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Pancreatic adenocarcinoma of the tail—Unveiling a rare presentation with venous thrombosis: A case report and literature review

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Abstract

Pancreatic cancer is a silent and lethal adversary that often conceals its presence until advanced stages. This report elucidates a distinctive case of a 46-year-old patient with pancreatic tail adenocarcinoma presenting with venous thrombosis, a rare manifestation. The patient's symptoms included severe left leg pain, swelling, and redness, accompanied by weight loss and decreased appetite. Laboratory findings indicated a prothrombotic state, whereas imaging revealed a substantial mass on the tail of the pancreas with hepatic metastasis. Elevated cancer antigen 19-9 and carcinoembryonic antigen supported the diagnosis which was confirmed by a liver biopsy. This case underscores the diagnostic challenges posed by pancreatic cancer, particularly in the tail, emphasizing the need for early detection. The intricate interplay between metastasis and thrombosis complicates the clinical landscape, requiring a comprehensive approach to management.

Keywords

Pancreatic tail tumor, venous thromboembolism, pancreatic metastasis, metastatic pancreatic adenocarcinoma, thromboembolism

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Introduction

Pancreatic cancer is the seventh leading cause of global cancer-related mortality, boasting a staggering 98% mortality rate and an incidence of 4.2 cases per 100,000 inhabitants.[1,2] Aptly coined the "silent" disease, pancreatic cancer often lurks asymptomatic in its early stages, revealing vague symptoms upon manifestation. The intricate landscape of pancreatic carcinomas unfolds, with 75% of the head, 15–20% of the body, and 5–10% of the tail, with the latter, particularly at a younger age, presenting rarer cases that tend to surface later and exhibit poorer survival rates due to delayed detection and advanced disease or metastasis.[3]

The uniqueness of pancreatic cancer extends beyond its low incidence to its remarkable ability to induce a hypercoagulable state, exponentially heightening the risk of venous thromboembolism (VTE). The prevalence of pancreatic cancer-associated VTE has doubled from 1997 to 2017, which is attributable to its increased prevalence, advanced age of patients, and enhanced detection through routine computed tomography (CT) scans.[4] Despite the enduring association between pancreatic cancer and hypercoagulability, the intricate pathological mechanisms and interplay among various pathways remain poorly understood. The International Initiative on Thrombosis and Cancer has raised awareness on this issue since 2013, advocating for the integration of the best supportive care to improve the quality of life for pancreatic cancer patients.[5]

In this report, we present a unique case of a 46-year-old patient diagnosed with adenocarcinoma of the pancreatic tail, showcasing a rare presentation with venous thrombosis. We intend to contribute to the growing body of knowledge surrounding this challenging-to-diagnose cancer characterized by high mortality and aspire to heighten awareness and

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facilitate earlier identification of pancreatic cancer, thereby improving the outlook for individuals grappling with this formidable disease.

Case report

In a 49-year-old male with a medical background marked by hypertension, diabetes, and hyperlipidemia, an acute onset of intense pain in the left lower leg, progressively escalating over the preceding 48 h, prompts medical attention. Simultaneously, the patient observed a surge in swelling, heightened warmth, and noticeable redness in the affected limb. The absence of any reported trauma or prolonged immobility, coupled with a denial of chest pain or shortness of breath, characterized the patient's clinical presentation. Noteworthy was the disclosure of a 10-pound weight loss over the past 2 months, concomitant with a discernible reduction in appetite. The patient's medication history encompassed aspirin 75 mg, rosuvastatin 10 mg, amlodipine 10 mg, and a combination of sitagliptin with metformin (50/500 mg) administered orally. Upon physical examination, the patient appeared well-oriented, adequately hydrated, and vitally stable. The abdominal assessment revealed a soft and non-tender abdomen with no evidence of visceromegaly. Bowel sounds were audible, and cardiovascular examination yielded unremarkable findings.

Laboratory investigations revealed significant abnormalities indicative of a prothrombotic state in a patient with suspected deep vein thrombosis (DVT) (Table 1). D-dimer levels were markedly elevated at 9.50 mg/L (reference range below 0.5 mg/L). In addition, there were elevated levels of C-reactive protein (12.6 mg/dL, reference range 0.0–0.5 mg/dL) and white cell count (20.74×10^9/L, reference range: 4.0–10.0×10^9/L). Coagulation studies showed a prolonged activated partial thromboplastin time of 43.3 s (reference range: 26.4–32 s), while prothrombin time was within normal limits at 14.2 s (reference range: 11.7–15.3 s), with an international normalized ratio of 1.0. Vascular studies of the left leg revealed dilation of the left femoral, great saphenous, and popliteal veins, along with echogenic material suggestive of thrombus without vascular flow (Figure 1). No arterial insufficiency was observed in the left leg. Based on these findings, the patient was admitted with a working diagnosis of DVT. A vascular surgeon review was conducted, and the patient was initiated on a comprehensive anticoagulation regimen, which included subcutaneous enoxaparin 60 mg twice daily, oral rivaroxaban 10 mg at bedtime, and continuation of oral aspirin 75 mg once daily.

Laboratory investigations conducted during the patient's hospitalization revealed significant deviations from normal metabolic parameters, notably an elevated blood glucose level of 240 mg/dL and an increased hemoglobin A1C of 10.3% (previous HbA1C done 1 year back was 6.7%). Concurrently, the patient reported mild abdominal pain, prompting a detailed assessment. Liver function tests displayed abnormal results, including total bilirubin 1.6, direct bilirubin 1.4, alkaline phosphatase 322, aspartate aminotransferase 74, alanine aminotransferase 656, and gamma-glutamyl transferase 366. Non-reactive results for hepatitis B and C were noted, and alpha-fetoprotein (AFP) levels were within the normal range at 2.11 (reference range: <7.22 IU/mL). A subsequent ultrasound scan of the abdomen revealed a liver measuring 17.3 cm with multiple hypoechoic lesions observed in both lobes of the

Table 1. Laboratory investigations reveal a prothrombotic state.

Investigation	Value	Reference value
D-dimer	9.50 mg/L	0.5 mg/L
C-reactive protein levels	12.6 mg/dL	0.0–0.5 mg/dL
White cell count	20.74×10^9/L	4.0–$10.0\ 10^9$/L
Activated partial thromboplastin time	43.3 s	26.4–32 s
Prothrombin time	14.2 s	11.7–15.3 s

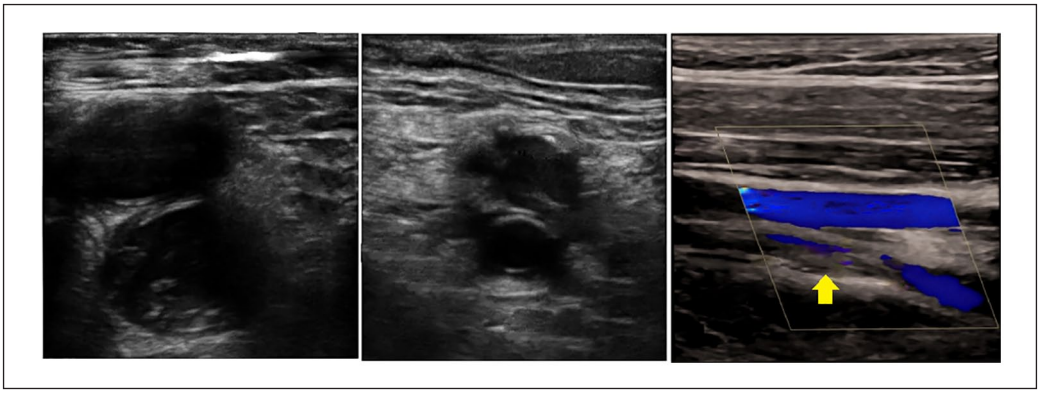

Figure 1. Ultrasound of the left leg showed dilated femoral vein (left image) (artery on top of vein) and dilated popliteal vein (center image) along with echogenic material suggestive of thrombus. Doppler ultrasound of left femoral vein with thrombus (yellow arrow) (right image).

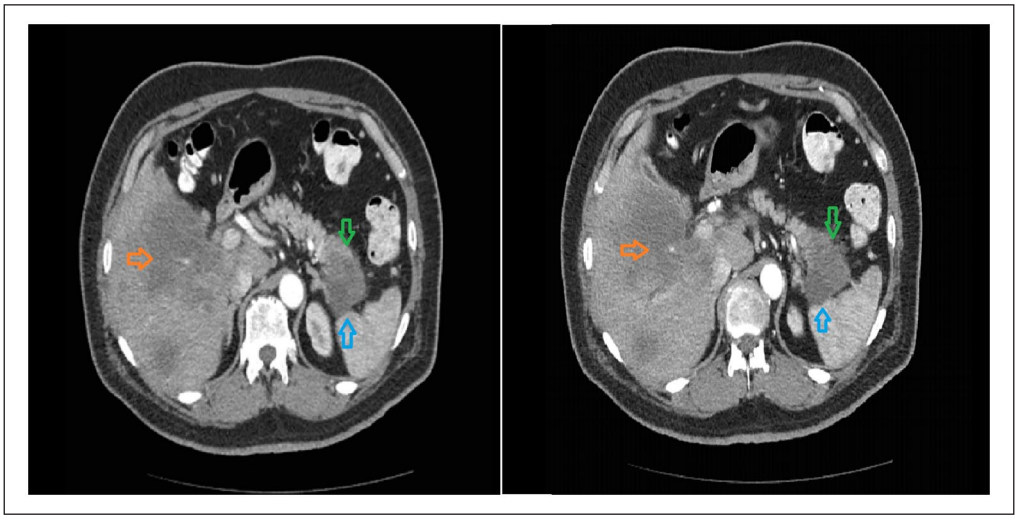

Figure 2. The CT scan of the abdomen shows heterogeneous soft tissue density mass (blue arrows) originating from the swollen tail of the pancreas (green arrows) with multiple hypo-dense lesions of varying sizes in the liver (orange arrows).
CT: computed tomography.

Table 2. Biopsy revealing liver metastasis secondary to pancreatic adenocarcinoma.

Aspect	Findings
Specimen	Trucut biopsy of the liver.
Gross	Two pale white linear cores of tissue collectively measuring 2 × 0.2 × 0.1 cm. Entirely submitted in a single cassette.
Microscopic description	Clusters of atypical cells exhibiting variable-sized hyperchromatic nuclei with prominent nucleoli and eosinophilic cytoplasm. Focally Lumina formation is observed.
Immunohistochemistry	Cytokeratin AE1/AE3, Cytokeratin 7, Cytokeratin 202, CDXZ, positive. HepPar-1 negative.

liver, giving the appearance of a target sign (the largest one measuring 3.9 × 3.7 cm in size). No intra- or extrahepatic biliary duct dilatation was noted.

A CT scan of the abdomen revealed a substantial heterogeneous soft tissue density mass (5.30 × 3.9 cm) with adjacent fat stranding originating from the tail of the pancreas (Figure 2). This mass, situated in close proximity to the spleen hilum, encased the splenic vessels. Notably, it exhibited an inferior abutment to the left adrenal gland, indicating a potential neoplastic lesion. Multiple hypodense lesions of varying sizes were evident in both liver lobes (Figure 2), with the largest lesion in segment V measuring 8.3 × 9.0 cm and encasing the right portal vein. The CT results, alongside an increased cancer antigen (CA) 19-9 tumor marker (45.7 U/mL; range = < 37 U/mL) and elevated carcinoembryonic antigen (CEA) levels (74.74 ng/ml; range = 3.0 ng/ml), robustly substantiate the diagnosis of pancreatic cancer originating in the tail with concurrent liver metastasis. Following a liver biopsy, the findings unveiled features indicative of a poorly differentiated primary pancreatic adenocarcinoma. Immunohistochemical analysis revealed neoplastic cells displaying a profile of CK7+/CK20+/TTF1-/HepPar-1-, accompanied by positive staining for CDX2, AE1/AE3, and PODXL1 (Table 2). These results compellingly signify a primary pancreatic-biliary neoplasm. A definitive diagnosis of stage IV pancreatic tail adenocarcinoma with multiple liver metastases was conclusively established.

Upon 1-month follow-up, the patient reported the resolution of epigastric pain and improved abdominal parameters, albeit still deranged. However, a new symptom—cough—emerged, prompting a contrast-enhanced CT of the chest that revealed mild pneumonitis without pulmonary metastasis. The patient was promptly referred to a pulmonologist. Subsequently, initiation of a FOLFIRINOX chemotherapy regimen, comprising 5-fluorouracil, leucovorin, irinotecan, and oxaliplatin, ensued. Tragically, the patient passed away at home in the first week of February 2024 due to cardiopulmonary arrest. Despite efforts to manage the disease with chemotherapy, the progression of the illness ultimately led to a fatal outcome.

Discussion

Pancreatic cancer represents a formidable clinical challenge, characterized by a dismal 5-year survival rate of 10%.[6] However, its research in Pakistan is sparse, with only 23 studies in the last 14 years. In comparison to 2012, there was a more than twofold rise in the incidence of pancreatic

cancers in 2020 in Pakistan with a 97.4% mortality rate and the majority of the patients dying in the first 6 months from the diagnosis.[7] Our patient's case tragically mirrors the alarming trend of pancreatic cancer in Pakistan, as, despite diligent treatment efforts, the aggressive nature of the disease led to their rapid decline, culminating in their unfortunate passing a mere 2 months following diagnosis. One of the molecular-focused studies employed immunohistochemistry to assess cell surface markers and two others employing bioinformatics and serum CEA analysis, yielded inconclusive results.[8,9] The limited findings are attributed to small sample sizes in these investigations. No other study to analyze molecular aspects of pancreatic cancers has been published in Pakistan. Despite constituting a mere 3% of annual new cancer cases, pancreatic adenocarcinoma demonstrates an alarming propensity for high mortality and is anticipated to become the second leading cause of cancer death by 2030.[10,11] Notably, tumors affecting the distal components of the pancreas, encompassing the body and tail, contribute significantly, comprising approximately one-third of pancreatic neoplasms.[12] In this context, our report emphasizes the crucial importance of recognizing diverse clinical presentations of pancreatic carcinoma involving the tail. This case underscores the imperative for healthcare practitioners to adeptly employ contemporary screening methods to facilitate early detection and prompt interventions. In doing so, we contribute to advancing medical knowledge and improving outcomes in the challenging landscape of pancreatic cancer.

Neoplasms originating in the pancreatic head predominate, manifesting pronounced symptoms such as weight loss, jaundice, dark urine, light-colored stools, nausea, and vomiting, leading to relatively early detection. By contrast, tail-derived neoplasms, although less frequent, present a diagnostic challenge with vague symptoms such as abdominal pain, back pain, and weight loss, often leading to delayed diagnosis and poor prognosis.[13] Approximately 10% of pancreatic neoplasms involve the distal gland, highlighting the potential for favorable outcomes through early surgical resection when promptly identified.[12]

The clinical spectrum of this condition encompasses left-sided abdominal pain, splenomegaly, ascites, gastrointestinal bleeding, migratory phlebitis, vascular embolism, and localized bruit. Distant metastases manifest as nodular liver lesions, pulmonary densities, and lymphadenopathy.[14] Notably, the detection of nodular liver lesions served as the initial diagnostic clue, prompting further investigation into tumor markers such as AFP, CEA, and CA 19-9. Confirmatory measures included CT CAP imaging and a trucut liver biopsy to determine the extent of metastasis. Importantly, our patient's chief presenting complaint, venous thrombosis, aligns with documented associations between thrombotic complications and carcinoma of the pancreatic tail. Only two studies reported the vascular status of pancreatic cancer patients, revealing that 45.6% had positive vascular invasion, with the superior mesenteric artery, coeliac artery, and common hepatic artery being commonly invaded. Notably, none of the studies reported presentations with DVT.[15,16]

In a recent 2021 cohort study, pancreatic cancer emerged with the highest 6-month cumulative incidence of VTE.[4] Notably, thrombotic complications in pancreatic cancers, particularly in the venous system, reach an incidence of up to 36%, attributed to elevated plasma levels of fibrinogen, factor 8, and D-dimers, coupled with decreased levels of protein C and antithrombin 3.[17] A historical analysis by Sprout in 1938, based on 4258 autopsies, revealed that among 16 cases of carcinoma in the tail of the pancreas, five exhibited venous thrombosis. Conversely, among 31 cases of pancreatic head cancer, only three manifested such complications.[14] The tail of the pancreas notably presents a heightened incidence of arterial embolization, which is attributed to the release of thrombocytosin, a tumor necrosis-derived factor.[17] This tissue factor, a key player in angiogenesis, correlates with disease activity by upregulating vascular endothelial growth factor expression and downregulating thrombospondin, an angiogenesis inhibitor. Additional factors contributing to these events include plasminogen activator inhibitor type 1, interleukin 1, tumor necrosis factor, platelet factor 4, thrombospondin 1, and heparanase enzyme.[18]

The cornerstone of pancreatic cancer diagnosis lies in the combined use of tumor markers and imaging modalities. Noninvasive imaging techniques, including helical CT, magnetic resonance imaging, and endoscopic ultrasonography, alongside minimally invasive procedures, such as laparoscopic ultrasonography, play pivotal roles in this diagnostic endeavor.[19] Tumor markers, such as serum CA 19-9, although characterized by low specificity, exhibit heightened levels indicative of aggressive tumor growth.[20] Notably, elevated CA 19-9 levels establish positive correlations with disease stage, survival duration, and thrombosis severity.[17] According to the European Society for Medical Oncology Clinical Practice Guideline, biopsy is pivotal for differential diagnosis, especially in patients starting chemotherapy, yet not routinely recommended if surgical resection is planned.[21] One attempt is advisable unless unsafe, and after two inconclusive attempts, treatment may begin without histological proof if multidisciplinary tumor board discussions, imaging, and CA 19-9 levels indicate malignancy. In our case, challenges, including the patient's high-risk status, staff shortage, and consent issues, prevented a pancreatic tail cancer biopsy. Despite opting for a liver biopsy as an alternative, bypassing the primary lesion biopsy contradicts the global medical standard, impeding accurate diagnosis. However, a percutaneous biopsy of the most accessible tumor site can confirm metastatic disease.[21] In treatment modalities, the overall prognosis hinges on surgical resection, a therapeutic avenue that not only enhances survival rates but also facilitates effective palliative care. Palliative interventions encompass pain management, chemoradiation, and surgical procedures such as stent placement for creating bypass routes, collectively contributing to a comprehensive

approach to alleviating symptoms and enhancing the quality of life of patients.[22]

A critical concern surrounding pancreatic cancers presenting with metastasis is the grim prognosis, as evidenced by a 3.3-fold higher risk of venous thrombosis compared with cases of localized disease. Remarkably, mortality rates underscore the severity of this scenario, with approximately 70%–90% of patients succumbing within 2 years of diagnosis.[17] The delayed presentation of the disease, coupled with its intricate anatomical location, significantly contributed to the observed unfavorable outcomes as depicted in our case. The enigmatic interplay between pancreatic cancer, liver metastasis, and thrombosis remains a subject of exploration, awaiting discovery and revelation. Furthermore, there is an imperative call for intensified research endeavors, focusing on genetic manipulations and pioneering chemotherapeutic trials. This concerted effort aims to address the challenges that pancreatic cancer continues to pose to the realm of medicine, promising advancements that may alter the trajectory of this formidable adversary.

Conclusion

In conclusion, the presented case underscores the challenges associated with pancreatic cancer, particularly when it arises in the tail and manifests as venous thrombosis. Delay in diagnosis and complex interplay between metastasis and thrombosis contribute to poor prognosis. The imperative for early detection through contemporary screening methods and the need for comprehensive management strategies, including surgical intervention and palliative care, are emphasized. As we navigate this intricate landscape, ongoing research efforts and awareness campaigns become pivotal especially in a country like Pakistan, offering hope for improved outcomes in the relentless battle against pancreatic cancer.

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Preprint available at https://www.researchgate.net/publication/376543477_Pancreatic_Adenocarcinoma_of_the_Tail_Unveiling_a_Rare_Presentation_with_Venous_Thrombosis_A_Case_Report_and_Comprehensive_Literature_Review.

Authors contribution

Conception and design: Syeda Mahrukh Fatima Zaidi and Syeda Abiha Rabab
Acquisition of data: Syeda Abiha Rabab, Ayesha Amjad, and Syeda Mahrukh Fatima Zaidi
Drafting of the manuscript: Paras, Maryam, Ayesha Amjad, and Syeda Mahrukh Fatima Zaidi
Critical revision for important intellectual content: Syeda Abiha Rabab.
Final approval of the study: Paras, Maryam, Ayesha Amjad, Syeda Mahrukh Fatima Zaidi, and Syeda Abiha Rabab
All authors have read and agreed to the final version of the manuscript.

Availability Of Data and Materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images before his death. Written informed consent was obtained from a legally authorized representative(s) for anonymized/in case of deceased patient for information to be published in this article. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Research Registration

None. Research Registration is not required. This case report does not detail a new surgical technique or new equipment/technology.

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