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**Simultaneous multiple primary malignancies diagnosed by endoscopic ultrasound-guided fine-needle aspiration: A case report**

Yang J *et al.* Simultaneous MPMs diagnosed by EUS-FNA

**Abstract**

**BACKGROUND**

Multiple primary malignancies (MPMs) refer to more than one primary malignancy in the same or separate organs of the same patient, and MPMs are considered when different histological characteristics are detected in epidemiological studies. Herein, we report a case presumed to be primary pancreatic cancer with multiple liver metastases by positron-emission tomography/computed tomography (PET/CT) and confirmed synchronous liver and pancreatic MPMs by endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA).

**CASE SUMMARY**

A 50-year-old male was referred to our hospital due to abdominal discomfort for two months. Abdominal computed tomography (CT) at his local hospital revealed a pancreatic mass with multiple liver nodules. After being transferred to our hospital, PET/CT confirmed all these lesions to have elevated metabolic activity, and therefore primary pancreatic cancer with multiple liver metastases was considered. EUS-guided liver aspiration unexpectedly found signet-ring cells with a high Ki-67 positive rate (20%), while EUS-guided pancreatic aspiration detected pancreatic neuroendocrine cells with a relatively low Ki-67 positive rate (1%). The final diagnosis from the Multidisciplinary Team (MDT) was simultaneous liver and pancreatic MPMs. The

patient returned to his local hospital for neoadjuvant chemotherapy and surgery, and he is still alive during a 6-month postoperative follow-up.

## CONCLUSION

Although rare, MPMs should be considered when treating pancreatic mass with suspected metastatic lesions, and EUS-FNA proved minimally invasive and accurate.

**Key Words:** Multiple primary malignancies; Endoscopic ultrasound; Fine-needle aspiration; Pancreatic cancer; Liver cancer; Case report

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**Core Tip:** We report a rare case of synchronous liver and pancreatic MPMs confirmed by EUS-FNA, although this patient was first diagnosed as primary pancreatic cancer with multiple liver metastases by CT and PET/CT. Although rare, multiple primary malignancies should be considered in patients with pancreatic mass and suspected metastatic lesions, and EUS-FNA has proven to be a minimally invasive and accurate preoperative diagnosis method.

## INTRODUCTION

Multiple primary malignancies (MPMs) refer to more than one primary malignancy in the same or separate organs of the same patient, and MPMs are considered when different histological characteristics are detected<sup>[1]</sup>. Simultaneous malignancies are defined as malignancies that are diagnosed at the same time or during the staging of the first malignancy, while synchronous and metachronous malignancies were usually distinguished by a 2-month or 6-month time point in different databases<sup>[2-3]</sup>. In patients with digestive MPMs, it is infrequent for liver or pancreatic cancer patients to have both

primary malignancies detected simultaneously<sup>[4]</sup>. Treatment strategies and associated prognoses of patients with digestive MPMs are significantly different from those patients with primary digestive cancer and distant metastasis.

Preoperative endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is an essential breakthrough in the endoscopic field and a substantial procedure to evaluate benign and malignant gastrointestinal tract lesions and nearby organs<sup>[5]</sup>. Taking pancreatic cancer as an example, the overall survival (OS) of the preoperative EUS-FNA group was significantly higher than that of the non-FNA group, and there was no remarkable difference in the tumor recurrence rate or peritoneal implantation rate between the two groups<sup>[6]</sup>.

Herein, we report a case presumed to be primary pancreatic cancer with multiple liver metastases by positron-emission tomography/computed tomography (PET/CT) and confirmed synchronous liver and pancreatic MPMs by EUS-FNA.

#### **CASE PRESENTATION**

##### ***Chief complaints***

A 50-year-old Chinese male was referred to our hospital due to abdominal discomfort for approximately two months.

##### ***History of present illness***

Approximately one month previously, this patient was admitted to a local hospital due to elevated blood amylase. He denied jaundice, vomiting, and gastrointestinal bleeding. He was diagnosed with acute pancreatitis, but CT revealed an enlarged pancreatic head and suspected liver metastases. Thus, he was referred to our hospital for further management.

##### ***History of past illness***

The patient had a clean medical history.

### ***Personal and family history***

This patient had a 30-year smoking history (half a pack per day) and has not quit smoking. He denied any family history of cancer.

### ***Physical examination***

After admission, the patient's physical examination revealed no abnormality.

### ***Laboratory examinations***

Blood analysis revealed elevated CA19-9 [106 U/mL (0-27 U/mL)], amylase [450 U/L (0-110 U/L)] and lipase [3795 U/L (0-300 U/L)]. Alpha-fetoprotein (AFP) was within normal limits.

### ***Imaging examinations***

After admission, PET/CT detected increased soft tissues with elevated metabolic activity in the pancreatic head (Figure 1) and multiple liver nodules with increased metabolic activity (Figure 2), and therefore the initial diagnosis was primary pancreatic cancer with multiple liver metastases.

EUS confirmed an enlarged hypoechoic pancreatic head (Figure 3A) and multiple hypoechoic liver masses (Figure 3B). A linear Pentax echoendoscope (Hoya co., Tokyo, Japan) and the color Doppler flow imaging were employed to determine the puncture site. No malignant cells were detected in the fluid inside the peripancreatic cystic lesion extracted by EUS-FNA. EUS-FNA biopsy (EUS-FNAB) was performed with two 19-gauge needles (Boston Scientific co., Natick, American), respectively. EUS-guided liver aspiration unexpectedly found signet-ring cells (Figure 4A) with a high Ki-67 positive rate (20%), while EUS-guided pancreatic aspiration with another aspiration needle detected pancreatic neuroendocrine cells (Figure 4B) with a relatively low Ki-67 positive rate (1%). Three senior pathologists in our medical university confirmed that the considerable differences in immunohistochemical results indicated that the pancreatic mass and multiple liver nodules were not metastatic lesions from the other.

The gastric mucosa punctured by the EUS-guided liver aspiration needle was further inspected by magnifying endoscopy. No abnormal microsurface or microvascular was identified, and no malignant cells were found in deep excavation biopsies. The possibility of gastric signet-ring cell carcinoma was excluded. The patient's colonoscopy was negative.

### **FINAL DIAGNOSIS**

A multi-disciplinary team (MDT) of pathologists, radiologists, and clinicians was convened. The final diagnoses were listed as follows: 1. Simultaneous liver and pancreatic MPMs (Hepatic signet ring cell adenocarcinoma and pancreatic neuroendocrine tumor); 2. Pancreatic pseudocyst.

### **TREATMENT**

The patient returned to his local hospital for neoadjuvant chemotherapy (apatinib, 500 mg, once per day) and left liver resection, and postoperative pathological results confirmed the diagnoses of hepatic signet ring cell adenocarcinoma, pancreatic neuroendocrine tumor, and post-necrotic pancreatic pseudocyst.

### **OUTCOME AND FOLLOW-UP**

The patient is still alive during a 6-month postoperative follow-up.

3

### **DISCUSSION**

To the best of our knowledge, this case report is the first report of simultaneous liver and pancreatic MPMs preoperatively diagnosed by EUS-FNA in Asian patients. This case will help prompt clinicians to consider other possibilities besides primary pancreatic cancer with liver metastasis when dealing with similar issues and raise their attention to routinely perform preoperative EUS-FNA in patients with presumed malignancies.

With the continuous progress of medical techniques and the extension of life expectancy, the incidence of MPMs has increased gradually. Most patients with MPMs were male and elderly patients (>50 years old), and the leading location in all MPMTs was the digestive system<sup>[7]</sup>. Compared with all other MPMs, liver malignancies revealed the fewest MPMs occurrences<sup>[8]</sup>, and it is rarer to confirm both liver and pancreatic malignancies by EUS-FNA simultaneously. Lai *et al.*<sup>[9]</sup> reported a 56 years old Caucasian female with a pancreatic mass and a single liver nodule. Her EUS-FNA cytology revealed pancreatic ductal adenocarcinoma, while she underwent a liver core biopsy and confirmed hepatocellular carcinoma. The absence of EUS-FNA for liver biopsy may be due to the location of her liver lesion. In addition, Zhang *et al.*<sup>[10]</sup> reported a 70 years old male with pathological confirmed pancreatic metastasis of hepatocellular carcinoma. Therefore, in patients with pancreatic masses and multiple liver nodules, clinicians should consider the following three possibilities: primary pancreatic cancer with liver metastasis, primary liver cancer with pancreatic metastasis, and MPMs.

Correct diagnosis is the first and essential step in treating patients with malignancies. PET/CT, one of the more sophisticated imaging methods that have been increasingly used in recent years, is playing a considerable role in the diagnosis of MPMs<sup>[11]</sup>. Compared with the inability to obtain specimens from PET/CT, the accuracy and safety advantages have been proven in the process of securing cell and tissue specimens *via* EUS-FNA <sup>[12-14]</sup>. EUS-FNA and associated procedures are expected to play an increasingly important role in the preoperative diagnosis of MPMs and other suspected malignancies.

This male patient in the present case had a smoking history of up to 30 years. Male and patients with smoking history were considered high-risk factors for developing multiple MPMs<sup>[1, 15]</sup>. Therefore, these patients need to be consciously inspected for the possibility of MPMs. Liver lesions are more often considered metastases than primary tumors<sup>[16]</sup>, and thus the presumed diagnosis of this patient was primary pancreatic cancer with multiple liver metastases. However, the pathological results of EUS-guided liver and pancreatic aspiration unexpectedly confirmed a rare case of MPMs. This case

also reminds us that a pathological biopsy should always be the final and definite diagnosis in patients with suspected malignancies <sup>[17]</sup>.

### **CONCLUSION**

A rare case of simultaneous liver and pancreatic MPMs was confirmed by pathological biopsies of EUS-guided liver and pancreatic aspiration. MPMs should be considered in patients with pancreatic mass and suspected metastatic lesions, and EUS-FNA is a minimally invasive and accurate diagnostic method.



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SIMILARITY INDEX

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