Decoding the diagnostic dilemma: Peripheral T-cell lymphoma presenting as acute pancreatitis: A case report

FNU VIKASH[1], SINDHU VIKASH[1], ANSH MEHTA[2], SANJANA NAGRAJ[1], SUNNY PATEL[3], SAMMY HO[4] and DONALD KOTLER[3]

Departments of [1]Internal Medicine, [2]Hematology and Oncology, and [3]Gastroenterology, Jacobi Medical Center; [4]Department of Gastroenterology, Montefiore Medical Center, Albert Einstein College of Medicine, New York, NY 10461, USA

Received August 14, 2023; Accepted November 10, 2023

DOI: 10.3892/ol.2023.14206

Abstract. Peripheral T cell lymphoma (PTCL) is a rare form of non-Hodgkin lymphoma characterized by the origin of mature T-cells. PTCL demonstrates atypical clinical features and involves both nodal and extra-nodal sites. The diagnosis and treatment of PTCL can prove to be challenging, as it is often detected at advanced stages and is resistant to conventional chemotherapy treatments. The present report describes a 55-year-old male patient who presented with acute pancreatitis, and imaging suggested a soft tissue mass in the pancreatic head indicating pancreatic adenocarcinoma. Further investigation through ultrasound-guided biopsy led to the diagnosis of pancreatic PTCL not otherwise specified.

Introduction

PTCL is a rare type of NHL that arises from mature T-cells. PTCL-NOS is a heterogeneous group comprised of predominantly nodal T-cell lymphomas that do not fit the criteria for the other subtypes of PTCL and carry a poor prognosis (1). Management is often challenging due to advanced-stage detection and resistance to standard chemotherapy. PTCL-NOS commonly affects systemic lymph nodes; however, extra nodal sites such as the liver, spleen, lungs, pancreas, and bone marrow are rare (2). At the same time, there are a few case reports of primary liver involvement in PTCL (3,4); however, there have been no documented cases of PTCL with primary pancreatic involvement. Here, we report an atypical case of primary pancreatic PTCL-NOS with secondary involvement of the liver presenting as AP without peripheral lymphadenopathy.

Correspondence to: Dr Fnu Vikash, Department of Internal Medicine, Jacobi Medical Center, Albert Einstein College of Medicine, 1400 Pelham Parkway South, Bronx, New York, NY 10461, USA
E-mail: vikashjs86@outlook.com

Key words: peripheral T-cell lymphoma, acute pancreatitis, non-Hodgkin lymphoma, epigastric pain, peripheral T-cell lymphoma not otherwise specified, chemotherapy

Case report

A 55-year-old male with no known medical history presented to the emergency room in November 2022 at Jacobi Medical center, with epigastric pain, nausea, non-bloody non-bilious vomiting, jaundice, and unquantifiable weight loss. He had no history of tobacco, alcohol, recreational drug use, abdominal surgeries, and no family history of gastrointestinal malignancy. Vital signs were within normal limits. The physical exam was remarkable for scleral icterus, generalized yellowish skin discoloration, and epigastric tenderness. Laboratory workup showed a white blood cell count of 1.09/nl (normal: 3.90-10.60/nl), absolute neutrophil count of 0.58/nl (normal: 1.90-8.70/nl), absolute lymphocyte count of 0.29/nl (normal: 0.65-4.20/nl), and platelet count 9/nl (normal: 150-440/nl). The liver function tests revealed a cholestatic pattern, with elevated levels of alanine aminotransferase 85 U/l (normal: 1-40 U/l), aspartate aminotransferase 146 U/l (normal: 1-40 U/l), alkaline phosphatase 225 U/l (40-129 U/l), total bilirubin 31 mg/dl (normal: 0.1-0.3 mg/dl), and direct bilirubin 24 mg/dl (normal: 0.1-0.3 mg/dl). Lipase and lactate dehydrogenase (LDH) were 876 U/l (normal: 7-60 U/l) and 805 U/l (normal: 100-210 U/l), respectively. Serologic tests, including human immunodeficiency virus, syphilis, and hepatitis panel, were within normal limits. Computed tomography (CT) scan abdomen/pelvis with contrast showed AP with localized peripancreatic fluid and ill-defined soft tissue mass within the pancreatic head (Fig. 1) without biliary or pancreatic duct dilatation. Magnetic Resonance Cholangiopancreatography (MRCP) revealed a T2 hypointense retroperitoneal soft tissue mass (4.4 cm) involving the pancreatic head with superimposed pancreatitis and pseudocyst (Fig. 2A and C) and extensive paraaortic lymphadenopathy (Fig. 2B) consistent with pancreatic adenocarcinoma. However, tumor markers carcinoembryonic antigen 19-9 and carcinoembryonic antigen levels were normal. At this point, the cause of bicytopenia (thrombocytopenia and neutropenia) was still unclear; hence bone marrow (BM) biopsy was performed, which revealed hypercellular marrow (60%) with scarce CD3-positive cells (Fig. 3B) and CD30-positive atypical lymphoid infiltration (~5%) (Fig. 3C). At this point, there was a strong suspicion of lymphoma, and considering abnormal liver enzymes and easy accessibility to the liver, an ultrasound-guided liver

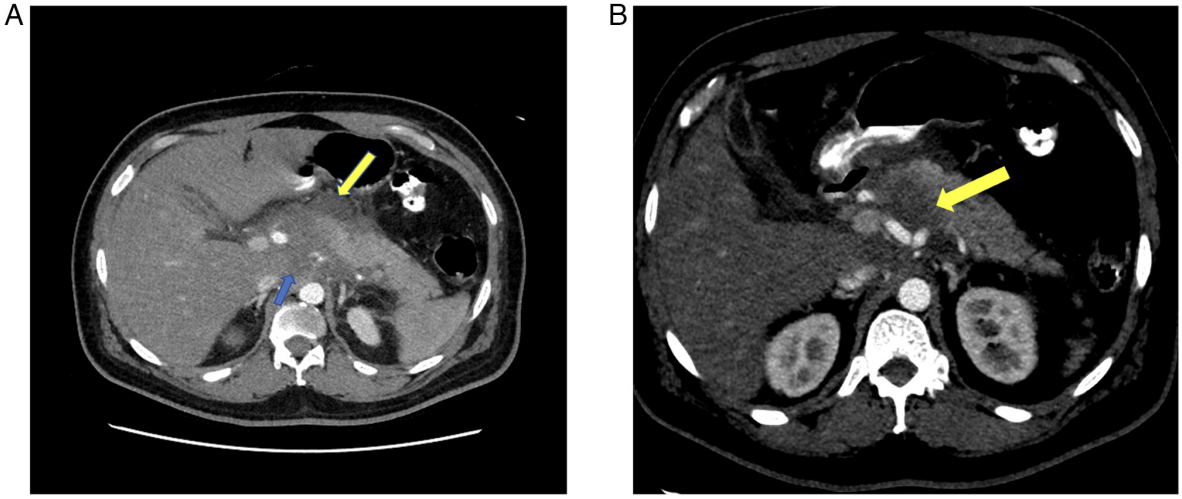

Figure 1. Axial CT scan with contrast. (A) Acute pancreatitis with peripancreatic fluid collection (yellow arrow) and an ill-defined mass in the pancreatic head (blue arrow). (B) Ill-defined mass in the pancreatic head (yellow arrow).

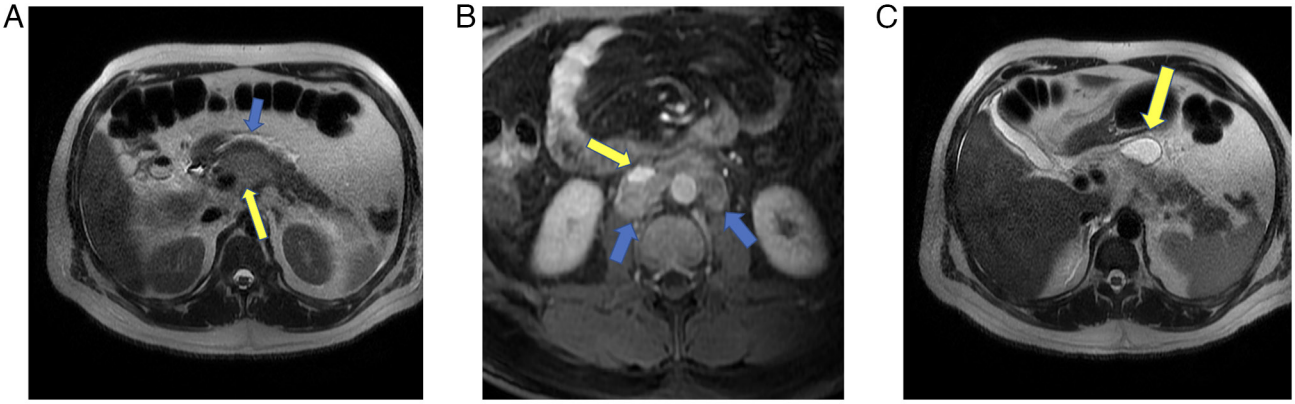

Figure 2. Magnetic resonance cholangiopancreatography. (A) T2 hypointense retroperitoneal soft tissue mass (4.4 cm) involving the pancreatic head (yellow arrow) with peripancreatic fat stranding (blue arrow), representing superimposed pancreatitis. (B) Para-aortic lymphadenopathy (blue arrows) displacing the inferior vena cava (yellow arrow) anteriorly. (C) Pancreatic pseudocyst (yellow arrow).

core biopsy was performed. However, before the biopsy, the patient received intravenous (IV) steroids and platelets transfusion to stabilize the platelet counts. A liver biopsy revealed the presence of mature T-cell lymphoma, characterized by co-expression of the markers CD4, CD30, and FOXP3 (Fig. 4). The CT scan for the head, neck, and chest was negative. Our patient's immunohistochemistry markers for mature T-cell lymphoma did not meet the criteria for specific types of mature T-cell lymphoma defined by the World Health Organization (WHO) (5). Therefore, the diagnosis of PTCL-NOS is favored. The patient was subsequently initiated on an ACHP regimen (brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone), per the ECHELON 2 trial (6). The patient is currently getting his chemotherapy sessions, with the tentative plan of hematopoietic stem cell transplantation.

Discussion

PTCL is an aggressive entity comprising 5-15% of all NHL (1). The median age at diagnosis is 60 years, with a higher incidence in men (2:1 ratio). Approximately 35% of patients diagnosed with PTCL exhibit B symptoms (fevers, diaphoresis, and anorexia), 50% have elevated LDH, and 14% demonstrate hypergammaglobulinemia (2). Our patient had no evidence of B symptoms, but LDH levels were elevated. PTCL is prevalent in immunosuppressed patients, such as patients with human immunodeficiency virus/human T-cell leukemia virus (HIV/HTLV) infections, lupus, or using immunosuppressive therapy (7). However, in this case, serologic tests were negative for HIV, HBV, HCV, and HTLV, leading to speculation that PTCL can occur in immunocompetent individuals.

AP is a well-documented complication of pancreatic adenocarcinoma reported in 14% of cases; however, it is a rare complication in pancreatic PTCL (8). The postulated pathogenesis underlying AP is pancreatic duct obstruction, rupture of the pancreatic duct with a direct parenchymal invasion, and ischemia secondary to vascular occlusion by the tumor (9,10). In our case, no pancreatic duct involvement was detected despite the extensive infiltration of lymphoma cells in the pancreatic head. Therefore, the probable pathogenesis of AP is attributable to tumor-induced ischemia resulting from vascular occlusion.

Primary hepatic lymphoma generally presents as a single, well-defined nodule, whereas secondary hepatic lymphoma

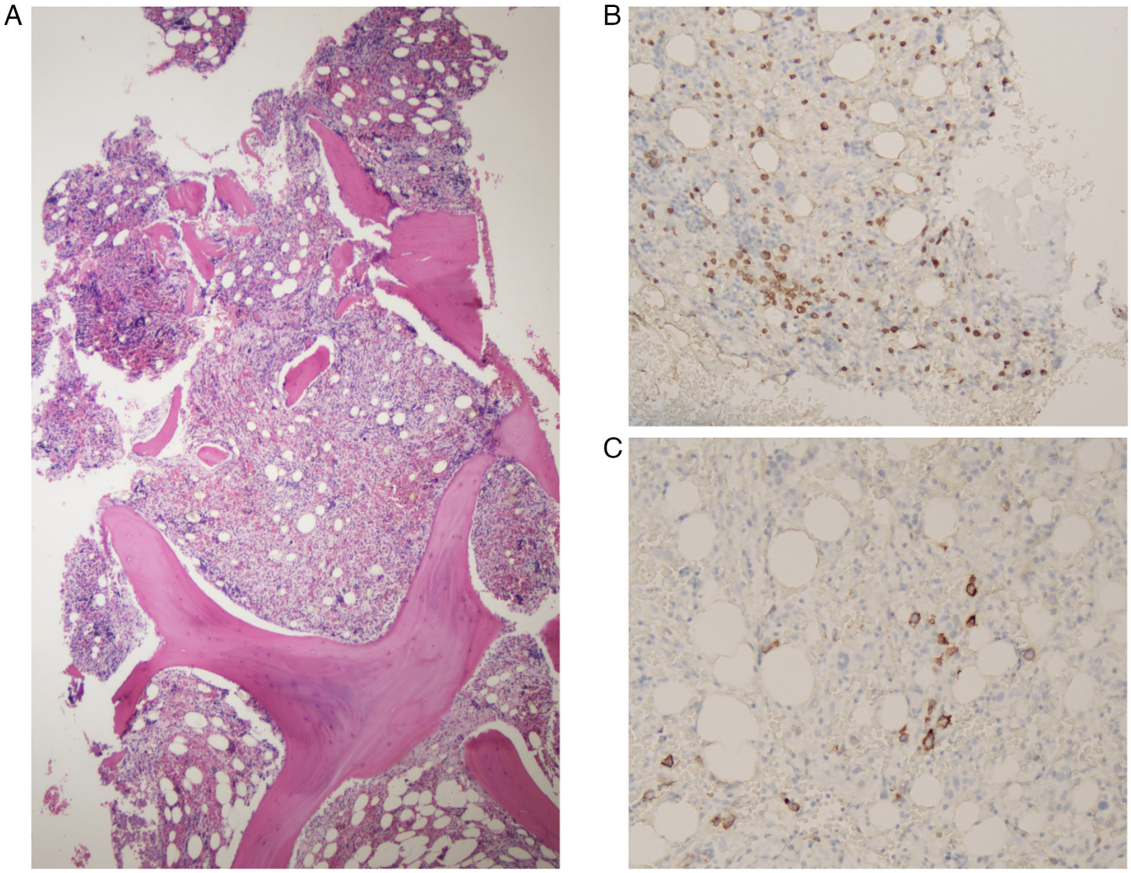

Figure 3. Bone marrow biopsy. (A) Hypercellular bone marrow (magnification, x4; H&E staining). (B) Scarce CD3-positive cells (magnification, x20; CD3 immune staining). (C) Scarce CD30-positive cells (magnification, x40; CD3 immune staining).

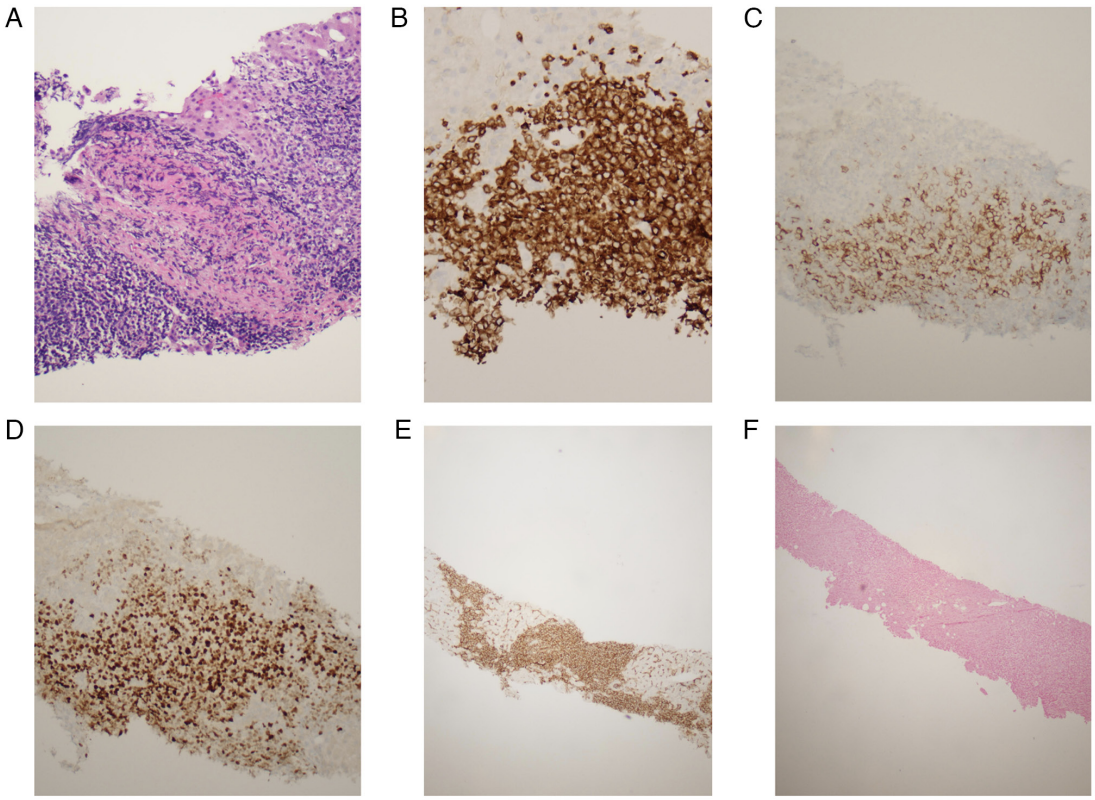

Figure 4. Liver core biopsy (magnification, x20). (A) Infiltration of lymphocytes involving portal triad and surrounding parenchyma (H&E staining). Immune staining highlighted abundant amounts of T-cells, positive for (B) CD3 (CD3 immune staining), (C) CD30 (CD30 immune staining) and (D) FOXP3 (FOXP3 immune staining). (E) CD4-positive T cells (CD4 immune staining). (F) Epstein-Barr encoded RNA-negative liver tissue (H&E staining). FOXP3, forkhead box P3.

can present in various forms, ranging from one or multiple nodules to diffuse infiltration (11). In our case, neither CT nor MRCP scan could identify liver lesions (possibly due to their small size) but revealed a hypointense retroperitoneal mass within the pancreatic head, indicating primary pancreatic involvement with secondary metastasis to the liver. At the same time, previous reports have documented several cases of primary hepatic PTCL (3,4). However, we present a unique case of primary pancreatic PTCL with an unusual clinical manifestation as AP, alongside liver and bone marrow involvement at the time of diagnosis.

Imaging, particularly CT scans, is crucial for diagnosing and characterizing pancreatic lymphoma. There are two morphologic patterns for pancreatic lymphoma: well-circumscribed tumors that may resemble pancreatic adenocarcinoma and diffuse infiltrating types that can mimic acute pancreatitis on CT scans. Key distinctions include the lack of pancreatic duct dilation in lymphoma, lymph node involvement below the renal veins, and invasive growth (12,13). Calcification or necrosis is not typical in untreated cases. MRI findings parallel CT, with well-circumscribed tumors showing low signal intensity on T1-weighted images and subtle enhancement (13). Diffuse infiltrating masses display low signal intensity on both T1 and T2-weighted images with mild-to-moderate enhancement (13). However, our patient CT scan showed ill-defined soft tissue mass within the pancreatic head and MRCP revealed a T2 hypointense retroperitoneal soft tissue mass (4.4 cm) involving the pancreatic head which was initially concerning for pancreatic adenocarcinoma, however our patient had no pancreatic duct involvement, and tumors makers like Carcinoembryonic Antigen (CEA) and Cancer Antigen 19-9 (CA 19-9) were also negative in our patient, leading us to a possibility of considering other diagnosis.

PTCL is often a perplexing diagnosis associated with poor outcomes (14). Literature reports a case series of 15 patients with nodal PTCL-NOS was found to have an aggressive clinical course. Of these patients, 10 passed away within 6 months of their diagnosis, with a median survival time of only 3.5 months (15). Moreover, Weisenburger *et al* (2) proposed that higher Kiel 67(Ki-67) was associated with poor response to therapy and worse prognosis. Several case reports have highlighted atypical presentation for PTCL, such as Liu *et al* (16) report PTCL presenting as rhabdomyolysis in a patient with alcohol abuse. Moreover, in another case, PTCL presented as peripheral neuropathy compatible with subacute demyelinating polyradiculoneuropathy (17). In essentially all of these cases, the diagnosis was delayed or complex due to the atypical presentation of a notoriously heterogeneous disease. In conclusion, considering the rapidly progressive nature of PTCL, prompt invasive biopsy should be performed. Early recognition of this uncommon tumor is crucial for remission and early stem cell transplantation. Furthermore, this case highlights the potential biases of radiologists towards more common diagnoses, as in our case, it was first diagnosed as pancreatic adenocarcinoma based on imaging findings. It emphasizes the need for a critical and discerning approach to an accurate diagnosis.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

FV and DK conceived and designed the study. FV, SV, AM, SN and SP obtained data and treated this patient. FV and SV analyzed the data and drafted the manuscript. FV and SH analyzed the data using pathological methods. FV and DK confirm the authenticity of the pathological data. FV and SH confirm the authenticity of all other raw data. SV, AM, SN, SP and DK revised the manuscript before submission. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed patient consent was obtained to publish the article.

Competing interests

The authors declare that they have no competing interests.

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