Abstract. We herein present the first case to be reported of synchronous quadruple primary cancer of the thyroid, breast, pancreas and stomach in a 70-year-old female. Fluorine-18-fluorodeoxyglucose (FDG)-positron-emission tomography/computed tomography (PET/CT) revealed increased FDG activity in the thyroid, left breast, pancreatic body and antrum of the stomach. To make a definitive diagnosis of synchronous quadruple primary tumors, ultrasound-guided fine-needle aspiration (FNA) cytology and biopsy of the thyroid, breast, pancreas and stomach were performed. FNA cytology and biopsy findings showed papillary carcinoma of the thyroid, invasive ductal adenocarcinoma of the breast, adenocarcinoma of the pancreas and gastrointestinal stromal tumor. To the best of our knowledge, this combination of synchronous multiple primary tumors has not been reported.

Recently, reports of multiple primary tumors occurring in the same patient have gradually been published. The majority of multiple primary tumors are metachronous, while multiple synchronous primary tumors in the same patient are extremely rare (1, 2). Recently, we experienced a case of synchronous quadruple primary cancer of the thyroid, breast, pancreas and stomach in a 70-year-old female. As far as we know, there has been no such case reported in the English language literature. We report the first case of synchronous quadruple primary tumors involving the thyroid, breast, pancreas and stomach, and a review of the medical literature.

Case Report

A 73-year-old female was admitted to Chonnam National University Hwasun Hospital (Jeonnam, Korea) with dyspepsia of one month. She suffered from essential hypertension and hyperlipidemia, but there was no previous history of peptic ulcer diseases, cholecystitis with gallstones, smoking, any alcohol ingestion, or abdominal surgery. Her family history was non-contributory. On admission, she was afebrile, with normal blood pressure and pulse, and she appeared well-nourished. Anemic conjunctiva and scleral icterus were not present. Her abdomen was not tender. There was no abdominal mass; the liver, gallbladder, and spleen were not palpable, and bowel sounds were normoactive. All laboratory examinations, including complete peripheral blood cell counts, blood biochemistry and tumor markers, were within normal range.

Esophagogastroduodenoscopy showed a protruding lesion about 5 cm in size, covered with normal mucosa in the antrum of the stomach, suggesting gastric submucosal tumor. Abdominal computed tomography (CT) revealed an approximately 5.0×4.0 cm sized mass in the antrum of the stomach and a 1.5 × 1.8 cm sized ill-defined mass with dilation of the main pancreatic duct in the pancreatic body. Endoscopic ultrasonography (EUS) showed a homogeneous hypoechoic mass originating from the proper muscle layer in the antrum, indicating gastrointestinal stromal tumor (GIST). Magnetic resonance imaging (MRI) showed an ill-defined inhomogeneous mass with invasion of celiac axis and dilation of the main pancreatic duct in the body, indicating pancreatic cancer.

We performed fluorine-18-fluorodeoxyglucose (FDG)-positron-emission tomography/computed tomography (PET/CT) to stage the pancreatic cancer and GIST. FDG-PET/CT revealed increased FDG activity in both thyroid lobes, left breast, pancreatic body and antrum of the stomach (Figure 1). Neck US revealed a 1.1×1.0-cm sized speculated isoechoic mass in the left lobe and a 1.3×1.5-cm sized speculated hypoechoic mass in the right lobe of the thyroid. Breast US revealed several irregular hypoechoic masses in the upper inner portion of the left breast.

To make the histological diagnosis of synchronous quadruple primary tumors, US-guided fine-needle aspiration (FNA) cytology and biopsy of the thyroid, breast, pancreas, and stomach were performed. FNA cytology and biopsy findings showed papillary carcinoma of the thyroid, invasive ductal adenocarcinoma of the breast, adenocarcinoma of the pancreas and gastrointestinal stromal tumor. To the best of our knowledge, this combination of synchronous multiple primary tumors has not been reported.

Key Words: Synchronous cancer, thyroid, breast, stomach, pancreas.
Figure 1. Fluorine-18-fluorodeoxyglucose (FDG)-positron emission tomography/computed tomography (PET/CT). Maximum intensity projection PET image shows the FDG-avid foci in both thyroid lobes, left breast, pancreatic body and antrum of the stomach (arrows) (A). PET/CT shows multiple masses with increased FDG uptake in both thyroid lobes, left breast, pancreatic body and antrum of the stomach (arrows) (B).

Figure 2. Microscopic examinations. Papanicolaou staining shows the characteristic Orphan Annie eye nuclear inclusions, intranuclear grooves and pseudoinclusion, indicating papillary carcinoma of the thyroid (A, x400). Routine histology, stained using hematoxylin-eosin (H&E), shows moderately differentiated invasive ductal carcinoma of the breast (B, x200). Routine histology, stained using H&E, shows moderately differentiated adenocarcinoma of pancreas (C, x200). Immunohistochemical staining of tumor cells is strongly positive for cluster of differentiation antigen 117 (CD117), indicating gastrointestinal stromal tumor (D, x100).
and stomach were performed. Microscopic examinations revealed papillary carcinoma of the thyroid (Figure 2A), invasive ductal adenocarcinoma of the breast (Figure 2B), adenocarcinoma of the pancreas (Figure 2C) and GIST positive for cluster of differentiation antigen 117 (CD117) (Figure 2D), respectively. The patient refused further evaluation and aggressive treatment such as surgery. We decided to treat the breast cancer and GIST by hormone therapy and chemotherapy, and provide supportive treatment for the thyroid and pancreatic cancer. Therefore, the patient was given letrozole (Femara® Tab 2.5 mg) and imatinib (Glivec® Tab 2.5 mg). The patient’s condition was getting worse, and she eventually died 8 months after the diagnosis.

Discussion

The incidence of synchronous and metachronous multiple primary tumors has increased in recent decades (1, 2). There are several possible explanations for this change. Firstly, recent improvements in the survival of patients with tumor have led to an increase in the incidence of second primary tumors, and the frequency of multiple primary tumors is expected to increase as the population ages. Secondly, changes of therapeutic modality and constant follow-up examinations for the primary tumor can affect the incidence of synchronous or metachronous multiple primary tumors (1, 2).

The criteria for multiple primary tumors were those proposed earlier (3), i.e. that each of the tumors should have a distinctively-different histology and the probability of one being a metastasis of the other must be excluded. The term synchronous is used in various ways, with an interval of two months, six months, one year, and two years in different studies (4). Our case had tumors with four different histologies, including the papillary carcinoma of the thyroid, invasive ductal adenocarcinoma of the breast, adenocarcinoma of the pancreas and GIST, coincidently.

The etiologies and epidemiologies of multiple primary tumors are under investigation, and relationships between some tumors are well-established. Multiple primary tumors are predominantly seen in both the genitourinary and gastrointestinal tracts (1, 3). Because breast, ovarian, and endometrial tissues are all hormonally-responsive, there are increased risks of synchronous primary tumors among tumors at these sites (5-7). Patients with ovarian cancer have a significant risk for synchronous breast cancer (5-7).

Pancreatic cancer was associated with tumors of the gastrointestinal tract, especially of the stomach (8-10). Some studies suggested that gastrectomy may be a risk factor predisposing a patient to the development of pancreatic cancer (11, 12). However, there was no clinical evidence to suggest that gastrectomy is associated with the development of pancreatic cancer. Previous studies also reported that v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog (KRAS) mutations occur in a considerable proportion of pancreatic and colon cancer cases (13, 14). Further investigations focusing on oncogenes are necessary to clarify the etiology of development of multiple synchronous primary tumors.

Previous studies reported that about 25% of patients with GIST were found to have at least one additional malignant tumor due to as increase in survival rate of patients with GIST (15). Several studies have reported that carcinoma in the gastrointestinal tract was the most common additional malignancy in GIST (15, 16). However, concurrent occurrence of non-familial GISTs with extra-gastrointestinal tract malignancies is a very rare episode, such as in our case (17).

Taken together, since synchronous quadruple primary tumors of the thyroid, breast, pancreas and stomach have not been reported, we suggest that the association between such tumors may not be one of these, and further studies are warranted to clarify the relationship between multiple primary tumors, including common etiological factors. 

References


Received March 9, 2013
Revised April 15, 2013
Accepted April 17, 2013