

## Synchronous Pancreatic Ductal Adenocarcinomas Diagnosed by Endoscopic Ultrasound-Guided Fine Needle Biopsy

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Cases of pancreatic ductal adenocarcinoma with multiple masses accompanying underlying pancreatic diseases, such as intraductal papillary mucinous neoplasm, have been reported. However, synchronous invasion without underlying pancreatic disease is very rare. A 61-year-old female with abdominal discomfort and jaundice was admitted to our hospital. Abdominal computed tomography (CT) revealed cancer of the pancreatic head with direct invasion of the duodenal loop and common bile duct. However, positron emission tomography-CT showed an increased standardized uptake value (SUV) in the pancreatic head and tail. We performed endoscopic ultrasound-guided fine needle biopsy (EUS-FNB) for the histopathologic diagnosis of the pancreatic head and the evaluation of the increased SUV in the tail portion of the pancreas, as the characteristics of these lesions could affect the extent of surgery. As a result, pancreatic ductal adenocarcinomas were confirmed by both cytologic and histologic analyses. In addition, immunohistochemical analysis of the biopsy specimens was positive for carcinoembryonic antigen and p53 in both masses. The two masses were ultimately diagnosed as pancreatic ductal adenocarcinoma, stage IIB, based on EUS-FNB and imaging studies. In conclusion, the entire pancreas must be evaluated in a patient with a pancreatic mass to detect the rare but possible presence of synchronous pancreatic ductal adenocarcinoma. Additionally, EUS-FNB can provide pathologic confirmation in a single procedure. (**Gut Liver 2015;9:685-688**)

**Key Words:** Carcinoma, pancreatic ductal; Neoplasms, multiple primary; Endoscopic ultrasound-guided fine needle aspiration; Biopsy, large-core needle

### INTRODUCTION

Accurate staging of pancreatic cancer is necessary to establish a therapeutic plan. Cases of pancreatic ductal adenocarcinoma with multiple masses accompanying underlying pancreatic diseases, such as intraductal papillary mucinous neoplasm (IPMN), have been reported. However, synchronous invasion without underlying pancreatic disease is very rare. Here, we report a case of synchronous invasion in the head and tail of the pancreas, which was confirmed by endoscopic ultrasound-guided fine needle biopsy (EUS-FNB) using a core biopsy needle.

### CASE REPORT

A 61-year-old female with abdominal discomfort and jaundice was admitted to our hospital. She had no history of alcohol use or smoking and no family history of pancreatic cancer. Physical examination showed icteric sclerae and skin and right upper quadrant tenderness. Blood tests revealed elevated levels of total bilirubin (9.33 mg/dL), direct bilirubin (7.41 mg/dL), aminotransferases (aspartate transferase/alanine transferase: 306/541 IU/L), alkaline phosphatase (183 IU/L),  $\gamma$ -glutamyl transpeptidase (658 IU/L), and carbohydrate antigen 19-9 (2,596 U/mL). Abdominal computed tomography (CT) revealed cancer of the pancreatic head with direct invasion of the duodenal loop and common bile duct and metastatic lymph nodes in the hepatic artery and gastrocolic trunk (Fig. 1A). However, fluorine-18 fluorodeoxyglucose (<sup>18</sup>F-FDG) positron emission tomography-CT (PET-CT) showed increased standardized uptake values (SUV) in the pancreatic head (SUV<sub>max</sub>, 10.6) and tail (SUV<sub>max</sub>, 5.5) (Fig. 1B and C). Before making a decision regarding further treatment, we evaluated the SUV in the pancreatic tail, a finding that did

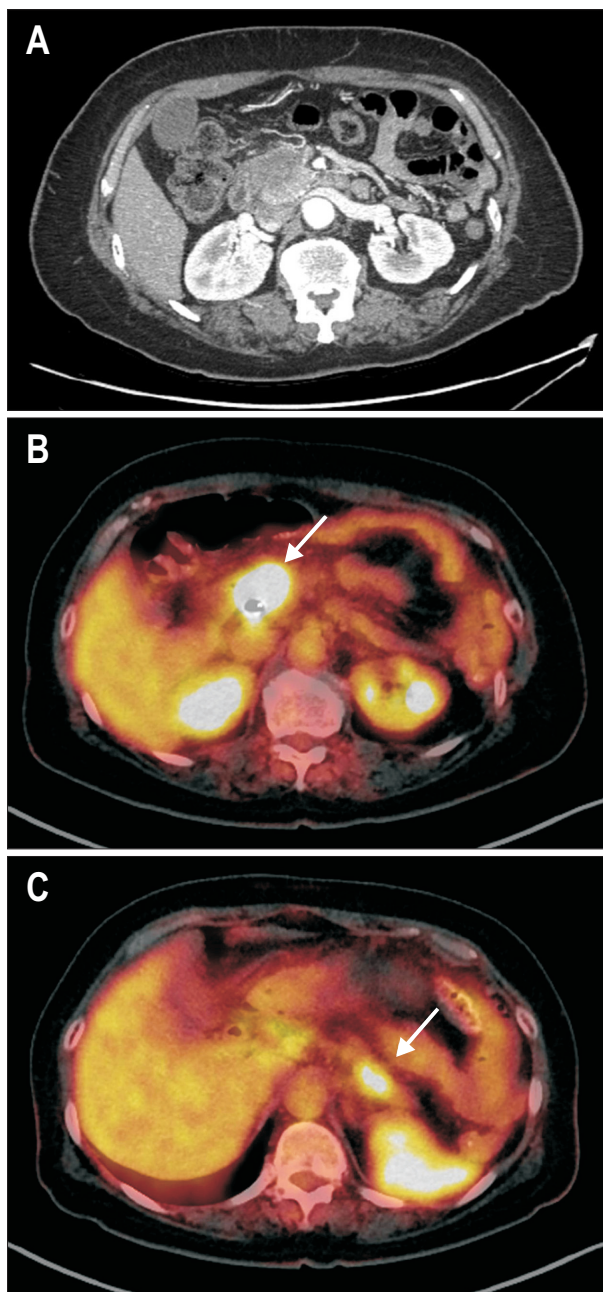
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**Fig. 1.** Imaging findings of the pancreatic masses. (A) Abdominal computed tomography (CT) revealed a mass in the pancreatic head with duodenal invasion. (B, C) Fluorine-18 fluorodeoxyglucose positron emission tomography-CT showed increased standardized uptake values (SUV) (arrow) in the pancreatic head (SUV<sub>max</sub>, 10.6) and tail (SUV<sub>max</sub>, 5.5).

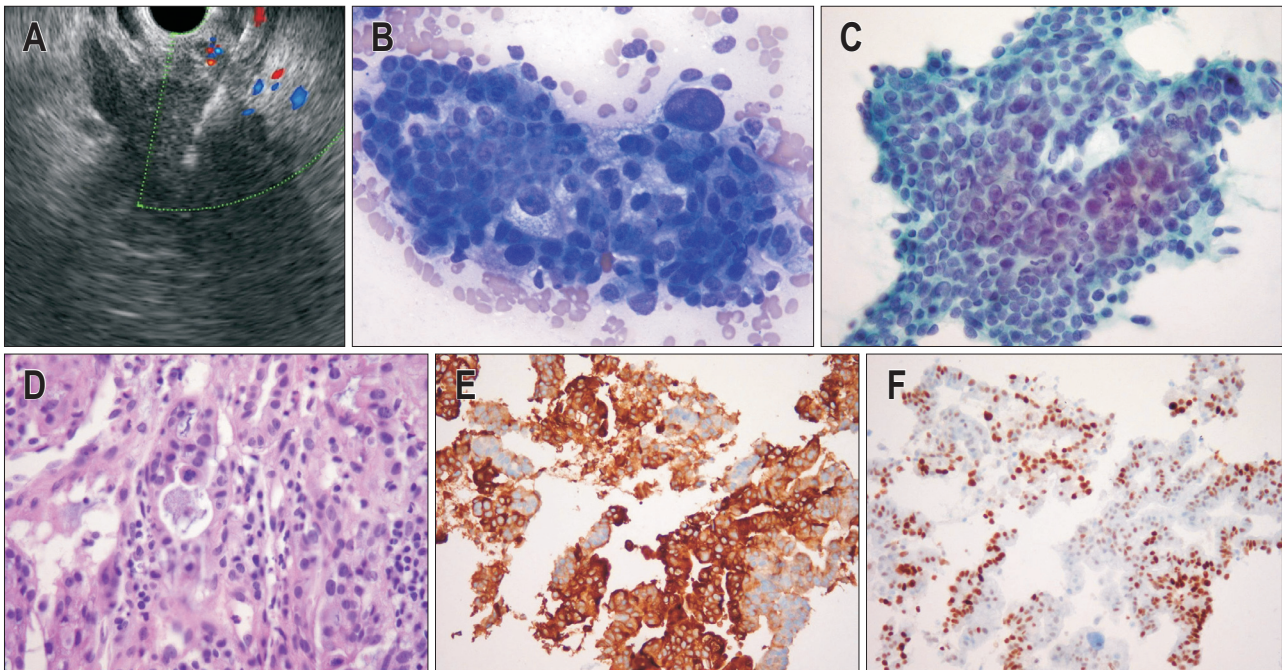
not correlate with the abdominal CT, because the characteristics of this mass could affect the extent of surgery. To accomplish this, EUS-FNB was performed using a linear array echoendoscope (GF-UCT240; Olympus Medical Systems Co., Ltd., Tokyo, Japan) for the histopathologic diagnosis of the pancreatic head and the evaluation of the increased SUV in the tail of the pancreas. EUS showed a heterogeneous hypoechoic mass (35×49 mm) in the head and another mass (24×20 mm) with similar

characteristics in the tail. There were no other specific findings that indicated underlying pancreatic disease. After color Doppler ultrasound, EUS-FNB was performed on the head and tail masses using a 25-gauge FNB device (Echotip ProCore; Wilson-Cook Medical, Winston-Salem, NC, USA) via the transduodenal and transgastric approaches, respectively (Figs 2A and 3A). A portion of the tissue obtained by EUS-FNB was air-dried and stained with Diff-Quik (International Reagents Co., Ltd., Kobe, Japan) for immediate on-site diagnosis. The residual tissues were then fixed with ethanol for cytological analysis and formalin for histological analysis. For the masses in the head and tail, on-site cytology revealed clusters of atypical cells with high cellularity (Figs 2B and 3B). Pancreatic ductal adenocarcinomas were also identified from cytological analysis using Papanicolaou staining (Fig. 2C) and from histological analysis using hematoxylin and eosin staining in both masses (Figs 2D and 3C). Immunohistochemical (IHC) analysis of the histological specimens was positive for carcinoembryonic antigen (Figs 2E and 3D) and p53 (Figs 2F and 3E) in both of the masses. The Ki-67 labeling index indicated high proliferative activity. The two masses were ultimately diagnosed as pancreatic ductal adenocarcinoma, stage IIB (T3N1M0), based on the EUS-FNB and imaging studies. The patient refused surgery and is subsequently being treated with combined chemotherapy and radiation therapy.

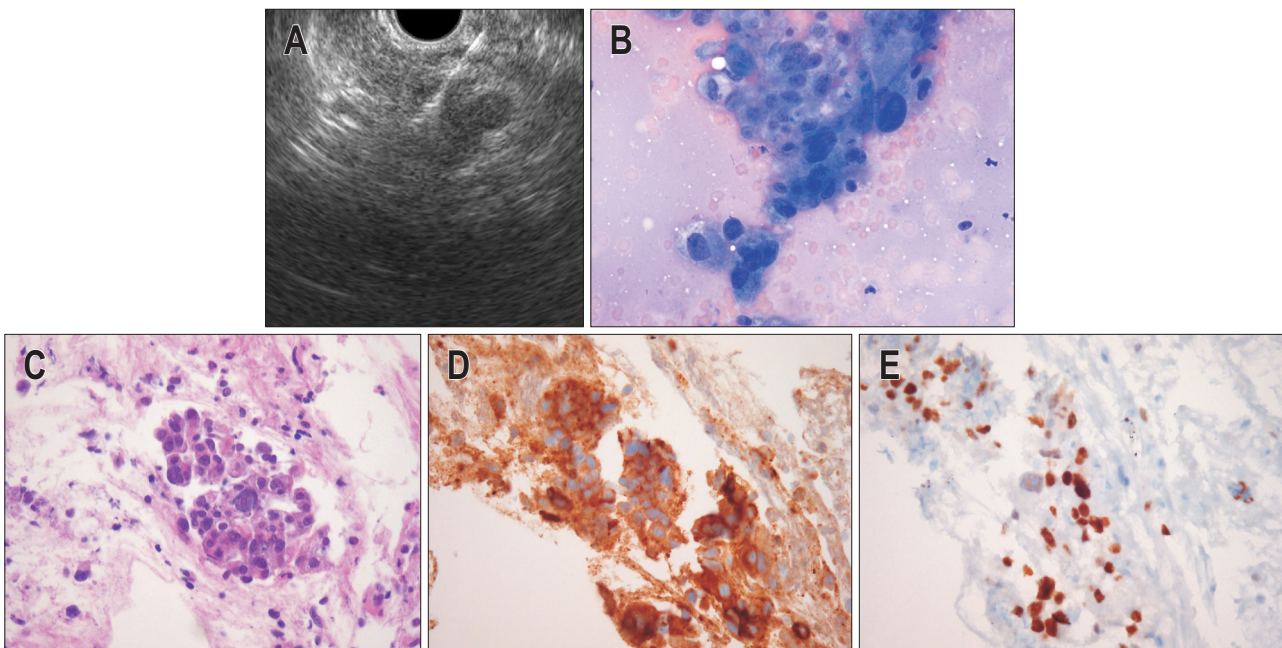
## DISCUSSION

The frequency of pancreatic ductal adenocarcinoma is 60% to 70% in the head, 10% in the body, 5% in the tail, 5% in the head and body, 10% in the tail and body, and up to 5% in the entire pancreas.<sup>1</sup> There are three precursor lesions of pancreatic ductal adenocarcinoma, known as pancreatic intraepithelial neoplasia (PanIN), intraductal papillary mucinous neoplasm, and mucinous cystic neoplasia (MCN).<sup>2</sup> IPMN and MCN occasionally demonstrate multifocal invasion.<sup>3</sup> However, even though PanIN is the most common type of precursor lesion in pancreatic adenocarcinomas, multifocal invasion has been rarely reported; however, even though PanIN is the most common type of precursor lesion in pancreatic adenocarcinomas, multifocal invasion has been rarely reported in the patients with a strong family history of pancreatic cancer. In addition, multifocal invasion of pancreatic cancer was diagnosed by histopathologic analysis of the surgical specimen in most of cases.<sup>4,5</sup> In the present case, where there was a definite malignant tumor on the head of the pancreas, we initially examined the possible presence of another malignant lesion within the tail of the pancreas because of the increased SUV in the pancreatic tail on <sup>18</sup>F-FDG PET-CT, a finding that did not correlate with the abdominal CT. However, increased SUV can also be observed in benign focal lesions, such as focal pancreatitis and autoimmune pancreatitis. Therefore, EUS was performed to evaluate the increased SUV in the pancreatic tail; simultaneous FNB was performed for histopatho-





**Fig. 2.** Endoscopic ultrasound-guided fine needle biopsy (EUS-FNB) of the pancreatic head mass. (A) EUS-FNB was performed on the head mass. (B) On-site examination with a Diff-Quik stain revealed clusters of atypical cells showing enlarged nuclei with anisonucleosis and prominent nucleoli ( $\times 400$ ). (C) Cytologic analysis with a Papanicolaou stain showed a sheet of cells with nuclear overlapping and crowding. The nuclei showed anisonucleosis and coarse chromatin ( $\times 400$ ). (D) Histologic findings using hematoxylin and eosin staining showed solid nests with occasional lumens, consistent with moderately differentiated adenocarcinoma ( $\times 400$ ). (E) An immunohistochemical stain for carcinoembryonic antigen revealed positivity in the tumor cells ( $\times 400$ ). (F) Immunohistochemical stain for p53 revealed positivity in the tumor cells ( $\times 400$ ).



**Fig. 3.** Endoscopic ultrasound-guided fine needle biopsy (EUS-FNB) of the pancreatic tail mass. (A) EUS-FNB was performed on the tail mass. (B) On-site examination with a Diff-Quik stain revealed the same characteristics as those of the head mass ( $\times 400$ ). (C) Histologic findings were consistent with moderately differentiated adenocarcinoma ( $\times 400$ ). (D) Immunohistochemical stain for carcinoembryonic antigen revealed positivity in the tumor cells ( $\times 400$ ). (E) Immunohistochemical stain for p53 revealed positivity in the tumor cells ( $\times 400$ ).

logic diagnosis. As a result, multifocal invasion was confirmed prior to surgery, in contrast to the previous case report.<sup>5</sup>

EUS-guided fine needle aspiration (EUS-FNA) has become a popular diagnostic tool and is used in a diverse range of diseases. Several studies have examined ways to increase the efficacy of the procedure.<sup>6-8</sup> EUS-FNB using a core biopsy needle was developed to improve histological diagnosis by EUS-FNA. In this case report, histological diagnosis combined with IHC using EUS-FNB core samples was useful to identify similar characteristics of the two different masses and to achieve a more accurate staging of pancreatic cancer before surgery. However, the complete separation of the two tumors could not be confirmed because the patient refused to undergo surgical resection.

In conclusion, the entire pancreas must be evaluated in a patient with a pancreatic mass to detect the rare but possible presence of synchronous pancreatic ductal adenocarcinomas. Additionally, EUS-FNB can provide pathologic confirmation in a single procedure.

#### CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

#### ACKNOWLEDGEMENTS

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