

## Quadruple Primary Malignancies in an Old Male Smoker Treated with Cooperative Surgery

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### — ABSTRACT —

The patients with head and neck cancers are frequently elderly with history of smoking that may harbor possibilities of multiple primary malignancies. Recent use of PET-CT as an initial diagnostic tool facilitates the finding of unexpected primary malignancies. Here we present a case of quadruple primary malignancies treated with cooperative surgery. A 66 year-old male presented with sore throat. He was identified as a current smoker and had a history of alcohol ingestion. Physical examination followed by office-based biopsy revealed supraglottic squamous cell carcinoma. Imaging studies including PET-CT found multiple suspicious malignant lesions involving thyroid gland, esophagus, sigmoid colon as well as the larynx. Further multidisciplinary consultation suggested that all of the evaluation lesions were primary malignancies without evidence of systemic spread. The patient underwent cooperative surgery ; supraglottic partial laryngectomy with neck dissection for supraglottic cancer, left hemithyroidectomy for thyroid cancer, Ivor Lewis operation for esophageal cancer, lower anterior resection for colon cancer. Careful postoperative care was provided without a complication. Office-based observation has been ongoing without an evidence of recurrence. (J Clinical Otolaryngol 2015;26:312-316)

**KEY WORDS** : Quadruple primary cancer · Multiple primary cancer · Head and neck cancer.

### Introduction

Multiple primary cancer is defined as the two or more malignancies in an individual that the possibility of relationship between to tumors are excluded.<sup>1)</sup> Most are double primary cancers, and the incidence decreases as the number of concomitant cancer increases.<sup>2,3)</sup> The incidence of multiple primary malignancies is increasing in recent years probably due to an increased age at diagnosis and improvements in diagnostic modalities including positron emission tomography-

computed tomography (PET-CT).<sup>4,5)</sup> Because therapeutic planning is usually complicated in case of multiple synchronous malignancies, careful multidisciplinary approach is crucial for proper therapeutic planning.<sup>6)</sup> In the head and neck cancer, the patients are generally elderly and harbor multiple risk factors including smoking and alcohol consumption.<sup>7)</sup> Thus, the incidence of synchronous multiple primary cancers are relatively high in patients with head and neck cancer compared with other site of cancers.<sup>2,8,9)</sup> In the present study, we report a case of quadruple primary malignancies in an old male smoker treated with cooperative surgery.

### Case Report

A 63 year-old male was presented with sore throat during 5 months. He also complained other symptoms

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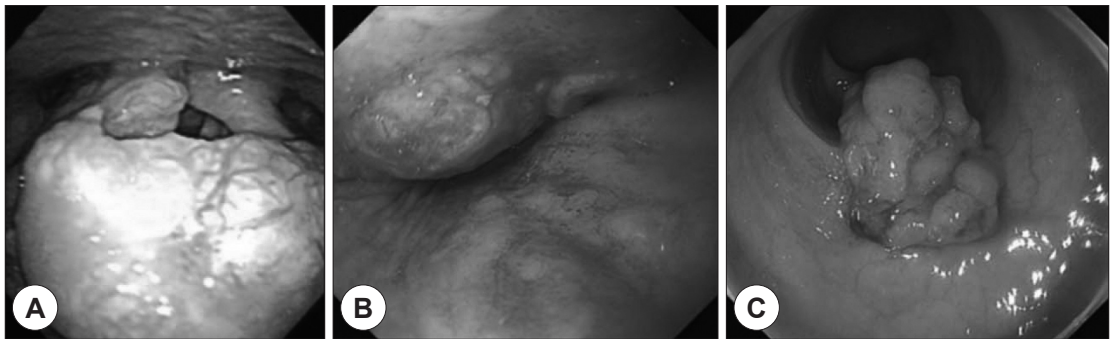
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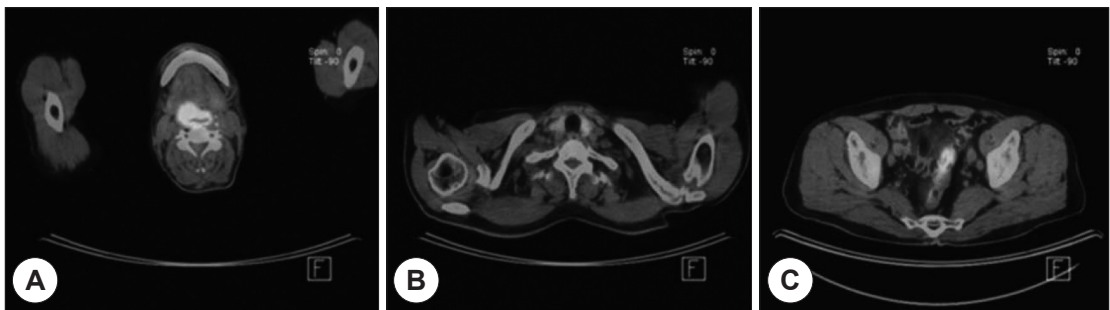
of voice change and globus sensation. He did not have past medical history except hypertension. He was a current smoker with a history of 50 pack-year and had a history of alcohol consumption. No specific family history was noted. Laryngeal evaluation revealed an exophytic mass at the laryngeal surface of epiglottis which was extended to the right aryepiglottic fold (Fig. 1A). Bilateral vocal folds were mobile without evidence of tumor invasion. Computed tomography showed a supraglottic mass with right paraglottic space invasion and a suspicious metastatic lymph node in the right lateral neck. Office-base biopsy revealed well-differentiated squamous cell carcinoma. Thus, initial diagnosis was made as supraglottic cancer with right lateral neck metastasis (cT3N1) and PET-CT was planned to evaluate presence of distant metastasis.

PET-CT results showed that increased fludeoxyglucose (FDG) uptake at the supraglottic mass with a

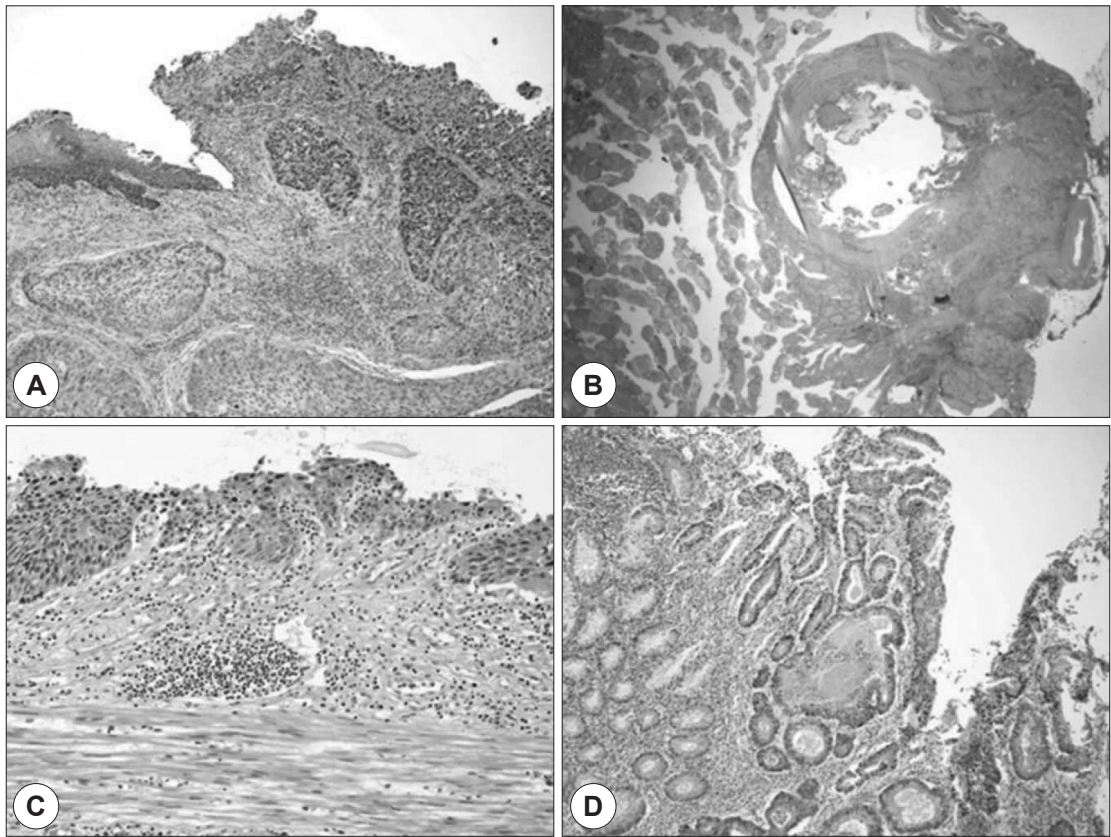
standardized uptake value (SUV) of 20.1 and right level III lymph node with an SUV of 3.6 (Fig. 2A). However, we unexpectedly found another multiple increased FDG uptake including left thyroid gland (SUV : 4.1), sigmoid colon (SUV : 15.5) (Fig. 2B, C). Multidisciplinary consultations were conducted and the patient was diagnosed as multiple synchronous malignancies including esophageal squamous cell carcinoma (cT1N0M0) and colon adenocarcinoma (cT1N0M0) (Fig. 1B, C). The patient refused to further evaluate regarding thyroid nodule. Cooperative surgical intervention was planned. First, head and neck surgical team performed supraglottic partial laryngectomy with right modified radical neck dissection for supraglottic cancer and left hemithyroidectomy for thyroid nodule. Next, Ivor-Lewis operation for esophageal cancer and lower anterior resection for sigmoid colon cancer were performed by two different surgical teams. After syn-



**Fig. 1.** Endoscopic images of primary tumors. A : Exophytic supraglottic mass originating from laryngeal surface of epiglottis. B : Ulcerative mass in distal esophagus. C : Polypoid mass in sigmoid colon.



**Fig. 2.** Images from PET-CT. A : Images showing increased FDG uptake in supraglottic cancer (SUV : 20.1). B : Images showing increased FDG uptake in thyroid nodule (SUV : 4.1). C : Images showing increased FDG uptake in sigmoid colon (SUV : 15.5).

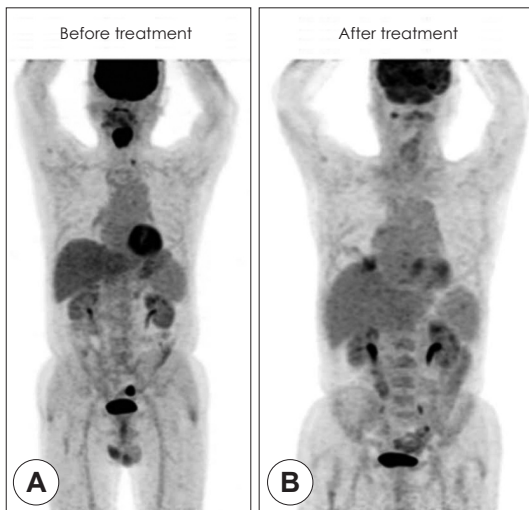


**Fig. 3.** Pathologic analysis of the quadruple primary malignancies stained with hematoxylin and eosin. A : Well-differentiated supraglottic squamous cell carcinoma invading the thyroid cartilage (magnification 100 $\times$ ). B : Thyroid papillary carcinoma with a size of 1.0 cm (magnification 12.5 $\times$ ). C : Esophageal squamous cell carcinoma with invasion of lamina propria (magnification 200 $\times$ ). D : Colon adenocarcinoma (magnification 200 $\times$ ).

chronous surgical intervention, the patient transferred to Intensive Care Unit (ICU) and recovered well without a complication. Final pathologic evaluation showed the quadruple primary malignancies including supraglottic cancer with invasion of thyroid cartilage and a metastatic lymph node in level IIA (pT4aN1) (Fig. 3). Pathological evaluations also indicated the thyroid gland having papillary thyroid cancer with a maximum diameter of 1.0 cm. Post-operative adjuvant radiotherapy was conducted for supraglottic cancer. Follow-up evaluations using PET-CT at 4 months after treatment showed no evidence of tumor recurrence (Fig. 4).

## Discussion

Since the first report of tumors in multiple organs in 1889, the incidence of multiple primary cancers have been increasing, mainly attributed by increased age at diagnosis and improvements of diagnostic modalities.<sup>3,4)</sup> The conventional diagnostic criteria of multiple primary cancer is, 1) Each cancer must be definitively malignant by histopathology, 2) they must be histologically different, and 3) the possibility of metastasis among the cancers must be excluded.<sup>3,4)</sup> Moertal et al classified multiple primary cancers observed at the same time or within six months as synchronous multiple primary cancers, and cancers developing with



**Fig. 4.** Comparisons of Images from PET-CT. A : Images showing multiple synchronous malignancies before treatment. B : Images showing no evidence of tumor recurrence after treatment.

more than six months as an interval as metachronous multiple primary cancers.<sup>10</sup> Here the patient was diagnosed as quadruple malignancies without an evidence of relationship of each tumor within 6 months. Thus, the final diagnosis was made as synchronous quadruple primary malignancies.

The main risk factors of multiple primary cancers are presence of family history and repeated carcinogen exposure such as tobacco smoking and alcohol ingestion. Huang et al. performed investigation of family history in a patient with multiple primary cancer and found hereditary non-polyposis colorectal cancer is the main risk factor of multiple cancers.<sup>11</sup> Although majorities of cases are not related with known hereditary syndrome, other unknown genetic susceptibilities might be involved in that multiple tumorigenesis.<sup>12</sup> Besides, older age itself is a risk factor of most of the malignancies, thus, it appears evident that increased age at diagnosis in recent years is one of factors of rising incidence of multiple primary malignancies.<sup>6</sup> Advancements of diagnostic modalities also contribute the rising incidence of synchronous multiple primary cancers.<sup>4,5</sup> Of note, preoperative use of PET-CT facilitates the unexpected findings of multiple pri-

mary cancers as well as distant metastasis. Here, repeated carcinogen exposure including 50 pack-year smoking and alcohol ingestion may contribute to the development of multiple primary cancers. Also, preoperative PET-CT facilitates unexpected discovery of multiple tumor foci such as thyroid malignancy.

Considering that the most of patients with head and neck cancers are elderly and have a history of smoking and alcohol ingestion, it is acceptable that the incidence of multiple primary cancer is relatively high in those patients compared with the patients with other type of cancers.<sup>6,13</sup> Carcinogenic insult, such as tobacco and alcohol, may increase the likelihood of multiple independent malignant foci developing in the mucosa epithelium.<sup>2</sup> The frequency of multiple primary tumors in the head and neck region is also supported by the field cancerization theory, which the carcinogenic agents can initiate the tumorous degeneration at other affected sites.<sup>2</sup> Thus, during management of head and neck cancer, physicians should keep in mind for the probabilities of other tumor foci.

There are no established therapeutic rules for multiple primary cancers, but the type, progression, response to therapy, and patient's general health status should be considered.<sup>3</sup> If each of the cancers has the possibility of cure, radical therapy is indicated. Because the patients with multiple primary cancers are typically elderly and harbor tumors in multiple organs, therapeutic plan should be made to reduce treatment-related morbidity while maintaining acceptable oncologic outcomes.<sup>6</sup> In the present case, esophageal and colon cancer showed early primary lesion with no evidence of metastasis. Multidisciplinary consultation indicated that radical surgical approach is possible option in management of each tumor. Thus, we could conduct cooperative surgical ablation for all of the multiple primary cancers synchronously without a complication.

In conclusion, we report quadruple primary malignancies in an old male smoker treated with cooperative surgery. The findings of unexpected primary malignancies should be considered especially in head and neck cancer patients. Prevention, early diagnosis,

and treatment would be important and multidisciplinary consultation is crucial for overall management of multiple primary malignancies.

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