Case Report

Lumbar metastases in nasopharyngeal carcinoma (NPC) patient with uncompleate chemoradiation

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Abstract

Nasopharyngeal carcinoma (NPC) is a tumor arising from the epithelial cells that cover the surface and line the nasopharynx. In Indonesia, NPC is the 4th most prevalent. Nasopharyngeal Carcinoma stage IVB as distant metastasis. The therapy in nasopharyngeal carcinoma (NPC) is Chemoradiotherapy. Concurrent chemoradiotherapy is either an established treatment modality or actively being investigated. Chemoradiotherapy have demonstrated decreased incidence of distant metastases compared with radiation only, however only if its treatment done completely. Here we present a rare case of unfinished chemoradiotherapy that caused metastases nasopharyngeal carcinoma patient. A 41-years-old consulted to ENT-HN department with main complaints of progressive cancer pain for 3 month and got worse in past 1 month. Patient also complaints for the pain at the waist, chest and headache currently. However, there was formal history of nasopharyngeal carcinoma for this patient since 2019 that had been treated with 3 cycles of chemotherapy and 26 cycles of radiotherapy. The patient was diagnosed with recurrent nasopharyngeal carcinoma post chemotherapy and radiotherapy with metastatic process. Unfortunately, the treatment underwent was not complete. A nasopharyngeal biopsy was performed and the histopathology result revealed a non-keratinizing squamous cell carcinoma nasopharynx. Lumbar CT-scan showed distant metastatic to lumbar vertebrae I-V. Nasopharyngeal carcinoma (NPC) represents a rare disease that showed as carcinoma that appears in the nasopharynx. The unfinished treatment of NPC leads to recurrent NPC and metastatic process to lumbar vertebrae I-V. Nevertheless, 20% of patients are radioresistant and experience a recurrence, which in most cases manifests with distant metastases.

Keywords: Nasopharyngeal carcinoma, chemoradiotherapy, metastasis lumbar vertebrae.

Introduction

Nasopharyngeal carcinoma (NPC) is a tumor arising from the epithelial cells on the surface and the lines of the nasopharynx (Brennan, 2006). the NPC annual incidence vary as 0.8-2.2/100,000 in female and male respectively. However, it is a significant health problem in several geographic areas including Southern China, Hong Kong, and South-East Asia (Bray et al., 2018). In Indonesia, NPC is the fourth most prevalent cancer after breast, cervical, and lung cancer (Adham et al., 2012; Bray et al., 2018). The etiology of NPC (particularly the endemic form) is multistep process, in which EBV, ethnic background, and environmental carcinogens posed an important role (Brennan, 2006). The non-viral risk factors include family history, history of chronic rhinitis, consumption of salted fish, alcohol consumption, herbal product use, smoking and occupation exposure (Chen et al., 2016).

The tumor, node, metastasis (TNM) classification system includes six groups of NPC based on tumor extension (T1-4), the involving nodal (No-3), and the presence of metastasis (Mo-1). Stages I-II are considered as early diseases, while stages III, IVA, and IVB as locoregional advanced diseases as distant metastasis (Edge, 2010). The tumor can extend within or out of the nasopharynx to the other lateral wall and/or
posterosuperior to the base of the skull or the palate, nasal cavity or oropharynx. It then typically metastases to cervical lymph nodes. Distant metastases may occur in bone, lung, mediastinum and, more rarely, the liver (Brennan, 2006).

One of the therapies of nasopharyngeal carcinoma (NPC) is chemoradiotherapy. Concurrent chemoradiotherapy is either an established treatment modality or actively being investigated. Chemoradiotherapy have demonstrated decreased incidence of distant metastases compared with radiation alone (Edge, 2010).

We report here the case of an Indonesian man with rarely lumbar metastases of NPC after an uncompleted concurrent chemoradiotherapy. We discuss the clinical features and diagnosis of these rare clinical conditions.

Case

A 41-year-old male presented to the Dr, Zainoel Abidin Hospital, Banda Aceh, Indonesia and consulted to the department of ENT-HN with a main complaint of progressive pain for about three month and worsening in recent weeks. The patient also complained for the pain in the waist and chest, recurring headache, severe weakness, but medically stable. No complaints of nose bleeding or double vision, but there was a complaint of buzzing sound in the ear, associated with hearing impairment, ear discharge and feeling of fullness in the ipsilateral ear, but no otalgia and no postural imbalance. He was a non-smoker.

There was a former history of nasopharyngeal carcinoma for this patient since 2019 underwent uncompleted protocols having only 3 cycles of chemotherapy and 26 cycles of radiotherapy... Physical examination found mildly painful and fixed enlarged lymph nodes at the left side of the neck with 5 x 2 x 1 cm of diameter (Figure 1).

![Figure 1. The patient and the enlarged lymph nodes.](image)

Laboratory findings showed increase leukocytes and platelets count, in contrary low level of hemoglobin, hematocrit and erythrocytes count. A nasopharyngeal biopsy was performed and revealed a non-keratinizing squamous cell carcinoma of nasopharynx in April 2021. Computerized axial tomogram (CT-scan) of the nasopharynx with contrast revealed soft tissue thickening on the left side of the
nasopharynx (Figure 2A). Abdominal CT-scan and bone lumbar vertebrae CT-scan showed further metastasis process on the first to the fifth lumbar vertebral corpus (Figure 2B).

The patient diagnosed with recurrent nasopharyngeal carcinoma stage IVb post chemotherapy and radiotherapy with metastatic process in lumbar vertebrae. Then the patient treated with two cycles of chemotherapy using regimen consist of carboplatin, docetaxel, and zoledronic acid as supportive therapy. Improvement of patient’s complaint were obtained, with pain and headache significantly decreased.

Figure 2. Computed tomography scan (CT scan) of the nasopharynx (A) and the vertebra (B) of the patient.

**Discussion**

NPC is a carcinoma that appears in the nasopharynx (the area above the throat and behind the nose), which shows evidence of mild microscopic or ultrastructure squamous differentiation (Brennan, 2006). The symptoms and signs related to NPC include neck masses, epistaxis, nasal obstruction and discharge, ear disorders, headache, and other non-specific indicators. Furthermore, because the cancer is in a silent anatomic site, and NPC exhibits a higher metastatic rate, NPC tends to present at an advanced stages (clinical stages III and IV) when diagnosed. It has been shown that >70% of patients were at advanced stage when diagnosed in clinics (Brennan, 2006; Wu et al., 2017). In the presented case, the patient has been diagnosed with NPC since 2019 and he got a few times for chemoradiotherapy before, but unfortunately the treatment not complete yet. The patient decided not to come to the treat until eventually he got these last signs and symptoms again.

NPC has a high propensity of cervical node metastasis 85% of NPC cases presented with lymphadenopathy. The most commonly involved regions include the retropharyngeal (69%) and level II lymph nodes (70%). The overall probability of levels III, IV, and V nodal involvement are 45%, 11%, and 27%, respectively (Kresno, 2011).

Hematogenous metastases occur when cancer cells reach the blood vessels. Penetrated blood vessels determine where metastases will occur, within capillaries of circulating cancer cells stopping as cancer emboli. This principle also explains the existence of a specific pattern of metastases or a specific site of metastasis. Cancer area manipulation, such as palpation, massage, and curettage increase the likelihood of the presence of such cells in the blood (Bosman, 1999).

Cancer cells are attached to the endothelium and surrounded by a network of fibrin, platelets, and leukocytes before penetrating the blood vessels. vascularity of the visited area and its ability to produce angiogenic factors. Metastasis can sometimes appear several years after the primary cancer has been completely removed. The
localization of the first hematogenous metastases is often determined by the localization of the first capillary network that the cancer cell reaches through the blood vessels (Liu et al., 2006).

Metastasis proceeds through 5 sequential stages as follows. Invasion and migration of cancer cells that break away from primary cancer and invade the surrounding healthy tissue, in this process the secretion of various lytic enzymes destroy the extracellular matrix, thereby facilitating migration. Intravasation is the entry of cancer cells into the blood and lymph circulation. Cancer cells are attached to endothelial cells through adhesion molecules, by secreting proteolytic enzymes that cause cancer cells to infiltrate blood vessels. Cancer cells circulate in the circulation and must face various conditions that exist in the blood. High oxygen concentration and cytotoxic lymphocytes immune surveillance, in this condition, there is a selection of resistant and aggressive cancer cells (Liu et al., 2006).

The use of intravenous zoledronic acid has been shown in several clinical trials to provide immediate and durable palliation of bone pain in patients with malignant bone disease. Among Japanese women with bone metastases from breast cancer, zoledronic acid reduced the mean composite Brief Pain Inventory (BPI) scores compared with placebo with significant reductions starting at week 4 and at every subsequent time point throughout. Zoledronic acid also prevented worsening of Eastern Cooperative Oncology Group performance status in a larger percentage of patients compared with placebo (28% vs. 36%, respectively) (Chen et al., 2016).

Radiotherapy remains the standard care for NPC treatment, either alone or in combination with chemotherapy. Radiation alone is applied in stage I disease. For stages II-IVB, guidelines recommend concurrent chemoradiotherapy (CCRT) with adjuvant chemotherapy (AC) (CCRT-AC), induction chemotherapy (IC) followed by CCRT (IC-CCRT), or CCRT alone. Combination chemotherapy and radiation treatment may apply sequentially. For stage IVC, platinum-based chemotherapy is the preferred strategy for chemo naive individuals with satisfactory performance, although chemoradiotherapy for locoregional disease can also be given (Brennan, 2006; Union for International Cancer Control, 2014).

Concurrent chemoradiotherapy is either an established treatment modality or actively being studied. Chemoradiotherapy has demonstrated decreased incidence of distant metastases compared with radiation alone, however, only if its treatment is done completely (Brennan, 2006; Edge, 2010; Union for International Cancer Control, 2014).

Unfortunately, there are about 20% of the patients suffer from a radioresistant disease that recurs after upfront therapy. In presented case, the unfinished treatment may eventually lead to recurrent NPC and further to the lumbar metastasis.

Re-irradiation and surgery are strategies that are more preferrable, albeit related to the high risk of morbidity. Immunotherapy and targeted therapy, such as heavy ions-based re-irradiations, are experimental but very intriguing options (Brennan, 2006; Edge, 2010; Perri et al., 2019; Union for International Cancer Control, 2014). Although NPC is highly prevalent in Indonesia, there is no comprehensive report on patients’ survival, and the determining factors affecting survival not widely reported (Adham et al., 2012; Adham et al., 2014).

Conclusion

NPC represents a rare disease that showed as a carcinoma that appears in the nasopharynx (the area above the throat and behind the nose). Symptoms related to the primary tumor include trismus, pain, otitis media, nasal regurgitation due to paresis of the soft palate, hearing loss, and cranial nerve palsies. Larger growths may produce nasal obstruction or bleeding. Metastatic spread may result in bone
pain or organ dysfunction. The variation of treatment modality may have an effect on survival. One of the therapies in NPC is Chemoradiotherapy. Concurrent chemoradiotherapy is either an established treatment modality or is actively being investigated. The unfinished treatment of NPC leads to recurrent NPC and metastatic NPC in another organ. Nevertheless, 20% of patients are radioresistant and experience a recurrence, which in most cases manifests with distant metastases. Systemic therapies are the gold standard in this case, but locoregional recurrences, localized in the nasopharynx or in the lateral cervical lymph nodes, should be managed differently.

**Authors’ contributions**

Conceptualization: AM and LS; Data curation: AM; Investigation: AM; Resources: AM and LS; Supervision: AM; Validation: AM and LS; Writing-original draft preparation: AM; Writing-review and editing: AM and LS.

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**Conflict of interest**

There is no conflict of interest was reported by the authors.

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Union for International Cancer Control. Cancer Medicines on the WHO List of...