

두경부 원발부위 불명암에서 치료 후 발견된 비인두암

김은지 · 홍기환 · 홍용태*

전북대학교 의과대학 이비인후과학교실

Nasopharyngeal cancer found after treatment of unknown primary cancer in the head and neck

Eun Ji Kim, MD, Ki Hwan Hong, MD, Yong Tae Hong, MD, PhD*

Department of Otolaryngology-HNS, Research Institute for Clinical Medicine of Chonbuk National University-
Biomedical Research Institute of Chonbuk National University Hospital, Chonbuk, 560-182, Korea

= Abstract =

Despite adequate diagnostic work-up, unknown primary carcinoma(UPC) of the head and neck cannot be detected in approximately 2- 3% of patients.(1,2) There are several explanations for a cervical metastasis in the absence of a primary tumor. Here in, we report 2 patients, who were diagnosed with nasopharyngeal cancer after treatment of unknown primary cancer of the neck. Both patients had radical neck dissections and chemoradiation therapy, but 1 patient showed nasopharyngeal cancers 4 years after treatment and the other patient at 9 months after treatment for the unknown primary cancer. Therefore, we report 2 cases of nasopharyngeal cancer, which were diagnosed after treatment of unknown head and neck primary site.

Key Words : Nasopharyngeal cancer, Unknown primary cancer

Introduction

Unknown primary carcinoma (UPC) of the head and neck is a unique clinical phenomenon found in approximately 2-3% of patients, despite appropriate diagnostic investigations.^{1,2)}

UPC is defined as a biopsy-proven malignancy, in the absence of an identifiable primary site after a complete history, physical examination, and other studies for cancer have been performed. UPC may be considered as metastases from a primary tumor that has not been found or that does not show

clinical signs or symptoms of the primary tumor. The common types of cancer associated with UPC are adenocarcinomas and poorly differentiated carcinomas. Only 5-8% of UPCs are squamous carcinomas and 2-5% are undifferentiated malignancies.³⁻⁵⁾

Diagnostic evaluation should be focused on the identification of the primary origin of the tumor, as this can lead to disease-directed treatment and a better-defined prognosis. There are many studies on the evaluation of patients with UPC, including endoscopic evaluations and radiologic images, such as computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET)-CT. Additional directed studies include monoclonal antibody panels and molecular profiling techniques to detect the specific genomic and phenotypic characteristics of the malignant cells involved.⁴⁻⁷⁾

The status of metastatic neck nodes, such as the size of

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+Corresponding author: Yong Tae Hong MD. PhD.

Department of Otolaryngology-HNS, Chonbuk National
University, Medical School, Chonju, Chonbuk, 561-712, Korea
Tel: 82-63-250-1990, Fax: 82-63-250-1986
E-mail: centennialman@hanmail.net

the neck mass, extracapsular spread, and lymph node ratio, should be considered before initiating treatment. In addition, the status of retropharyngeal nodes and human papilloma virus(HPV) or Epstein Barr virus(EBV) provide useful information for treatment.^{3,4)} Treatment should be decided using a multidisciplinary team approach. If there is advanced neck node status without any evidence of abnormalities on physical and imaging examinations, upfront neck dissection is preferred. The next step is to determine whether adjuvant radiotherapy/concurrent chemoradiotherapy should be given. In this study, we report 2 extremely rare cases of delayed detection of nasopharyngeal carcinoma and a review of relevant literature. These patients received proper evaluation for UPC in the head and neck, but detection of nasopharyngeal carcinoma was delayed, which was found after the treatment of UPC.

Case report

In the first case, a 78-year-old man presented with a headache and voice change. He had a hard tender mass on his right neck in level III area 2 cm in size. He underwent

core needle biopsy and was diagnosed with metastatic carcinoma in the neck. However, on fibrotic laryngoscopy, neck CT (Fig. 1A, B), and PET-CT (Fig. 1C) images, there was a metastatic neck mass on the right neck, level III, with no abnormal suspicious primary site in head and region. He was diagnosed with metastatic carcinoma of the head and neck with unknown primary site. Radical neck dissection was performed in his right neck.

Immunohistochemical study revealed negative for Synaptophysin, Chromogranin, CD56 and CK20 marker. Unfortunately, evaluation for EBV, HPV markers were not performed and metastatic carcinoma was confirmed. Postoperative radiation therapy was performed 1month after the operation. Follow-up evaluation was done every 3 months in the first year and then every 6 months. However, at 4 years after the treatment, an irregular margin mass with yellowish crust was found on the right lateral nasopharynx (Fig. 1D). We performed a punch biopsy of the nasopharyngeal mass and it was reported as a nonkeratinizing nasopharyngeal carcinoma. A 4.0 x 4.0 cm sized mass was noted on right nasopharynx with parapharyngeal extension on neck CT (Fig. 1E), and PET-CT (Fig. 1F). He received che-

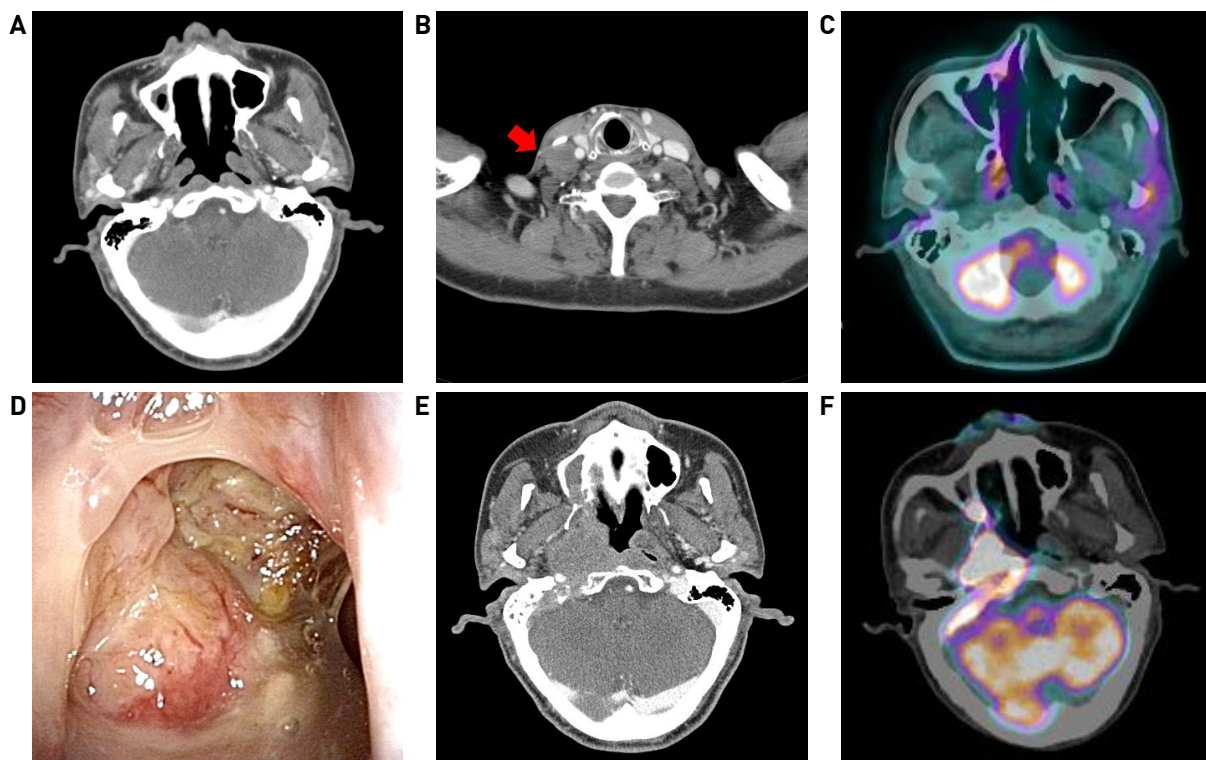


Fig. 1. Case 1. Before detection of right nasopharyngeal cancer, normal CT on the nasopharynx(A) and right metastatic neck mass(B) and normal PET-CT image on nasopharynx(C). After detection of nasopharynx cancer, endoscopic finding of right nasopharyngeal cancer(D), right nasopharyngeal mass on CT(E) and PET-CT(F) images.

motherapy, but experienced seizures and aggravation of his general condition. He passed away during the period of chemotherapy.

In the second case, a 57-year-old man presented with a hard fixed non-tender mass on the left neck level IB, approximately 3 cm in size. On neck CT, there were multiple lymph nodes with necrotic change on the left neck level IB to IIA, and the largest lymph node diameter was 1.7 cm (Fig. 2A). However, there was no mass on the left nasopharynx (Fig. 2B) with no abnormal suspicious primary site in head and region., We performed fine needle aspiration and the pathological result was reported as poorly differentiated carcinoma in the neck. He received radical neck dissection and postoperative chemoradiation therapy in the neck. Immunohistochemical study revealed negative for CK7, CK20 marker and positive for P63, Cytokeratin marker. Unfortunately, evaluation for EBV, HPV markers were not performed and metastatic carcinoma was confirmed. Follow-up evaluation was done every 3 month after the treatment. At 9 months after the treatment, left nasopharyngeal mucosa showed protrusion on endoscopic view but the mucosa seem

to be normal (Fig. 2D). We performed a punch biopsy on the nasopharyngeal mass after incision of the protruded mucosa of the left nasopharynx. The specimen was reported as nonkeratinizing nasopharyngeal carcinoma. On CT (Fig. 2E) and PET-CT (Fig. 2F) images, a 4.0 x 3.0 cm sized mass was noted on the left nasopharynx. He received chemotherapy, but over time, he complained of diplopia, dizziness and facial palsy. His general condition and symptoms worsened and died 10 months after the recurrence.

Discussion

Head and neck cancer patients frequently present with cervical lymph node metastases. Despite adequate diagnostic work-up, the primary tumor cannot be detected in approximately 2-3% of patients. There are several hypotheses for cervical metastasis in the absence of a primary tumor.¹⁻⁵⁾ Small tumors in particular areas, such as the tonsillar fossa or the base of tongue, can be easily missed, both on physical and radiographic exams, due to the anatomical complexity of the region and the intrinsic limitations of di-

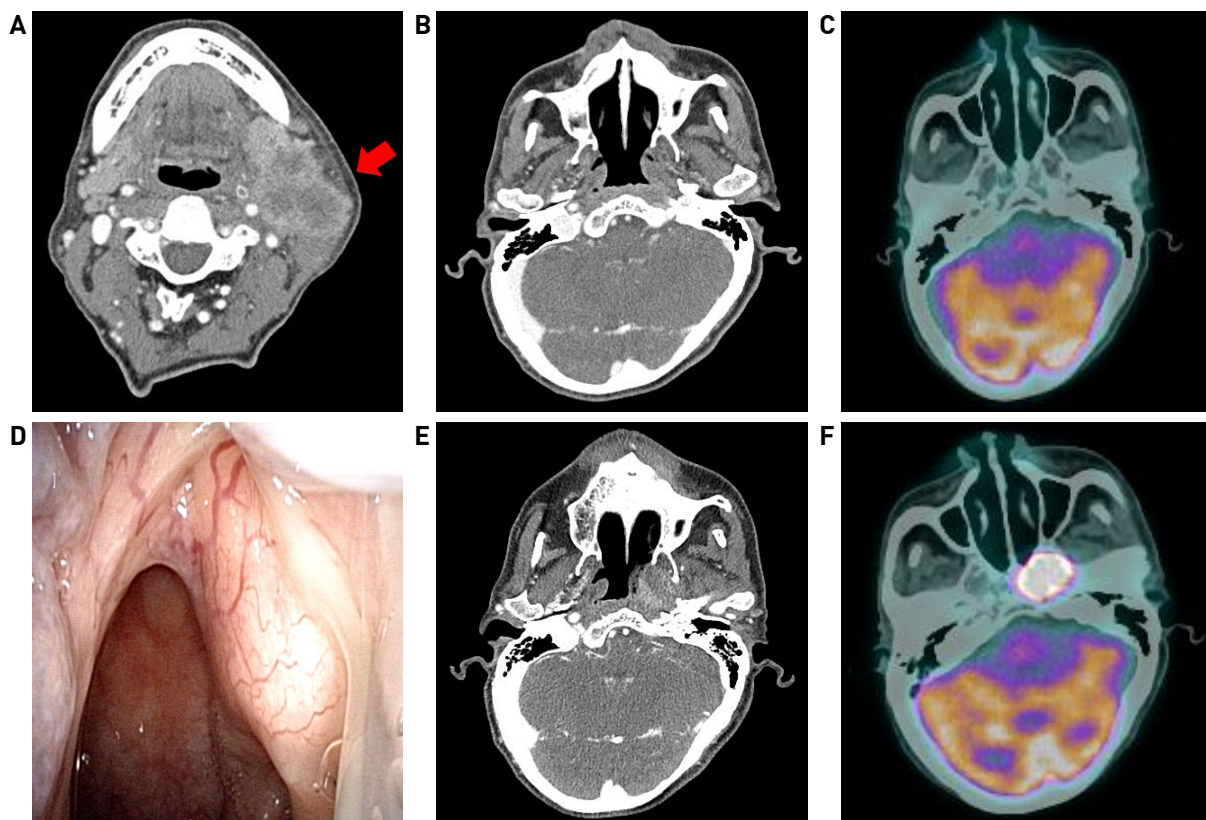


Fig. 2. Case 2. Before detection of nasopharyngeal cancer, normal CT on the nasopharynx(A) and left metastatic neck mass(B) and normal PET-CT image on nasopharynx(C). After detection of left nasopharynx cancer, endoscopic finding of left nasopharyngeal cancer(D), left nasopharyngeal mass on CT(E) and PET-CT(F) images.

agnostic techniques.³⁻⁶⁾ A small tumor hidden in the crypts of the lymphoid tissue of the tonsillar fossa and base of tongue can acquire an early metastatic phenotype and spread to regional lymph nodes while remaining undetectable.^{6,7)} Cianchetti et al³⁾ reviewed 236 patients of UPC of the head and neck and found the tonsillar fossa(44.7%) was most common primary location followed by base of tongue (43.9%) and 1 case documented from the nasopharynx (0.7%). Advances in the understanding of the basic biology of unknown primary cancers in the neck may have a direct impact on clinical care. When patients are diagnosed with neck metastases of an unrecognized primary, the diagnostic evaluation should concentrate on the identification of the primary origin of the tumor. This identification can lead to disease-directed treatment and a better-defined prognosis.^{7,8)} As seen in our 2 patients, the neck node was found before the nasopharyngeal cancer was diagnosed. Therefore, if an unknown primary cancer is diagnosed, there is a need for regular physical examination with radiologic examination of the nasopharynx. In the first case, nasopharyngeal mass was detected 4 years after the initial treatment. Thus, it has a possibility of metachronous second primary cancer of nasopharynx. But, considering the size of nasopharyngeal mass and clinical course, we think this patient is a UPC of the head and neck with delayed detection of primary site.

At present, the radiologic exams for clinical diagnosis of nasopharyngeal cancer include CT, MRI, and PET-CT. Each procedure has different characteristics, as they are different forms of imaging. MRI is superior in the depiction and delineation of local invasion of a primary tumor, when combined with the diagnostic characteristics of distant metastasis on PET/CT. This combination is the best clinical strategy to guide diagnosis and treatment. Thus, further evaluation should be focused on developing tools for better detection, such as the use of MRI and PET scanning. However, in our cases, we could not find the primary site using CT,

MRI, PET-CT and endoscopy. Nasopharynx is rare location found in UPC of the head and neck and delayed detection of primary site leads to poor outcome as in our cases. Nowadays, Immunostaining of biopsy specimens is also very important for the diagnosis of UPC. For example, in AJCC, a positive Epstein-Barr virus can be considered as a nasopharyngeal carcinoma without a nasopharyngeal mass. Therefore, molecular studies to detect the specific genomic and phenotypic characteristics of the malignant cells involved are important. Further, when follow up after treatment of unknown primary cancer, continuous care and examination is required as delayed primary site recurrence may occur.

References

- 1) Million RR, Cassisi NJ, eds. *Management of Head and Neck Cancer: A Multidisciplinary Approach*. Philadelphia, PA: JB Lippincott Co; 1994. p.311-20.
- 2) van de Wouw AJ, Jansen RL, Speel EJ, Hillen HF. *The unknown biology of the unknown primary tumour: a literature review*. *Ann Oncol*. 2003;14:191-6.
- 3) Cianchetti M, Mancuso AA, Amdur RJ, Werning JW, Kirwan J, Morris CG, et al. *Diagnostic Evaluation of Squamous Cell Carcinoma Metastatic to Cervical Lymph Nodes From an Unknown Head and Neck Primary Site*. *Laryngoscope*. 2009;119:2348-54.
- 4) Hainsworth JD, Greco FA. *Management of patients with cancer of unknown primary site*. *Oncology (Huntingt)*. 2000;14:563-74.
- 5) Greco FA, Burris HA III, Erland JB. *Carcinoma of unknown primary site*. *Cancer*. 2000;89:2655-60.
- 6) Greco FA, Hainsworth JD. *Cancer of unknown primary site*. In *DeVita VT Jr, Hellman S, Rosenberg SA (eds): Cancer: Principles and Practice of Oncology, 5th edition*. Philadelphia, PA: Lippincott; 1995. p.2072-92.
- 7) Lembersky BC, Thomas LC. *Metastases of unknown primary site*. *Med Clin North Am*. 1996;80:153-71.
- 8) Abbruzzese JL, Abbruzzese MC, Hess KR, Raber MN, Lenzi R, Frost P. *Unknown primary carcinoma: natural history and prognostic factors in 657 consecutive patients*. *J Clin Oncol*. 1994; 12:1272-80.