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CASE REPORT

Pulmonary Embolism in Long Standing Diabetes: A Hint Towards Pancreatic Carcinoma

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Abstract

Pancreatic carcinoma has remained one of the leading causes of cancer-related mortality worldwide. Cancer originating in the head of pancreas is often detected early in the disease due to biliary obstruction resulting in jaundice. In contrast, cancer of the pancreatic body and tail remains indolent, presenting late with significantly increased tumor burden and distant metastasis. Unfortunately, a single laboratory screening study is neither sensitive nor specific for early detection of pancreatic cancer. In this report, we present a patient with longstanding diabetes incidentally detected to have pancreatic tail carcinoma while presenting with pulmonary embolism, emphasizing the need for pancreatic cancer screening studies in population with longstanding diabetes.

Keywords: Pancreatic cancer, CA19-9, Pulmonary embolism, Anticoagulation failure

1. Introduction

Pancreatic cancer is the fourth leading cause of cancer death globally as per the American Cancer Society cancer facts of figures, 2023. It has a high mortality rate, with a five year survival rate of 12%.[1] Tumors in the head of pancreas are more common than in its body or tail. However, when present in the body or tail, they tend to present late, and at higher stages with symptoms of metastasis or local regional spread.[2,3] Presentations of tumors of body and tail of the pancreas are non-specific and include asthenia, anorexia, weight loss, and/or symptoms from distant metastasis or complications as demonstrated in our report.

2. Case presentation

A 93-year-old woman presented to the emergency department with a 3-week history of nonproductive cough and left lower pleuritic chest pain. She denied fevers, chills, sick contacts, or recent travel. Additional history revealed a 12-pound unintentional weight loss over the past 3 months accompanied by early satiety and left-sided dull abdominal pain. Medical history was notable for longstanding type 2 diabetes mellitus of more than 5 years (Hemoglobin A1C: 7.3 at presentation), atrial fibrillation, and breast cancer for which she underwent mastectomy, radiation, and hormonal therapy. Home medication included warfarin as a treatment of atrial fibrillation.

Upon presentation to the emergency department, the patient was mildly tachycardic (100 bpm), with a preserved blood pressure, respiratory rate, and oxygen saturation on room air. Physical examination was unremarkable except for an irregularly irregular rhythm consistent with her known atrial fibrillation. Laboratory diagnostics demonstrate an unremarkable CBC and BMP, with a therapeutic INR of 2.2. Diagnostic imaging included an EKG that confirmed atrial fibrillation with rapid ventricular rate and a chest radiograph that demonstrated a patchy infiltrate of the right lower lobe suggestive of pneumonia. A subsequent computed tomographic angiography demonstrated a left atrial appendage thrombus with multiple right lung pulmonary nodules measuring about 5 mm and scattered pulmonary artery emboli in the right middle and right lower lobes (Figs. 1 and 2). Incidentally, a pancreatic tail mass encasing the splenic artery associated with splenic infract and multiple hepatic nodules suspicious for malignancy were observed

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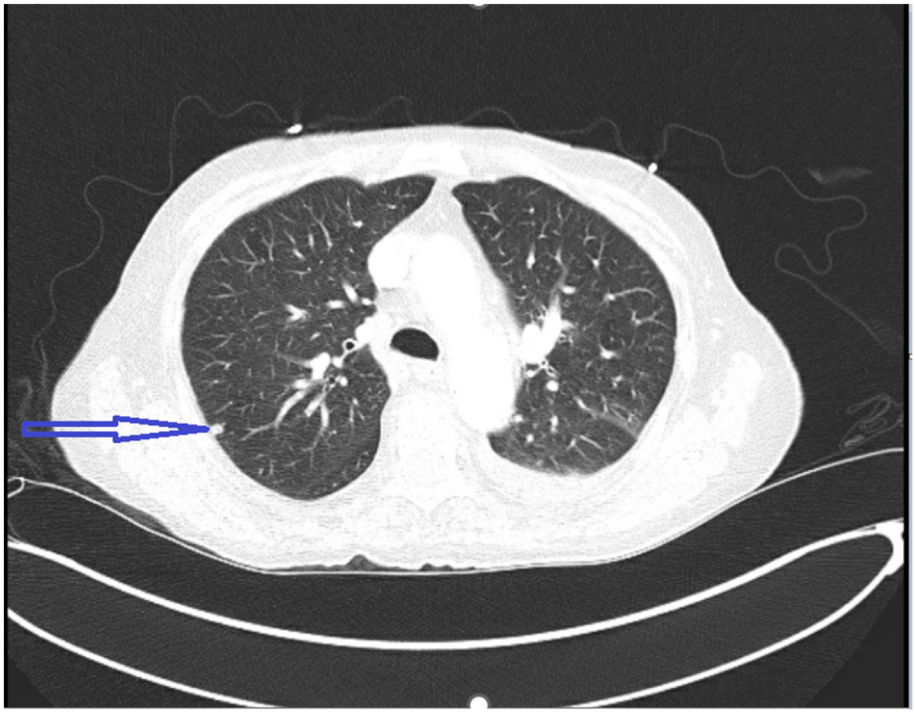

Fig. 1. Contrast enhanced computed tomography of chest showing pulmonary micronodules presumably related to metastasis.

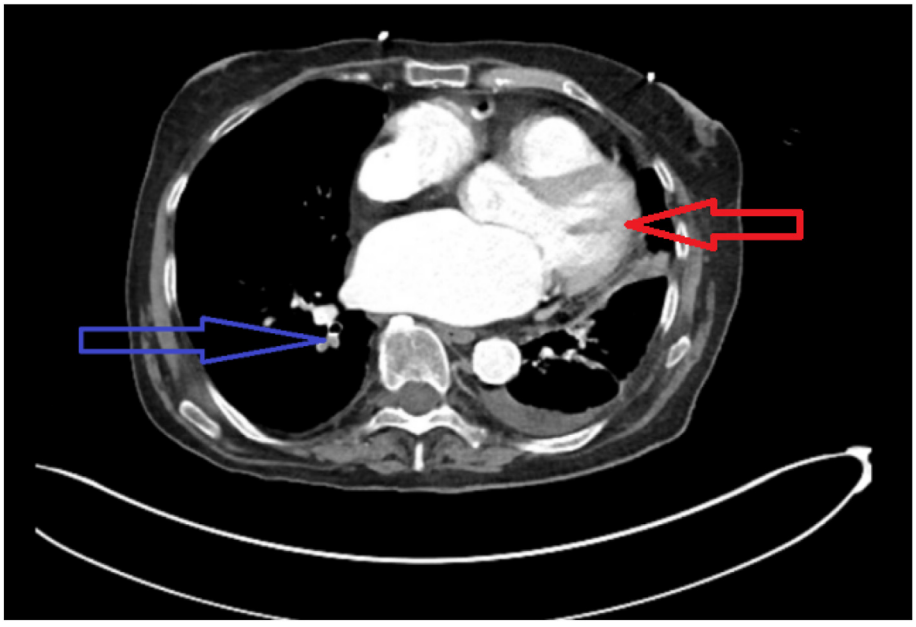

Fig. 2. Heart size is enlarged. There is a filling defect in the left atrial appendage (red arrow), concerning for thrombus. There are scattered pulmonary arterial filling defects (blue arrow) in the right middle lobe and right lower lobe pulmonary arterial segmental branches. There is a small left-sided pleural effusion with adjacent atelectasis. Minimal right basilar subsegmental atelectasis.

(Fig. 3). A lower extremity venous Doppler ultrasound was unremarkable. CA 19-9 was elevated at 11,544.3 units/mL. She was then transitioned from warfarin to low molecular weight heparin and subsequently discharged as she declined additional intervention given her advanced age.

3. Discussion

Risk factors for pancreatic carcinoma can be divided into non-modifiable and modifiable risk factors. A history of diabetes mellitus is considered a non-modifiable risk factor for pancreatic carcinoma.[4] Epidemiological studies indicate that the

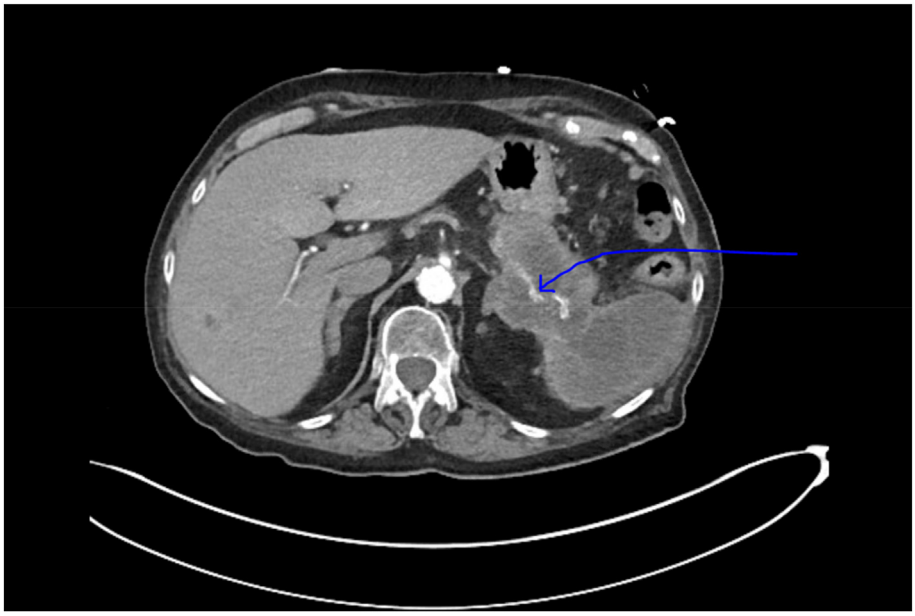

Fig. 3. Contrast Enhanced CT scan showing splenic artery (blue arrow) being encased by a large heterogeneously enhancing mass within the pancreatic tail measuring 7.6 × 6.3 cm leading to splenic infraction.

risk of pancreatic carcinoma is increased in patients with type 2 diabetes mellitus. American Cancer Society "Cancer Facts and Figures 2023" stated that about 25% of patients with pancreatic cancer had type 2 diabetes at the time of diagnosis of pancreatic cancer, and roughly another 40% had prediabetes.[5] From a pathophysiologic perspective, high insulin related to type 2 diabetes, obesity, and insulin resistance leads to an increase in IGF-I mediated effects in the nearby acinar cells resulting in increased survival and proliferation.[6] Multiple studies have concluded a causal relationship between diabetes and pancreatic carcinoma. Antwi SO et al. concluded a 3.09-fold increasing the risk of pancreatic cancer with diabetes mellitus compared to nondiabetics.[7] Furthermore, the association of diabetes and pancreatic cancer has been noted irrespective of body mass index (BMI) status, with long standing diabetes still posing as a significant risk factor for pancreatic cancer with a hazard ratio (HR) of 2.29 even in those of BMI less than 25. Similarly, in the same study, the age-adjusted HR was still high in patients with long standing diabetes than in patients without diabetes.[8] A meta-analysis done by Bosetti et al. also concluded an increased risk of pancreatic cancer with an odds ratio of 1.9 in those diagnosed with diabetes for over 2 years duration and an odds ratio of 1.3 in those diagnosed with diabetes for over 20 years. They further concluded that oral antidiabetic agents are associated with decreased risk of pancreatic cancer whereas insulin was associated with an increased risk of pancreatic cancer in the short-term (less than 5 years) underscoring the role of increased insulin in the pathophysiology of pancreatic cancer.[9]

Currently, there are no guidelines regarding pancreatic cancer screening in patients with long-term diabetes. CA 19-9 is a tumor marker commonly used in the diagnosis and treatment of pancreatic carcinoma. Although it has a sensitivity and specificity of 80% when a cut-off of 37 U/mL is used, it is a poor screening tool as it is elevated in several benign and malignant conditions including benign cholestatic diseases, liver fibrosis, and pancreatitis.[10,11] The International Cancer of the Pancreas Screening Consortium recommends MRI along with MRCP or EUS combination as preferred screening modality for pancreatic cancer in high-risk individuals such as those with hereditary breast and ovarian cancer syndrome, Lynch syndrome, and Puet-Jeghers.[12] Due to the high cost of pancreatic cancer screening modalities, the United States Preventive Service Task Force (USPSTF) has recommended against screening for pancreatic cancer in asymptomatic individuals including those with multiple risk factors.

Pancreatic carcinoma, which carries 2 points on the Khorana score (a risk stratification tool used for guiding venous thromboembolism prophylaxis in cancer patients), is recognized as a high-risk cancer for venous thromboembolism (VTE).[13] The incidence of VTE in pancreatic cancer varies from 5% to 57% in

retrospective studies, depending on the study population.[14] Levels of CA 19-9 seem to be associated with an increased risk of VTE with the highest risk being in those with CA-19-9 > 1000 U/ml.[15] In this report, we have highlighted VTE as a presenting feature that was associated with a diagnosis of pancreatic cancer. It further supports the use of CA 19-9 levels to predict patients at high risk of VTE; in our case, CA 19-9 level was 11, 544.3 U/ml.

On literature review, patients with VTE related with cancer has been shown to do better on LMWH rather than warfarin.[16,17] The 2022 international clinical practice guidelines for treatment and prophylaxis of VTE in cancer patients also supports the use of LMWH or novel anti-coagulants for treatment of VTE in cancer patients.[18] In this regard, our case report supports this statement with presentation of pulmonary embolism in the background of warfarin therapy having a therapeutic INR of 2.2.

4. Conclusion

Through this report, we highlight long standing diabetes as a risk factor for pancreatic carcinoma and emphasize the need of a cost-effective screening tool for pancreatic cancer. VTE in patients with long standing diabetes should prompt a search for pancreatic cancer as a cause especially in the elderly. Furthermore, we support the use of low molecular weight heparin and novel oral anti-coagulants in preference to warfarin for prevention and treatment of cancer related VTE.

Ethical statement

Informed written conset was taken.

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Disclaimer

This article has not been submitted to other journals for publication or presented at a conference.

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Conflict of interest

None.

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