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NASOPHARYNGEAL CARCINOMA WITH INTRACRANIAL INVOLVED

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Abstract

Introduction: Nasopharyngeal carcinoma (NPC) is an aggressive carcinoma come from postnasal space. Histology type of nasopharyngeal cell carcinoma and the staging that affect with management therapy. Nasopharyngeal carcinoma can be controlled by implementing evidence-based strategies of cancer and management of patients.

Case report: Reported a case in 47-year-old man, diagnosis squamous cell carcinoma of nasopharynx with intracranial involvement.

Conclusion: Histology type of nasopharyngeal carcinoma and the staging determined the modality of therapy and nasopharyngeal carcinoma prognosis

Article Info

Keywords:

Nasopharyngeal carcinoma, histology cell, tumour staging, intracranial involvement, prognostic

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1. CASE REPORT

Nasopharyngeal Carcinoma (NPC) is a malignant tumor from nasopharyngeal epithelium. The etiology of this malignant tumor is multifactorial, ethnic and geographical factors influence the risk of this disease [1]. The main etiology of nasopharyngeal malignancy always associated with Epstein Barr virus, genetic and environmental factors [2-4].

Nasopharyngeal Carcinoma are the fourth most common malignant tumors after cervical, breast and skin cancer and are the most common tumors in the head and neck [5].

Based on epidemiological data, NPC can be found in all countries where the highest incidence is in southern China, especially in Guangdong province and found in Europe and North America [6].

Incidence in Guangdong province in men reaches 20-50 per 100,000 population per year [1]. In Cantonese in Guangdong province and Guangxi region it reaches more than 50 per 100,000 population per year [7]. NPC incidence in America is 1-2 cases per 100,000 men and 0.4 cases per 100,000 women [8]. The geographical pattern of tumor events shows the interaction of environmental factors and genetic factors [9].

Nasopharynx is a cuboidal structure that is limited by the nasal cavity in the anterior, the skull base in the superior, the cervical spine in the posterior and the upper surface of the palate in the inferior. Eustachian tubes open toward the nasopharynx, some cranial nerves are also located nearby [10]. These malignancies can arise from various places in the nasopharynx, but are more common in the fossa of rosenmueller, which is located to the medial crura of the eustachian tube [11].

The nasopharynx is an area rich in lymphatic glands and blood vessels. This anatomic factor influence diagnosis, staging and treatment NPC [12]. The nasopharynx structure anatomy of Chinese and Asian is generally narrow compared to Caucasian so that make aerosol deposits and direct irritation leads to recurrent infections such as chronic pharyngitis which causes nasopharyngeal mucosa over a period of time certain changes to carcinoma [13].

Etiology of NPC is multifactorial. There are three main etiological factors associated with NPC, genetic, environmental and Epstein Barr virus infection. Epstein Barr virus infection factors are very dominant for nasopharyngeal carcinoma. Environment and genetics were also reported to be related to the incidence of NPC [2, 14].

Genetic related to geographical variations. Although the pathogenesis mechanism of nasopharyngeal carcinoma is still unclear, familial aggregation has been well documented by many epidemiology study. Environmental factors include food factors, especially consumption of salted fish [15, 16]. Nitrosamines in salted fish are carcinogens for the development of NPC. In addition to other food factors such as smoking, exposure to formaldehyde, wood dust and chemicals are also risk factors for NPC begin with chronic inflammation of the nasopharynx [17].

Epstein-Barr Virus (EBV) infections occur in almost all cases of nasopharyngeal carcinoma, so individuals will have some antibodies against EBV [18]. Viral DNA join tumor cells. The 10 years risk of developing nasopharyngeal carcinoma estimated to be 200 times higher in the group with positive antibodies [15].

Presence of dysplasia in early lesion, which is a response to some environmental carcinogens. The area of dysplasia which is the origin of carcinoma but may not stand alone to cause further development. At this stage latent EBV infection causes development become more severe [9].

Epstein Barr Virus can be latent or lytic phases in host cells. Both phases are involved in carcinogenesis. In the latent phase, EBV encodes the onco-protein latent membrane protein, the Latent Membrane Protein 1 (LMP1). Latent onco-protein 1 membrane protein is present in almost all nasopharyngeal carcinoma tissues. LMP1 is a 386-amino-acid protein and its active C-terminal region (CTAR) mediate some oncogenic signals, which contribute to oncogenic effect [19].

Nasopharyngeal carcinoma arises in the lateral wall, especially from the rossenmuller fossa [20]. Based on its anatomic location, NPC presents with one or more of 4 main symptom groups; first, nasal symptoms such as epistaxis, nasal obstruction and rhinorea; second, ear symptoms such as fully ears, hearing loss and tinnitus associated with eustachian tube dysfunction caused by tumor expansion lateral-posteriorly; third, cranial nerve paralysis, most commonly nerves 3,5,6 and 12, which are associated with superior expansion of tumors to the skull base. Patients complain of headaches, diplopia, facial pain and facial numbness; fourth, namely the symptoms of neck, usually appear enlarged lymph nodes at the top of the neck [11].

NPC patient could have one or more four groups symptoms. These groups of symptoms are related to primary tumors, infiltration to structures around the nasopharynx or metastasis to the neck lymph nodes. Clinical symptoms generally consist of a lump in the neck, saliva mixed with blood, nasal obstruction and rhinorea, headache, neurological symptoms and hearing symptoms such as tinnitus and hearing loss [21].

When patient come with NPC symptoms, clinician should do, ENT physical examination, performed enlargement of lymph nodes, fluid in the middle ear and cranial nerve examination. Clinical examination together with endoscopic examination can provide valuable information about tumor extension on the mucosal surface in the nasopharynx [21].

Primary tumors can be evaluated either by Computed Tomography (CT) scan or by Magnetic Resonance Imaging (MRI). MRI examination is more

sensitive than CT scanning to detect primary tumor and direct spread of soft tissue. Blood vessels are also clearly visible even without contrast. Although the diagnosis can be made based on clinical symptoms, it is recommended to confirm with histopathological examination with a biopsy [9].

Another investigation for diagnosis NPC is the estimation of antibody levels against EBV [21]. Immunoglobulin (Ig) A titer against Viral Capsid Antigen (VCA) EBV is now used as a screening test for high risk populations or NPC famiy patients [22].

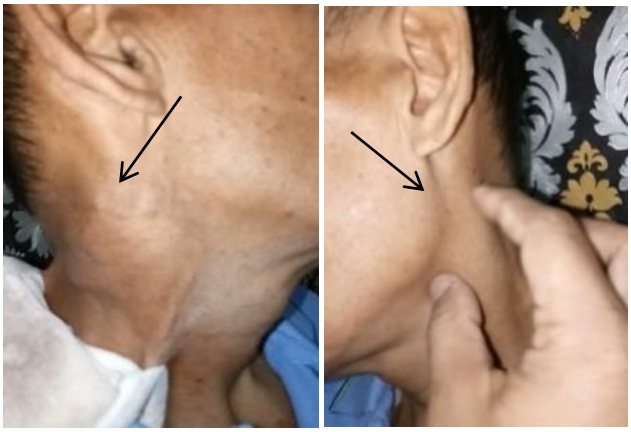
Strategic location of the NPC and tumor tendency to invade surrounding tissue, first line therapy for NPC is radiotherapy. Local and regional NPC can managed adequate by radiotherapy, whereas the role of chemotherapy usually carried out for spreading tumors such as lymphatic and hematogenous [16].

Epstein Barr Virus is important factor related to cancer. Knowledge about EBV can be used to identify genotypes and biomarkers to be applied in primary prevention, early detection, and predictions of t severity [19].

Male, 47 years old came to outpatient clinic on August 15, 2018 with the chief complain having a swollen neck since 4 months and double vision. Patients refer from oncologist with post incisional lymph node abscess with suspected nasopharyngeal cancer.

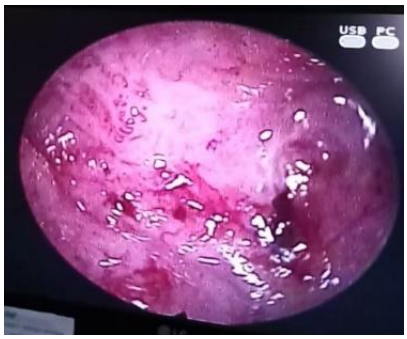
Physical examination, the general condition moderate, compos mentis, blood pressure 130/80 mmHg, respiration rate 20, heart rate 84, temperature within normal limit. Left and right ear within normal limit. External nose no deformity. Right nasal cavity wide, inferior turbinate within normal limit, no septum deviated. Left nasal cavity wide, inferior turbinate within normal limit, no septum deviated. Examination of the throat within normal limits. On posterior nasal endoscopy there is a mass in the nasopharynx. Eye examination: Ptosis (+), eye movement OD lateral-oblique superior inferior (-).

Right cervical lymph node region, 4x4x2 cm lymph node was obtained, the consistency of solid, no pain in palpation and there was an incisional scar matrix. Left cervical lymph node region, 2x2x1 cm lymph node was obtained, the consistency of solid, no pain in palpation. (Picture 1).



Picture 1. Right and left limph node examination

Right nasal endoscopy examination (Picture 2): wide nasal cavity, inferior, medial, turbinate within normal limit, medial meatus medial widely open, there was no nasal discharge, there was no septum deviated. Left nasal endoscopy examination: wide nasal cavity, inferior and medial turbinate within normal limit, medial meatus medial widely open, there was no nasal discharge, there was no septum deviated. Nasopharynx there was mass in left and right fossa rosenmueller granular, hyperemic, there was post nasal drip.



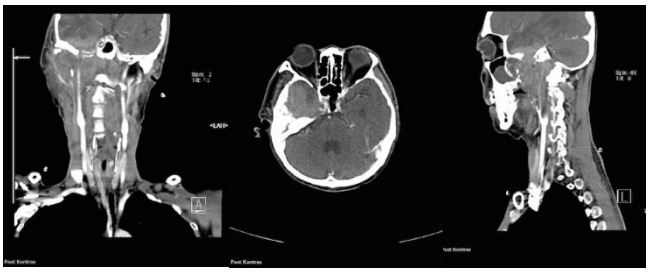
Picture 2. Nasoendoskopi from right nasal cavity

Base on that data we made working diagnostic nasopharyngeal mass. We plan for underwent biopsy. Laboratory examination hemoglobin 14.2 g/dl, leukocytes 9,400/mm3, hematocrit 42%, platelets 444,000/mm3, Bleeding Time 2 second, Clothing Time 7 second. Patient consult to Anesthesia Department, result: no contraindication.

Pathology anatomy result Nasopharyngeal Squamous cell carcinoma. Patient plan to staging with CT Nasopharynx, thorax x-ray, Abdomen Ultrasonography and bone survey.

CT Nasopharynx with contras result: appears right nasopharyngeal mass obliterated rosenmueller fossa, torus tubarius and right parapharyngeal space, infiltrating right masticator muscle, destructing right temporal bone, destructing right sella bone, infiltrating intracranial with hypodense on the right frontoparietal-temporal bone, contrast enhanced.

Thorax Rontgen, Abdomen ultrasonography and bone survey within normal limit and no sign of metastatic. Patient Diagnostic with NPC T4N2M0 Stage IVA and get management chemotherapy and radiotherapy.



Picture 3. Nasopharynx computed tomograpy with contras

2. DISCUSSION

Male, 47 years old was diagnostic with Nasopharynx Squamous Cell Carcinoma, Age distribution for cases that have developed to NPC varies between countries in the world [13]. In Indonesia the incidence of NPC at 1-30 years is 21%, with a peak occurrence at the age of 30-50 years [5].

Based on Indonesian cancer histopathology registration data in 2003, NPC was first ranked of all primary malignant tumors in men and eighth in women [23]. The male NPC incidence around 2-3 times higher than female [23].

Chief complain in this patient, swollen neck and double vision. Nasopharynx has many regional lymphatic vessels, metastases often found and cervical lymphadenopathy often the only clinical manifestation complained of by patients with NPC [24]. In Lee et all study cited from Wei in 4,768 NPC patients the most common symptom neck swelling (75,8%), nasal symptoms (73.4%), ear symptoms (62.4%), headaches (34.8%), diplopia (10.7%), facial numbness (7.6%), weight loss (6.9%) and trismus (3.0%) [11]. Complaints and clinical symptoms in children with adults are generally the same.

Nasal endoscopy examination this patient found a visible mass in the left and right rosenmueller fossa area. Endoscopic procedures cannot determine the third dimension of tumor growth, which is deep extension and includes erosion at the base of the skull and intracranial spread. This information can only be obtained by radiology examination. This investigation is very important to document the transmission of nasopharyngeal tumors and the involvement of surrounding tissues [21].

The patient was biopsy, with the impression of a nasopharyngeal squamous cell carcinoma. The type of cell carcinoma very important on the

management and prognosis of subsequent patients. The World Health Organization (WHO) in 1991 grouped NPC into 3 subtypes. Type 1) Squamous cell carcinoma with keratin, Type 2) Squamous cell carcinoma is not differentiated, and type 3) Squamous cell carcinoma is not differentiated [25-29]. In 2005 WHO made the most recent NPC classification into: 1) Keratinous squamous cell carcinoma, 2) Basaloid squamous cell carcinoma [30]. The tumor's histopathology type also determines a non-differentiated squamous cell carcinoma and 3) undifferentiated squamous cell carcinoma. where undifferentiated carcinomas have a higher level of local tumor control with radiotherapy [20, 30].

This patient is undergoing tumor staging, based on clinical symptoms and physical examination such as double vision, limited eyeball movement and ptosis, intracranial involvement. CT Nasopharynx result: intracranial intervention, Thorax Rontgen, Abdomen ultrasonography and bone survey within normal limit and no sign of metastatic. From this examination can be concluded, patient with T4 and no metastatic.

There were several stadium systems in NPC. The American Joint Committee on Cancer (AJCC) and International Union Against Cancer (UICC) systems are preferred in Europe and America. The old stadium system continues to be developed and revised, this is based on various experiences and clinical review obtained from various cancer centers in the world. The developed staging system must be based on several prognostic factors, such as the involvement of the skull base, cranial nerves, expansion of the primary tumor into the paranasopharyngeal space and the size of the lymph nodes of the neck [11].

Base on American Joint Committee on Cancer (AJCC) 8th edition 2018 citated from National Comprehensive Cancer Network (NCCN) guidelines 2019 [31]. NPC stage system:

T Stage (T)

Tx	Primary tumor cannot be assessed
T0	No tumor identified, but EBV-positive cervical node(s) involvement
Tis	Carcinoma in situ
T1	Tumor confined to the nasopharynx, or extenion to oropharynx and/or nasal cavity without parapharyngeal involvement
T2	Tumor with extension to parapharyngeal space, and/or adjacent soft tissue involvement (medial pterygoid, lateral pterygoid, prevertebral muscles)
T3	Tumor with infiltration of bony structures at skull base, cervical vertebra, pterygoid structures, and/or paranasal sinuses
T4	Tumor with intracranial extension, involvement of cranial nerves, hypopharynx, orbit, parotid gland, and/or extensive soft tissue infiltration beyond the lateral surface of the lateral pterygoid muscle

N Stage (N)

Nx	Regional nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Unilateral metastasis in cervical lymph node(s) and/or unilateral or bilateral metastasis in retropharyngeal lymph node(s), 6 cm or smaller in greatest dimension, above the caudal border of cricoid cartilage
N2	Bilateral metastasis in cervical lymph node(s), 6 cm or smaller in greatest dimension, above the caudal border of cricoid cartilage
N3	Unilateral or bilateral metastasis in cervical lymph node(s), larger than 6 cm in greatest dimension, and/or extension below the caudal border of cricoid cartilage

M Stage (M)

M0	No distant metastasis
M1	Distant metastasis

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T1,T0	N1	M0
	T2	N0	M0
	T2	N1	M0
Stage III	T1,T0	N2	M0
	T2	N2	M0
	T3	N0	M0
	T3	N1	M0
	T3	N2	M0
Stage IVA	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
	Any T	N3	M0
Stage IVB	Any T	Any N	M1

Patient with staging IVA get management chemotherapy and radiotherapy this corresponding NCCN guideline that patient with T4N2M0 get concurrant systemic therapy/RT followed by adjuvant chemotherapy.

Prognostic this patient for 5 years survival around 30-55% life expectancy it all depends on recurrence and the presence of distant metastases in stage 1 and 2 NPC is around 72-90% [2]. NPC sufferers often have poor prognosis, it's because late detection of clinical symptoms, lack of use of biomarkers for early detection and the low response of therapy that has been available so far [32].

3. CONCLUSION

The histological type of NPC, Staging, modality therapy management that will be given is important role in determining the prognosis of the disease. The life expectancy of patients with nasopharyngeal malignant tumors with intracranial or metastatic involvement lower than nasopharyngeal malignant tumors in the absence of distant metastases or intracranial involvement.

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