Case Report

Running Title: Pancreatic Metastasis from Esophageal SCC
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Solitary Synchronous Pancreatic Metastasis from Esophageal Squamous Cell Carcinoma: A Rare Case Report
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Abstract
Pancreas is an organ that is hardly affected by metastasis from other primary cancers; also, pancreatic metastasis from esophageal squamous cell carcinoma (ESCC) is an extremely infrequent entity. Metastatic esophageal cancer has a poor prognosis and the five-year survival rate is less than 5%. Here, we described a rare case of a 78-year-old woman presented with abdominal bloating, intermittent mild nausea, and loss of appetite and weight. Esophagogastroduodenoscopy revealed ESCC in the upper part of esophagus. A mass lesion between the head and body of pancreas was detected during metastatic workup. Endoscopic ultrasound-guided fine needle aspiration was performed, morphologic features and immunohistochemistry confirmed metastatic SCC from esophagus. Definitive chemoradiotherapy with curative intent was done on both oesophageal and pancreatic lesion. Interestingly, after nine months of treatment, the patient had no issues either in esophagus or in abdomen. In conclusion, local therapy could be considered as one of the best choices to improve the overall survival in ESCC with single metastasis to pancreas.

Keywords: Definitive chemoradiotherapy, Esophagus, Pancreas neoplasm, Solitary metastasis, Radiotherapy
Introduction
Esophageal cancer is a poor prognosis malignancy often diagnosed at an advanced stage due to inability to detect early symptoms. According to the data from GLOBOCAN database (2018), esophageal cancer is the ninth most prevalent malignancy and the sixth most common cause of cancer-related mortality worldwide. Esophageal squamous cell carcinoma (ESCC) is the most common type (90%) of esophageal malignancy in Asian countries; however, in western counties such as the United States, esophageal adenocarcinoma accounts for more than 60% of all esophageal cancers. Smoking and alcohol consumption are among the major risk factors associated with esophageal cancer; meanwhile, Barrett’s esophagus with intestinal metaplasia, obesity, and smoking are the risk factors for adenocarcinoma.

Case presentation
A 78-year-old woman presented with a five-month history of abdominal bloating, intermittent mild nausea, and loss of appetite and weight (12 kg). There was no family history for malignancy and hereditary disease. She had no history of smoking or alcohol consumption, and her BMI (Body Mass Index) was 20. The subject reported a 20-year history of diabetes mellitus with regular follow-up and the cardiac resynchronization therapy (CRT) implanted due to threatening tachyarrhythmia for 10 years. No abnormalities were detected in initial abdominopelvic ultra-sonography and physical examination. Esophagogastroduodenoscopy revealed a polyploidy infiltrative lesion without oozing in 20cm from incisor (figure 1); multiple biopsies were taken and the histopathology was consistent with a well-differentiated squamous cell carcinoma (figure 2). Further evaluation and metastatic workup with abdominal computed tomography (CT) demonstrated a mass lesion measuring 39x31 mm between the body and head of the pancreas (figure 3). Core needle biopsy (CNB) could not be performed because the mass was fragile; therefore, she underwent endoscopic ultrasound (EUS) for fine needle aspiration (FNA); multiple slides and two bottles of cell block were further taken (figure 4). The pathology examination showed that the tumor was metastatic squamous cell carcinoma with morphologic features similar to the previous ESCC. Immunohistochemistry (IHC) was positive for P65 and CK5. Liver function tests and cell blood count were within the normal limit. The patient underwent CRT for pancreas mass (5040 cGy in 28 fractions with capcitabin 1.5 gr daily). Symptoms were reduced and she was subjected to CRT to esophagus (4500 cGy in 25 fraction with capcitabin 1.5gr daily) followed by brachy therapy (10 Gy in tow fraction). Nine months after treatment, the pancreatic lesion size decreased from 42×36 mm to 26×26 mm; the patient had no problem swallowing and upper-endoscopy revealed no sign of recurrence in esophagus.

Discussion
More than 50% of patients have either unresectable cancer or metastases to distant organs at preliminary diagnosis. These patients have a dismal prognosis, and the median overall survival (OS) is six and five months for patients with a solitary site of distant metastasis (DM) and several sites of DM, respectively. It has been reported that esophageal cancer has a special propensity for unexpected specific site metastasis; this has been attributed to the particular anatomical esophageal features considered as having a key role in elucidating esophageal cancer with distinctive and extremely aggressive nature.
In general, 58.6% of patients with de novo stage 4 esophageal cancer have DM to a single organ. Esophageal cancer most commonly spreads to the liver (33.4%), followed by distant (non-regional) lymph nodes (26.6%), lung (20.5%), bone (15.7%), and brain (3.8%). Most malignant tumors in the pancreas are primary, only 20% are metastatic lesions, squamous cell carcinoma, small cell carcinoma, and acinar cell carcinoma, and the others are adenocarcinomas. Solitary pancreatic metastases from non-pancreatic primary cancers are highly uncommon, roughly causing only 2% of all pancreatic tumors. To the best our knowledge, only two cases of solitary synchronous pancreatic metastasis from ESCC have been reported in English literature. We reported a case of isolated synchronous pancreatic metastasis from ESCC diagnosed during preoperative metastatic workup for the treatment of primary esophageal cancer. In our case, it was difficult to distinguish a synchronous pancreatic carcinoma from a solitary pancreatic metastasis from primary ESCC. Given its rarity, SCC of the pancreas is supposed to be the result of metastasis from other primary sites until confirmed otherwise. The final diagnosis of metastatic ESCC to the pancreas was confirmed only after conducting FNA through endoscopic ultrasound (EUS), followed by pathology and IHC examination.

Overall, local therapy is not routinely suggested for metastatic cancer, ESCC or otherwise; however, several reports have indicated that the resection of pancreatic metastatic lesions in patients with diverse primary cancer increases disease-free interval and enhances patients' OS. The effectiveness of pancreatic resection is mostly associated with the biology of the primary cancer metatrasizing to the pancreas. It has been suggested that pancreatic metastasectomy can be a useful treatment for solitary pancreatic metastasis of ESCC without the possibly of spreading to another site.

In such cases, local therapy seems logical for treating and enhancing the overall survival of patients. In our case, the pancreatic lesion was unresectable due to the encasement of superior mesenteric artery. Thus, definitive chemo-radiotherapy with curative intent was performed as one of the best alternatives for oesophageal and pancreatic lesion.

Conclusion
In conclusion, we reported this case because solitary pancreatic metastasis of ESCC is very rare, and only a handful of cases have been reported to date. It is important to determine whether local therapy is an appropriate treatment regimen for isolated pancreatic metastasis from ESCC; due to its rarity, more research is required to confirm the usefulness of local therapy in these cases.

Informed Consent
Written informed consent for publishing the case report was signed by the patient.

Conflicts of Interest
None declared.

References
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Figure 1. Upper endoscopy showing a lesion with an irregular nodular surface in 22 cm from the incisors.

Figure 2. Histological examination of esophagus (A) and pancreas (B), suggesting well differentiated squamous cell carcinoma (H & E stain, ×400).
Figure 3. Abdominal Axial CT-scan revealing a contrast-enhanced pancreatic metastasis from ESCC with encasement of celiac artery.

Figure 4. Endoscopic ultrasound and elastography showing a 42 mm to 36 mm hypoechoic lesion in pancreatic genue with invasion to port and superior mesenteric artery (SMA).