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Case Report

The First Reported Case of Pulmonary Embolism and Deep Vein Thrombosis Associated with Intraductal Papillary Mucinous Neoplasm: A Case Report

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Abstract

Background: Reported cases of Intraductal papillary mucinous neoplasm (IPMN) are becoming more and more frequent. The risk of hypercoagulability associated with IPMN is not clearly established in the literature as it was only reported in four cases. Therefore, we present a unique case of a patient with IPMN who subsequently developed acute pulmonary embolism (PE) and deep venous thrombosis (DVT).

Case presentation: A 70-year-old healthy female patient complained of palpitation, chest pain, and dyspnea at rest. She had normal vital signs and findings on physical examination. Laboratory tests showed an increase in the D-Dimer level of 3,730 ng/mL fibrinogen equivalent unit (FEU). Bilateral DVT ultrasound (DVT-US) of the lower extremities was positive for acute calf DVT in the right lower extremity involving the soleal vein. CT-PE chest with IV contrast was remarkable for segmental and subsegmental pulmonary arteries thrombosis. She was started on a heparin drip and then transitioned to rivaroxaban for the treatment of PE and DVT. She was discharged in stable condition with outpatient follow-up.

Conclusion: IPMN of the pancreas is an exocrine pancreatic neoplasm often detected on Computed Tomography (CT) scan or Magnetic Resonance Imaging (MRI). It is usually non-malignant but was found to be more prone to progress into cancer in contrast to the other types of pancreatic cysts. An increased risk of hypercoagulability with pre-malignant pancreatic lesions such as IPMN has not yet been well established. As far as we know, this case report is the first article presenting IPMN associated with both acute DVT and PE in a relatively healthy individual with no prior risk factor for hypercoagulability. Although there is scattered evidence suggesting an increased risk of thromboembolic events with IPMN, this unique case of DVT and PE associated with IPMN highlights the importance of close monitoring of these patients, especially those who have risk factors for thrombosis.

Keywords: Intraductal papillary mucinous neoplasm, Deep vein thrombosis, Pulmonary embolism, Pancreas, Cancer

Introduction

Intraductal papillary mucinous neoplasm (IPMN) is known to have the highest prevalence among pancreatic cysts [1]. Its incidence has been rising [2,3] and especially in tertiary care facilities [3]. IPMN is a benign tumor [4,5] but its risk of progressing into a malignant form increases over the years after the initial diagnosis [5]. Individuals with IPMN usually do not experience any symptoms as the lesions are often discovered incidentally on imaging. When they occur, they include abdominal pain, nausea, vomiting, pancreatitis, and jaundice [1]. Therefore, most recent guidelines recommend close monitoring with frequent imaging [4,6–9]. Despite the fact that the risk of hypercoagulability is increased in cancer [10–13], it has not yet been established to be elevated in premalignant pancreatic tumors such as IPMN. Only a few articles reported the possible increased risk of hypercoagulability in patients with IPMN [14,15]. Therefore, we present the first reported case of a relatively healthy individual with IPMN who subsequently developed DVT and PE.

Case Report

A 70-year-old Caucasian female who was previously diagnosed with intraductal papillary mucinous neoplasm, gastroesophageal reflux disease, major depressive disorder (MDD) not on medication, and alcohol abuse, presented with sudden onset palpitation.

Her symptoms started three days prior to presentation and were described as pleuritic chest pain with dyspnea at rest. The pain was not radiating and was exacerbated by ambulation. She denied fever, cough, lightheadedness, syncope, lower extremities swelling, trauma, recent surgery or travel, immobilization, excessive weight gain, history of cancer or thromboembolic events, smoking, or drug use. She reported drinking one to two alcoholic beverages every night. Her family history was significant for breast cancer but negative for heart diseases, pulmonary embolism, deep venous thrombosis, or any other significant comorbidity. Her last CT scan of the pancreas done three months prior to presentation showed a stable cyst compared to the previous scan done two years ago and ruled out any evidence of pancreatic duct dilation (Figure 1).

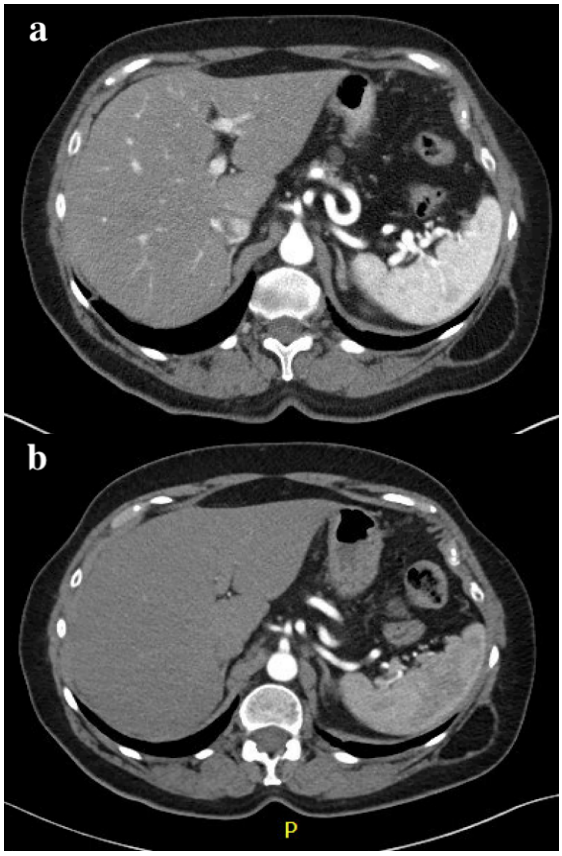

Figure 1: a. CT scan of the pancreas with IV contrast showing a stable 1.3 x 1.0 cm exophytic cystic lesion within the pancreatic body with additional subcentimeter cystic lesions within the uncinated process without evidence of main pancreatic duct dilation (2022). b. CT scan of the pancreas with IV contrast showing a stable 1.2 x 1.1 cm exophytic cystic lesion within the pancreatic body with additional questionable additional cystic lesion within the uncinated process of the pancreas measuring 1 x 0.8 cm without evidence of main pancreatic duct dilation (2020).

Vital signs were stable as the patient was normotensive and afebrile. Her heart rate was within normal range and the patient was oxygenating well on room air. Electrocardiography (ECG) was negative for acute findings.

On physical examination, she did not have any lung crackles or wheezing. Cardiac and

neurological exams were also normal. Lower limb examination was negative for erythema, swelling, and tenderness. She had palpable pulses bilaterally in all her extremities. Laboratory results were unremarkable except for a D-Dimer level of 3,730 ng/mL FEU. Bilateral deep venous thrombosis ultrasound (DVT-US) of the lower extremities was positive for acute calf DVT in the right lower limb involving the soleal vein. CT-PE chest with IV contrast was remarkable for segmental pulmonary arteries thrombosis in the left upper, right upper, and right lower lobe with subsegmental pulmonary arteries thrombosis in the right upper, right middle, right lower, left upper, and left lower lobes without any proof of pulmonary artery dilation (Figure 2). Echocardiography was done and showed a left ventricular ejection fraction of 60% without focal wall abnormalities or right ventricular strain.

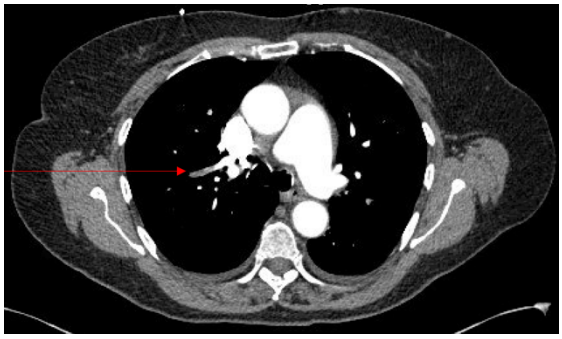

Figure 2: CT-PE chest with IV contrast showing filling defect in the right pulmonary artery involving the posterior segment of the upper lobe consistent with pulmonary embolism (red arrow pointing at the filling defect).

The patient was started on an intravenous heparin drip for the treatment of acute bilateral PE with deep vein thrombosis of the right soleal vein, and transitioned to rivaroxaban the next day. Subsequently, she was discharged in stable condition and instructed to follow up as an outpatient with her primary care physician and gastroenterologist.

Discussion

Pancreatic Intraductal papillary mucinous neoplasm (IPMN) is an exocrine pancreatic neoplasm often detected on CT-scan or MRI imaging [9]. It is characterized by dysplasia of the intraductal mucin-secreting epithelial cells of the main pancreatic or branchial ducts and is distinguished from other types of mucinous cysts by the absence of ovarian-type stroma. In the majority of cases, pancreatic cysts are benign entities that rarely develop into cancer [9]. Similarly, IPMN is usually non-malignant but was found to be more prone to progress into cancer in contrast to the other types of pancreatic cysts [4,9].

IPMN is divided into three categories: main duct (MD-IPMN), branch duct (BD-IPMN), and mixed-type IPMN. Interestingly, this classification can predict the malignant potential of IPMN. In fact, MD-IPMN has the highest malignant potential with a risk of 36 to 100%, while BD-IPMN has the lowest risk (11 to 33%) [4]. In addition, multifocal BD-IPMN has an increased risk of cancerous transformation compared to solitary BD-IPMN lesions. Alternatively, IPMN can also be classified based on their histology, including gastric, intestinal, pancreaticobiliary, and oncocytic [9].

Due to the fact that CT-scan and MRI are 47 to 78% accurate in differentiating between pancreatic cysts type, and 73 to 97% accurate in distinguishing between benign, premalignant, and malignant pancreatic cystic neoplasms [16,17], several approaches have been developed to monitor IPMN with low risk of malignancy. The American Gastroenterology Association (AGA) recommends the use of MRI to follow up on IPMN. Notably, The American College of Radiology (ACR) and the International Association of Pancreatology (IAP) support the solitary use of imaging modalities such as MRI or CT-scan for follow-up. On the other hand, the European Guidelines recommend the use of MRI and/or endoscopic ultrasound (EUS) with Serum Cancer Antigen 19-9 (CA19-9,) along with a clinical evaluation to monitor patients with IPMN who have no indication for surgery [4,9].

Cancer is characterized by a hypercoagulable state, resulting from the stimulation of the coagulation cascade and

the disturbances in fibrinolysis [13,18]. Thromboembolic events are common in malignancy as cancer is linked to a 7-fold increase in the risk of venous thromboembolic events (VTE) [18]. For instance, PDAC is estimated to increase the risk of VTE to 14 events per 100 patients per year. Splanchnic vein thrombosis is common in PDAC and has been shown to predict a bad prognosis [19].

In the current literature, an increased risk of hypercoagulability with pre-malignant pancreatic lesions such as IPMN has not yet been well established. One editorial presented a case of a patient with IPMN who was also found to have splenic vein thrombosis. Interestingly, there were no clear etiologies explaining this event [15]. A relatively recent abstract from 2020 reported three cases of two men and one woman who were admitted to the hospital with DVT and were found to have IPMN on a CT scan [14]. In contrast to our case, these patients were not known to have a history of IPMN, and the latter was found incidentally during workup for PE on imaging. Moreover, there was no evidence of pulmonary embolism reported. As far as we can tell, this is the first reported case of IPMN associated with both acute DVT and PE in a relatively healthy individual with no prior risk factor for hypercoagulability. It is important for clinicians to closely monitor patients with IPMN who develop an episode of thromboembolism as it could indicate a potential malignant transformation of the mass.

Conclusion

In conclusion, IPMN is a benign pancreatic cyst with a risk of progression to malignancy. Although the risk of thrombosis in patients with cancer in the pancreas is well established in the literature, there is scant evidence supporting an increased risk of thromboembolic events with IPMN. This unique case of DVT and PE associated with IPMN highlights the importance of close monitoring of these patients, especially those who have risk factors for thrombosis. Future studies will be needed in order to reinforce the association between IPMN and thromboembolic events.

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