF yang memenuhi kriteria dibagi berdasarkan kategori usia, jenis kelamin, klasifikasi histopatologi, stadium, dan respon pasca terapi. Dari 192 penderita ditemukan sebanyak 22 penderita memiliki data respon pasca terapi berdasarkan histopatologi. **Kesimpulan:** Penderita KNF di RSUD Dr. Soetomo tahun 2016-2019 ditemukan pada rentang usia 14-77 tahun dengan penderita terbanyak pada rentang usia 41- 50 yaitu 66 (34%) serta lebih banyak terjadi jenis kelamin laki-laki yaitu 140 (73%). Gejala klinis yang paling banyak dialami penderita adalah benjolan pada leher 158 (82%), keluhan lokal telinga

151 (79%), dan lokal hidung 144 (75%). Subtipe histopatologi terbanyak adalah nonkeratinizing squamous cell carcinoma undifferentiated yaitu 181 (94%) penderita. Stadium terbanyak penderita adalah IV A yaitu 122 (64%) penderita. Sebanyak 18 (82%) dari 22 penderita ber kriteria baik pada respon terapi berdasarkan histopatologi.

Kata kunci: karsinoma nasofaring, profil klinis, profil patologi, profil demografi, respon pasca terapi

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INTRODUCTION

Nasopharyngeal carcinoma (NPC) is one of malignant tumors in the neck on the nasopharyngeal surface cells, which is commonly arise from the fossa of Rossemuller.¹ The number of NPC new cases globally reaches 133,354 cases annually, with an incidence ratio of males against females is 2.2: 0.8 according to the world age-standardized rate (ASR).² The main factors studied as the etiology of NPC are genetic factors, infection of Epstein-Barr Virus (EBV), environment-related consumption pattern, and smoking habit.³

The symptoms of NPC are varied, but the difficult anatomic position allows cancer to be clinically undiscovered for a long time. Even though the patients feel disturbances in their nasal cavity, the symptoms will be more noticeable when it affects the surrounding organs causing symptoms in the ear or lump in the neck.⁴

Endoscopy is performed as an initial detection of NPC, confirmed by the biopsy of the primary tumor site and imaging for the staging.⁵ Histopathological classification of NPC consists of Keratinizing Squamous Cell Carcinoma, Non-keratinizing Squamous Cell Carcinoma, and Basaloid Squamous Cell Carcinoma, which is rarely found. The non-keratinizing category is still classified into differentiated and undifferentiated, but it does not affect clinical value and prognosis.⁶

This study aimed to find out the clinical and pathological profile of NPC in Dr. Soetomo General Hospital in the year 2016-2019.

METHOD

This was a retrospective descriptive study using medical records of NPC patients at Dr. Soetomo General Hospital, Surabaya, from 2016 to 2019. All samples met the inclusion criteria. The data was processed and presented in tables and descriptions.

RESULT

A total of 192 NPC patients from 2016 to 2019 met the criteria as study samples. The 140 (73%) patients were male, and 52 (27%) were female. Most patients were in the age range of 41-≤50 years old (66%) (Table 1). The clinical symptoms of patients were mainly the local metastatic complaint in the form of a lump in the neck (82%), local complaint in the ear (79%) and nose (75%), headache (51%), double vision (34%), cheek swelling (13%), dysphagia (6%), facial/cheek pain (4%), and choking while eating/drinking (2%). The 4% of patients complained of metastasis symptoms in the form of dyspnea, back pain, nausea, vomiting, or limbs and body weakness (Table 2).

Most NPC patients were classified into a histopathological classification of non-keratinizing undifferentiated squamous

cell carcinoma (94%), non-keratinizing differentiated squamous cell carcinoma (5%), and keratinizing squamous cell carcinoma (1%). There was no patient with basaloid squamous cell carcinoma (0%) (Table 3). Most NPC patients were classified as stage IV A (64%). The rest were stage III (21%), stage IV B (12%), and stage II (3%) (Table 4). There were no patients in stage I.

Based on the obtained data, out of 192 NPC patients, 22 patients had histopathological post-therapy response. The 82% of patients were classified as good criteria, recurrence (14%), and bad criteria (4%) (Table 5). Most of the good criteria responses were in the age range of 41-≤50 years old, (10 out of 18 patients). The poor criteria were found in one patient in 61-≤70 years old group, and

recurrence was found in 2 patients in 61-≤70 years old group. Moreover, a good response was found in 4 patients in the age range of 51-≤60 years old, 2 patients in the age range of 11-≤20 years old, 2 patients in the age range of 31-≤40 years old, and one recurrence patient in the age range of 11-≤20 years old. Most gender of the patients with good response criteria were males, 12 of 18 patients, while in the poor therapy response and recurrence in male gender were only 1 and 3 patients, respectively. Histopathological classification of 22 patients with therapy response data was a subtype of undifferentiated non-keratinizing squamous cell carcinoma. Most stages of the patients with good response were in stage IV A group (11 out of 18 patients) and 7 patients in stage III. One patient with a bad response was in stage IV A.

Table 1. Distribution of characteristics

Characteristics	Total	
	Frequency	%
Gender		
Male	140	73
Female	52	27
Age		
0 - ≤ 10	0	0
11-<20	5	3
21-≤30	12	6
31-≤40	26	14
41-≤50	66	34
51-≤60	53	28
61-≤70	22	11
71-≤80	8	4
81-≤90	0	0
91-≤100	0	0

Table 2. Clinical symptoms

Clinical symptoms	Total	
	Frequency	%
Local Symptoms		
Ear symptoms	151	79
Nasal symptoms	144	75
Local Metastasis Complaints	158	82

	Headache	97	51
	Double vision	66	34
Infiltration Symptoms	Dysphagia	12	6
	Eating / drinking choking	4	2
	Face / cheeks pain	8	4
	Numbness in cheeks	25	13
Distant metastasis symptoms		8	4

Table 3. Histopathological classification

Histopathological classification	Amount	
	Frequency	%
Keratinizing squamous cell carcinoma	1	1
Differentiated non-keratinizing squamous cell carcinoma	10	5
Undifferentiated non-keratinizing squamous cell carcinoma	181	94
Basaloid squamous cell carcinoma	0	0
Total	192	100

Table 4. Staging

Stages	Number	
	Frequency	%
Stage I	0	0
Stage II	6	3
Stage III	41	21
Stage IV A	122	64
Stage IV B	23	12
Total	192	100

Table 5. Therapy response

Therapy response based on histopathology	Number	
	Frequency	%
Good criteria	18	82%
Bad criteria	1	4%
Recurrence	3	14%
Total	22	100%

DISCUSSION

In this study, NPC patients were in the range age of 14-77 years old, with the highest age group of 41- ≤50 years old (34%). There were more male patients (73%) than females. This is in accordance with several other studies that NPC commonly occurs at 40

years old to 50 years old.⁷⁻⁸ NPC at young age is associated with the carcinogenic agent in early life, in which patients with first-degree relatives have 4-10 times risks genetically.⁹ The prognosis survival rate of patients with younger age is related to performance status and less comorbid in the patients.¹⁰

The ratio of incidence among males against females is 2:1.^{1,7,11} Lifestyle and biological factors affect the difference in the NPC incidence according to gender.^{1,2} Males are often exposed to a carcinogen from work.¹³ Estrogen is a female protective factor against NPC through NAG7 repressor as a negative regulator of tumor cells growth.¹⁴

The most common clinical symptoms of NPC patients in this study were local metastasis in the form of masses in the neck (82%), followed by local infiltration symptoms in the form of ear complaint (79%) and nasal complaint (75%). The mass in the neck becomes one of the three most common symptoms experienced by NPC patients.^{1,7} The mass in the neck with enlarged cervical lymph nodes is often unilateral and painless, except accompanied by inflammation or infection.³

The most common histopathological subtypes in this study were undifferentiated non-keratinizing squamous cell carcinoma. Naomi et al.¹¹ stated that 76.5% of NPC patients had undifferentiated subtypes. Lifestyles, such as smoking and consuming alcohol, are assumed as risk factor of NPC keratinizing type, while the consumption of salted and preserved foods with nitrosamines and EBV infection involved in NPC of non-keratinizing type, especially in endemic areas.⁶

In several other studies, NPC patients mainly were found at stage IV.^{1,11} The NPC staging that represents the local control and distant control becomes the important prognostic factor for survival. The more advance the stage, the more limited the life expectancy of the patients. Symptoms in the early stage of NPC related to nasal and ear complaints are not specific and insignificant that is often ignored by patients, or wrong interpretation by clinical practitioners, which cause the majority of patients are diagnosed in advanced stage.⁹

Endoscopy for tumor biopsy is a gold standard to examine response after NPC therapy.⁹ About 82% of NPC cases had good response criteria, indicated by the absence of viable tumor cells histopathologically. The cause of NPC patients being difficult to follow up is because the patients dropped out or stopped the initial therapy due to the treatment side effects.¹⁵ The median time for the recurrence of NPC patients is 2 years and is more common in male patients. NPC recurrence can occur by the regeneration of tumor cells in subclinical lesions after therapy.¹⁶

This study showed that the most NPC occurred in patients aged 41-50 years old and were more common in males. The most clinical symptom was a lump in the neck. The most common histopathology was undifferentiated non-keratinizing squamous cell carcinoma type and most patients were diagnosed in stage IV A. According to histopathology examination, 18 out of 22 patients had a good response after therapy.

REFERENCES

1. Dawolo A, Utama D, Kasim B. Profil Klinis Karsinoma Nasofaring di Departemen THT-KL RSUP Dr. Mohammad Hoesin Palembang Tahun 2014-2015. *Majalah Kedokteran Sriwijaya*. 2019;49(1):1-9.
2. Ching LJ. Prognostic Factors In Nasopharyngeal Cancer. *Multidisciplinary Management*. 2010; 95-136.
3. Lu JJ, Cooper JS, Lee AWM, eds. *Nasopharyngeal cancer. Multidisciplinary management*. Berlin: Springer; 2010.
4. Wang K. *Nasopharyngeal Carcinoma Diagnostic Challenge in a Nonendemic Setting: Our Experience with 101 Patients*. 2017.
5. Bercin S, Yalciner G, Muderris T, Gul F, Deger H, Kiris M. Pathologic Evaluation of Routine Nasopharynx Punch Biopsy in the Adult Population: Is It Really Necessary?. *Clinical and Experimental Otorhinolaryngology*. 2017; 10(3): 283-87.

6. El-Naggar A, Chan J, Grandis J, Takata T, Slootweg P. WHO classification of head and neck tumours. France: International Agency for Research on Cancer; 2017.
7. Adham M, Kurniawan A, Muhtadi A, Roezin A, Hermani B, Gondhowiardjo S et al. Nasopharyngeal carcinoma in Indonesia: epidemiology, incidence, signs, and symptoms at presentation. *Chinese Journal of Cancer*. 2012; 31(4): 185-96
8. Arditawati Y. Hubungan Antara Faktor Risiko dengan Tipe Histopatologi pada Karsinoma Nasofaring. Semarang: Fakultas Kedokteran Universitas Diponegoro; 2011.
9. Valerie JL, David JH, William I W. Tumors of the nose, sinuses, and nasopharynx. 1st ed. Thieme; 2014.
10. Xiao G, Cao Y, Qiu X, Wang W, Wang Y. Influence of gender and age on the survival of patients with nasopharyngeal carcinoma. *BMC Cancer*. 2013; 13(1).
11. Naomi S, Dewi Y, Agustina H. Association between Histopathological Grading and Clinical Staging in Nasopharyngeal Carcinoma. *Journal of Medicine & Health*. 2018; 2(2).
12. Salehiniya H, Mohammadian M, Mohammadian-Hafshejani A, Mahdavi N. Nasopharyngeal cancer in the world: epidemiology, incidence, mortality and risk factors. *World Cancer Research Journal*. 2018; 5 (1): e1046.
13. Hamita H, Yusuf M, Wiyadi M. The correlation between IL-10 expression and histopathological type in nasopharynx carcinoma patients. *Oto Rhino Laryngologica Indonesiana*. 2020; 50(1): 52.
14. Xie S, Yu I, Tse L, Mang O, Yue L. Sex difference in the incidence of nasopharyngeal carcinoma in Hong Kong 1983–2008: Suggestion of a potential protective role of oestrogen. *European Journal of Cancer*. 2013; 49(1): 150-55.
15. Wildeman M, Fles R, Herdini C, Indrasari R, Vincent A, Tjokronegoro M et al. Primary Treatment Results of Nasopharyngeal Carcinoma (NPC) in Yogyakarta, Indonesia. *PLoS ONE*. 2013; 8(5): e63706.
16. Li J, Lu T, Huang Y, Han F. Clinical Characteristics of Recurrent Nasopharyngeal Carcinoma in High-Incidence Area. *The Scientific World Journal*. 2012; 2012: 1-8.