Pancreatitis Panniculitis and Polyarthritis Syndrome: A Rare Misdiagnosed Case of Septic Arthritis Successfully Managed with Corticosteroids

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ABSTRACT

Background

Pancreatitis Panniculitis and Polyarthritis (PPP) syndrome is a rare triad of pancreatitis, subcutaneous fat necrosis (panniculitis), and polyarthritis, caused by the extravasation of pancreatic enzymes into the bloodstream. This can result in fat necrosis within various tissues, including bone and joints, leading to painful, swollen joints and skin lesions. Given its rarity, PPP syndrome is often misdiagnosed, and there is no established management protocol. We present a case of PPP syndrome that was initially misdiagnosed and treated as septic arthritis, highlighting the importance of recognizing this uncommon entity.

Case Presentation

A 35-year-old Indian male presented to the emergency department with diffuse joint pain, redness, and swelling for more than 20 days. His medical history was significant for chronic pancreatitis, anemia, pleural effusion, portal vein thrombosis, tuberculosis, and alcohol consumption. He had no recent trauma, travel history, or contact with infectious diseases, including COVID-19. The patient was febrile, tachycardic, and normotensive, with diffuse swelling and tenderness in multiple joints, including the knees, ankles, elbows, and wrists. Laboratory findings showed leukocytosis, elevated inflammatory markers, and elevated amylase levels.

Initial diagnostic imaging, including X-rays, showed no joint abnormalities, and arthrocentesis yielded purulent fluid that tested negative for microorganisms but revealed lipid crystals. This ruled out septic arthritis and raised suspicion for a pancreatic origin. A CT scan of the abdomen confirmed the diagnosis of chronic pancreatitis, with multiple calcifications in the pancreas and portal vein thrombosis. A joint biopsy was performed, and histopathology revealed extensive fat necrosis and the characteristic “ghost cells” of PPP syndrome.

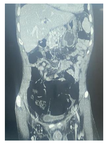
The patient was started on a course of prednisolone, which led to significant clinical improvement, and he was discharged after 29 days of hospitalization. He was placed on a tapering regimen of steroids over six weeks.

Conclusion

PPP syndrome is a rare but important differential diagnosis in patients with recurrent joint effusion, especially in the setting of chronic pancreatitis. Timely recognition and appropriate management can prevent unnecessary surgeries and reduce morbidity. Though there is no established treatment protocol, corticosteroids may offer a promising treatment option for managing extra-pancreatic manifestations. Further research is needed to establish guidelines for the diagnosis and management of PPP syndrome.

Introduction

Pancreatitis Panniculitis and Polyarthritis (PPP) syndrome is a rare entity first noticed and described in 1908 by Berner, it is a rare complication of pancreatic pathology that presents as a triad of Pancreatitis, Panniculitis and Polyarthritis. There have been few cases reported in the literature since and still no clear protocol in managing this syndrome. We present this case highlighting how misdiagnosis can lead to unnecessary surgery and lead to an increase morbidity and mortality rate. The article has been reported in line with the SCARE [10] criteria.



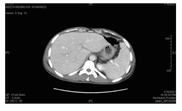


Figure 1: Abdomen CT Scan
- Multiple calcific foci seen in the head and uncinate process with pancreatic duct dilation, no evidence of necrosis/ collection.
- Chronic thrombosis and total occlusion of the Porto-Splenic-Mesenteric venous axis with extensive cavernous transformation
- Spleen enlarged, measuring 14.4cm
- Normal distension of stomach with thickened wall of the pylorus and congested vessels around its fundus.
- Minimal free fluid in the pelvis

CASE PRESENTATION

A 35-year-old Indian male presented to the hospital emergency room for diffuse joint pain and redness for more than 20 days in January 2021.He has a history of pancreatitis, anemia, pleural effusion and portal vein thrombosis, tuberculosis and was an alcohol consumer.
There was no history of recent travel, illness prior to pain, trauma or contact history with COVID-19. Pain was severe in nature, worse during night accompanied with shortness of breath with exertion without chest pain. There was no history of abdominal pain, nausea or vomiting, altered bowel habits, urinary symptoms, skin rash, morning stiffness of the joints or oral ulcers. Clinical examination revealed a febrile, tachycardiac and normotensive patient with diffusely swollen and tender joints involving knees, ankles, elbows, wrists and hands (Right 2nd MCP) associated with restricted motion. There was no signs of edema or deep vein thrombosis or skin rashes noted, nor epigastric tenderness or cardiopulmonary manifestation. Positive laboratory findings showed leukocytosis, elevated inflammatory markers and elevated amylase levels. Further lab results are shown in [Table 1 and 2].
On further assessment X-ray evaluations did not show any joint space or bone abnormality as a result of unremarkable finding Arthrocentesis of both knees was preformed which yielded a purulent fluid, which was negative for microorganisms and white cells but included lipid liquid crystals, which ruled out septic arthritis. Duo to high amylase level and history of pancreatitis and portal vein thrombosis computers tomography (CT) scan of the abdomen was done revealing a picture of chronic pancreatitis.

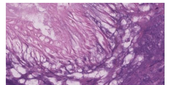
Patient was admitted under medical unit as a case of Acute on top of Chronic Pancreatitis and Polyarthritis for further evaluation. Initial treatment of pancreatitis showed improvement with clinical and biochemical markers. However, on Day 3 during hospital stay, he developed severe pain with passive and extensive motion with restriction of movement of the knee joints, aspiration was repeated of the joint revealing pus appearing fluid. He was taken for incision and drainage of both knees with impression of septic arthritis, drainage of the turbid fluid and sent for culture and sensitivity and kept on Meropenem and Vancomycin post
operatively.

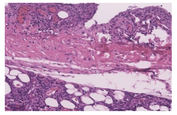
He was recovering well until symptoms recurred on day 8, underwent ultrasound guided aspiration of the left elbow which revealed no growth. On day 9, left knee was swollen again, ultrasound guided aspiration was done liberated bloody aspirate thus repeat incision and
drainage was done. Fluid sent for virology was negative.

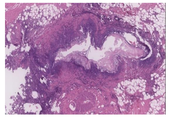
His clinical condition didn’t show improvement, with diffuse joint swelling recurring especially at the knees. On day 10, he underwent bilateral incision and drainage of knees. Intraoperatively, the retinaculum was noted to be eroded without signs of infection. Additionally, spontaneous rupture of skin swelling overlying the left ankle joint was seen revealing “cheesy brown sticky” substance that appeared as tissue destruction rather than infection. [Figure 2] Fluid sent for histopathology showed benign synovial cells and polymorph neutrophils consistent with benign fluid and acute inflammation. [Figure 3]

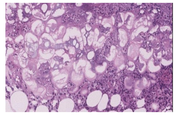
Moreover, during his course of stay his Hemoglobin dropped from 13.4 to 7.9, transfused 1 unit of PRBC and underwent upper GI endoscopy, which revealed multiple deep ulcers seen in the antrum, about 3 - 4 ulcers observed, largest measured 1 cm, clean based without active bleeding. Biopsy for H. Pylori was negative. Concomitant Endoscopic ultrasound of the pancreas was done, revealed no masses or significant lymph nodes.

On day 19, Histopathology report of the joint tissue revealed extensive enzymatic fat necrosis,
“ghost cell”, amorphous granular debris and stippled basophilia due to calcification accompanied by neutrophilic infiltration. and chronic inflammation with granulation tissue formation. Fibrinoid necrosis secondary in nature. [Figure 4]









A: Panniculitis with fat necrosis (H &E)
B: Higher power using fat necrosis, neutrophilic infiltrate and ghost cells
C: Necrosis with ghost cells
D: Inflamed synovium

DISCUSSION

Pancreatitis Panniculitis and Polyarthritis (PPP) syndrome is a rare entity. It’s typically apparent in middle aged males with a history of heavy alcohol abuse. [2,3] Underlying pancreatic pathology is the reason, it can be in the form of acute or chronic pancreatitis, pancreatic carcinoma, neuroendocrine carcinoma, insulinoma, ischemic pancreatic disease, abdominal trauma or pancreatic duct stenosis. [4] The exact etiology is still unclear. Multiple authors assumed that pancreatic enzyme extravasates into the systematic circulation through the thoracic duct, portal circulation or through lymphatic channels. Extra pancreatic manifestation appears when enzymes penetrate the peripheral fatty tissue, periarticular fat, and synovial spaces causing fat necrosis and secondary inflammation, resulting in panniculitis and polyarthritis.[1,6] Thrombosis of the portal vein as an association with PPP syndrome has been reported in the literature,[8] our patient had a history of portal vein thrombosis 3 years prior to admission, with a CT scan of the abdomen suggesting a diagnosis of chronic portal vein thrombosis. We theorize that occlusion of the portal vein may facilitate pancreatic enzymes extravasation to the systematic circulation. Narváez et al in his review of 25 documented cases with PPP syndrome, found that 75% of patients had absent or mild abdominal symptoms.[3] Pancreatic panniculitis is a complication of acute pancreatitis occurring in 2-3% of all patients, characterized by a tender edematous, red to brown in color subcutaneous nodule that appears most commonly in the lower limbs especially over the leg.[5] Subcutaneous nodules my rupture spontaneously and secretion of oily brown viscous material is described.[4] Typical histopathological features confirms the diagnosis, showing pathognomonic “Ghost cells”.[4,5,9] “Ghost cells” is anucleate adipocyte that have a thick wall with a fine basophilic granular material within their cytoplasm from dystrophic calcification.[5] Multiple lab abnormalities are present in PPP syndrome, elevated inflammatory markers and pancreatic enzymes are described. [2,4] Lipase levels is elevated in almost all of the cases that has been reported in the literature. [4,7,9] Dieker et al used lipase level to monitor the success of treatment modalities. [4] Unfortunately lipase was not used as a monitoring tool, because it was not available in the hospital.

In regard to arthritis, it is seen in approximately 75% of patients. [7,8] Polyarthritis is the presenting symptom in 25% of patients, prior to developing abdominal symptoms and recognition of pancreatic pathology. [8] Joint involvement can present as monoarticular or polyarticular; most commonly it involves the knee, ankle and wrist joints, although other joint involvement is reported. [1,4,7] It’s usually symmetrical and transient while it also can be migratory. Synovial fluid analysis is sterile and may contain creamy viscous materiel with high lipid content and high neutrophilic count. [2,4] Kim E et al analyzed 31 cases with PPP syndrome. It was observed that more than 70% of patients had a chief complaint other than abdominal pain. Arthralgia was the most common symptom counting for 71%. Of the 31 patient’s misdiagnosis rate was exceptionally high counting for 32.3% of the cases. [9] Unspecific joint involvement can be misleading, differential diagnosis include septic, gouty and rheumatoid arthritis must be ruled out. Early in the disease plain radiographs of the joints are usually normal. Late radiographic changes include bony osteolytic lesions, bone sclerosis and loss of joint space. [1,3] The most sensitive imaging modality is Magnetic Resonance Imaging (MRI). MRI detects abnormalities of the bone marrow early in the disease, prior to developing osteonecrosis. [1,3]

In terms of management, targeting the pancreatic pathology must be the aim. If conservative therapy failed to treat the pancreatitis, aggressive modalities of treatment must be targeted to resolve the pancreatitis and its complications. Surgery is advised for pancreatic tumors and gallbladder disease. [2] Trials of steroids and non--steroidal anti-inflammatory drugs for extra-pancreatic manifestation showed poor to moderate response. [3,6] Our patient showed a promising response after the administration of prednisolone. In order to determine prednisolone efficacy on polyarthritis, a more detailed analysis should be carried out. It is reported that panniculitis resolved after treatment of the pancreatic pathology, while arthritis showed variable responses. [3,6] In almost 45% of patients, arthritis was independent to pancreatic disease resolution, leading to chronic joint destruction which resulted in significant morbidity. [3] The nature of this disease and its multi-- system involvement requires a multidisciplinary approach, involving orthopedic surgeons, general surgeons, internist, dermatologist and histopathologist. This approach will facilitate the early recognition and treatment, thus it will lead to decrease in morbidity and mortality. Two consecutive reviews were done by Narváez et al and Kim E et al, during 1970 to 2008 and 2009 to 2019 respectively. The mortality rate was concluded to be 24.3% for the former and 30% for the latter. [3,9]

CONCLUSION

Recurrent joint effusion in patients with pancreatitis should raise suspicious among physicians to consider investigating for PPP syndrome as an etiology, especially the histopathology biopsy is the standard for achieving final diagnosis, being aware of this rare entity will help avoiding misdiagnosis or future complication by delaying management. However, still there is no established management protocol, more research is needed to demonstrate the efficacy of steroid management.

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