5-1-2023

Pancreatitis, panniculitis and polyarthralgia syndrome: A rare complication of pancreatic pathology

Harjinder Singh

Parth Patel

Shamik Parikh

Hassan Zreik

Neil Caliman

See next page for additional authors

Authors
Harjinder Singh, Parth Patel, Shamik Parikh, Hassan Zreik, Neil Caliman, and Vivek Kak

Radiology Case Reports 18 (2023) 2001–2004

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Pancreatitis, panniculitis and polyarthralgia syndrome: A rare complication of pancreatic pathology ☆

Harjinder Singh, MD[a,*], *Parth Patel, MD*[a], *Shamik Parikh, MD*[a], *Hassan Zreik, MD*[a], *Neil Caliman, MD*[b], *Vivek Kak, MD, FACP*[a]

[a] *Henry Ford Health, Department of Internal Medicine, Henry Ford Jackson Hospital, 205 N East Ave, Jackson, MI, 49201, USA*

[b] *Henry Ford Health, Department of Pathology, Henry Ford Jackson Hospital, 205 N East Ave, Jackson, MI, 49201, USA*

ARTICLE INFO

Article history:
Received 9 February 2023
Revised 23 February 2023
Accepted 26 February 2023

Keywords:
Pancreatitis
Panniculitis
Polyarthralgia
Ghost cells
Bone necrosis

ABSTRACT

Pancreatitis, panniculitis, and polyarthralgia (PPP) syndrome is a rare complication of chronic pancreatitis and occurs due to leakage of pancreatic enzymes in the systemic vasculature. This enzyme leakage leads to multiple manifestations such as polyarthralgia, panniculitis, and bone necrosis due to tissue autodigestion.The inciting pancreatic pathology may be masked, and the presentation may be due to one of the systemic consequences of enzyme leakage, which can present as a diagnostic challenge for clinicians. Here we present a patient who presented with nodular lesions and bone necrosis, and was found to have PPP syndrome. Therefore, a proper understanding of pathophysiology and radiology findings can help with prompt diagnosis and early exploration of management options.

Introduction

Polyarthritis, panniculitis, and pancreatitis (PPP) is a triad described in patients with pancreatic pathologies such as acute and chronic pancreatitis, pancreatic tumors, and ischemic pancreatic disease. The typical patient with PPP syndrome is a middle-aged male with chronic alcohol use [1]. The hypothesized pathogenesis for this syndrome is the leakage of pancreatic enzymes into the systemic circulation that leads to digestion of soft tissue, joints, and even bone necrosis [2]. In a previously described case report [3], the causative nature of pancreatic enzyme leakage was deemed to bea fistulous connection between a pancreatic pseudocyst and superior mesenteric vein, which was successfully treated with surgical resection of the fistulae. These tiny fistulae are challenging to identify on imaging, and the presence of superior mesenteric vein thrombosis may be an indirect manifestation [1]. This

☆ Competing Interests: The authors have declared that no competing interests exist.

* Corresponding author.
E-mail address: Hsingh8@hfhs.org (H. Singh).

https://doi.org/10.1016/j.radcr.2023.02.056

report highlights a patient who presented with nodular skin lesions masquerading as infection which clinically did not improve with antibiotics and further imaging and pathology findings helped steer the diagnosis towards PPP syndrome.

Case report

A 64-year-old male presented to the emergency department with purulent and painful nodular lesions on his lower extremities that first appeared 3 months ago. This was accompanied by polyarthralgia in his bilateral hips and shoulders. A diagnosis of erythema nodosum was made in the outpatient clinic, and he was started on glucocorticoids and ibuprofen without relief. The lesions became increasingly painful with purulent drainage which led him to seek care in the emergency department. The patient denied any fever, chills, rigor, or travel history. He had no history of autoimmune disease or malignancy. There was no past medical history or use of any chronic medications. The patient had a history of alcohol use averaging about ten standard drinks a week but denied smoking or illicit substance use. Family history was negative for autoimmune disorders or malignancy. He works in a casino as a security guard.

The patient was hospitalized due to concern about a possible infectious process. On evaluation, he was afebrile with normal vitals. Physical examination showed multiple nodules on bilateral lower extremities and a draining ulcer in the right heel. The lesion on the heel was tender and reddish-brown with purulent discharge. Other lesions were ulcerative with a necrotic floor and serosanguinous discharge.

Laboratory tests included an unremarkable complete blood count and basic metabolic profile, erythrocyte sedimentation rate of 75 mm/h (normal 0- 15 mm/h), C-reactive protein level of 5.7 mg/dL (normal <0.9 mg/dL), slightly elevated transaminases, and elevated lipase of 2328 U/L (normal 0-160 U/L). A lipase level was obtained due to the patient's history of chronic alcohol use and elevated inflammatory markers. A computed tomography scan of the abdomen showed acute pancreatitis with peripancreatic inflammatory changes and partial occlusion thrombosis of the portal and superior mesenteric veins (Fig. 1). Notably, the patient did not have any abdominal pain on presentation.

Gadolinium contrast MRI (Magnetic Resonance Imaging) of the right calcaneus showed findings concerning osteomyelitis (Fig. 2). Significant bone edema with surrounding soft tissue inflammation was seen on STIR (Short Tau Inversion Recovery) sequence (Fig. 3) and T2 FS (Fat saturated) sequence (Fig. 4). Due to the presence of bone marrow edema and periosteal separation of the cortex in the given clinical context, a diagnosis of osteomyelitis was made. He was started on piperacillin-tazobactam in the hospital for possible osteomyelitis. A superficial wound culture grew *Escherichia coli* and *Enterococcus faecalis* and the patient was discharged on oral amoxicillin and intravenous ertapenem. He continued his care at infectious disease and podiatry clinics for intravenous antibiotic infusions and wound care.

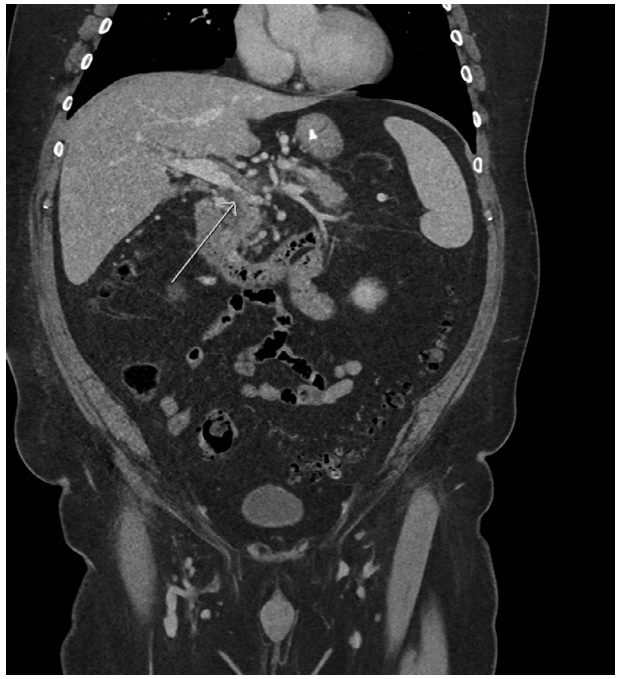

Fig. 1 – CT (Computed Tomography) of the abdomen (coronal view) showing pancreatitis with portal vein thrombosis (arrow).

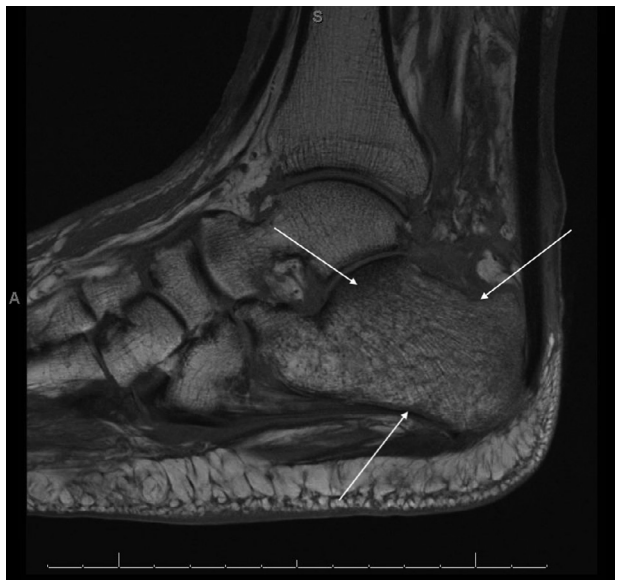

Fig. 2 – T1 MRI of right calcaneus (sagittal view) showing evidence of osteomyelitis.

After 6 weeks of antibiotics, the purulent discharge improved minimally, and there was no change in the size of the lesions. Therefore, ertapenem and amoxicillin were continued for another 6 weeks. Due to the nonresponse of lesions with the long course of broad-spectrum antibiotics, additional workup of the the nodular lesions was pursued. A biopsy of

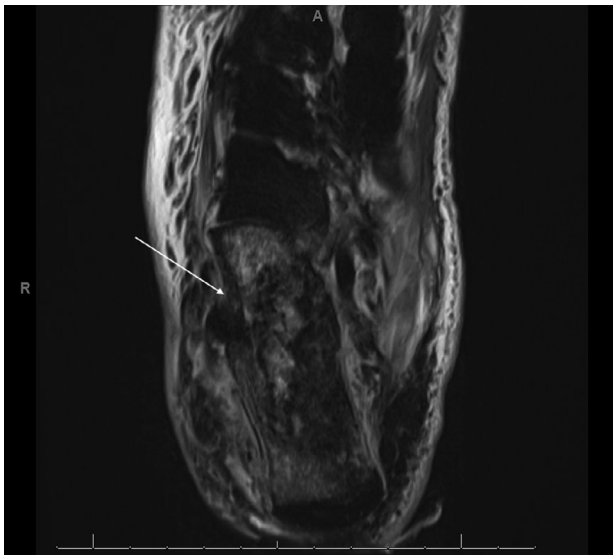

Fig. 3 – STIR MRI sequence of right calcaneus (coronal view) showing bone marrow edema and surrounding soft tissue edema.

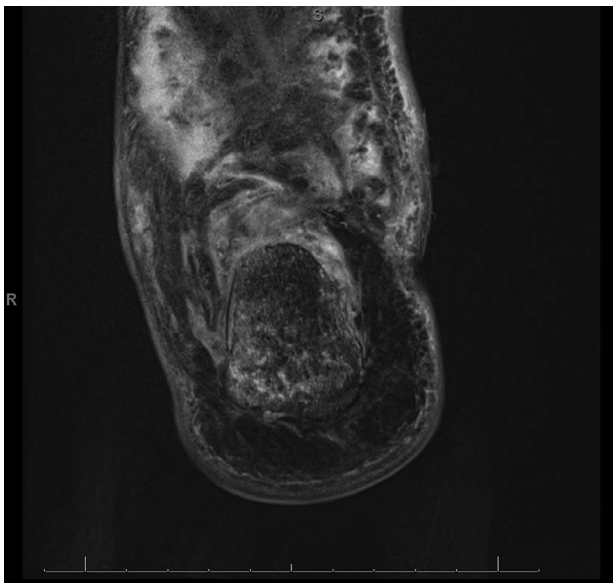

Fig. 4 – T2 FS (Fat Saturation) MRI sequence of right calcaneus (coronal view) suggesting osteomyelitis.

those lesions showed lobular panniculitis and ghost cells, suggesting pancreatic panniculitis (Fig. 5). This made the clinical team to make a diagnosis of pancreatitis, panniculitis and polyarthritis (PPP) syndrome.

After the diagnosis of PPP syndrome, antibiotics for the presumed osteomyelitis were stopped. The patient's lesions improved with regular wound dressings and podiatry follow-up. A decision was made not to pursue any surgical intervention, as the patient remained largely asymptomatic.

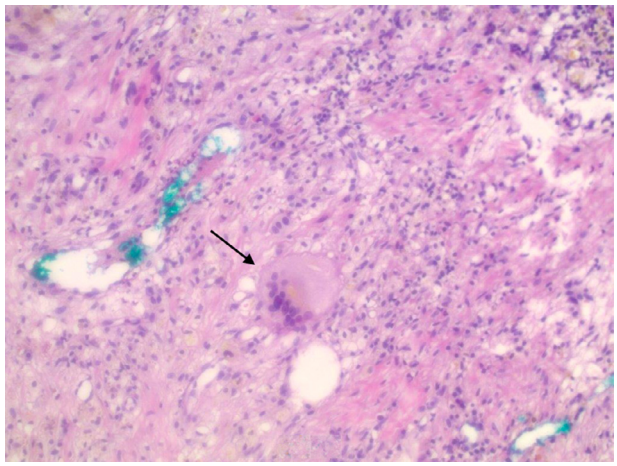

Fig. 5 – Multinucleated adipocyte termed as 'ghost cell' (arrow) in the background of inflammation suggesting pancreatic panniculitis; Hematoxylin and Eosin (H&E) stain, 10x20x (200x) magnification

Discussion

In the initial assessment, the patient met the necessary 2 of the 3 criteria for the diagnosis of pancreatitis including radiographic findings and an elevated lipase level. The likely cause of pancreatitis was chronic alcohol use. Initially, the findings of pancreatitis were not thought to be connected to the skin manifestations. He had painful, nodular, and purulent lesions, which were presumed to be erythema nodosum and were unsuccessfully treated as such. Then, an MRI led to the diagnosis of osteomyelitis, but treatment with antibiotics did not fully resolve the lesions. Subsequently, a biopsy of the nodular lesions showed lobular panniculitis and ghost cells which were pathognomonic for pancreatic panniculitis and suggested a connection with pancreatitis.

Hence, the cause of panniculitis and bone necrosis was likely due to the intravascular leakage of lipase due to PPP syndrome. Panniculitis is believed to be caused by the autodigestion of adipocytes in subcutaneous tissue by lipase. On biopsy of the skin lesions, the presence of ghost adipocytes is pathognomonic. Those cells are the adipocytes which have lost their nuclei and have thick shadowy walls due to coagulative necrosis by pancreatic enzymes [1,4]. The reactive bone changes are caused by circulating pancreatic enzymes and can be falsely diagnosed as osteomyelitis on imaging. Polyarthritis is due to the deposition of free fatty acids in joints that were released by fat autodigestion [4,5]. Although the lipase levels in the blood can be significantly elevated, patients usually present with no or mild abdominal symptoms. This could delay the diagnosis and recognition of pancreatitis.

This case highlights the importance of bone biopsy as the gold-standard diagnostic for osteomyelitis. It also reflects on the necessity of an interdisciplinary approach for a multisystem syndrome like PPP. In addition, it is important to

recognize that reactive changes on bone imaging could be seen in non-infectious pathologies, such as PPP syndrome and rheumatologic diseases, which could lead to unnecessary antibiotic use and possibly delay the diagnosis. Furthermore, in situations where osteomyelitis does not clinically improve with 4-6 weeks of systemic antibiotics, further workup such as bone biopsy should be considered before continuing treatment.

In other reported cases of PPP, management was focused on pancreatic pathology to reduce the translocation of lipase in the bloodstream and further systemic symptoms. NSAIDs and corticosteroids are usually ineffective in controlling skin inflammation. Along with surgical resection of fistulae, some cases have been treated with octreotide to decrease pancreatic stimulation, and plasmapheresis to clear out the circulating lipase [3,6,7].

For the evaluation of nodular skin lesions such as erythema nodosum, a broad differential including infections, inflammatory bowel disease, and malignancy should be considered. Diagnosis or further workup of rare disorders such as PPP should be considered after the exclusion of common etiologies. In this scenario, checking lipase and pancreatic imaging was essential in diagnosing pancreatitis and subsequently PPP syndrome. Additional case reports would further contribute to the knowledge of this rare disorder and would help clinicians better understand evolution of the disease and patient outcomes.

Patient consent

It is confirmed that a written informed consent for publication was obtained from the patient.

Author contribution

All authors had a role in writing the manuscript and had access to data.

REFERENCES

[1] Narváez J, Bianchi MM, Santo P, de la Fuente D, Ríos-Rodriguez V, Bolao F, et al. Pancreatitis, panniculitis, and polyarthritis. Semin Arthritis Rheum. 2010;39(5):417–23. doi:10.1016/j.semarthrit.2008.10.001.

[2] Fine Robert M. The fine page: subcutaneous fat necrosis, pancreatitis, and arthropathy. Int J Dermatol 1983;22(10):575–6. doi:10.1111/j.1365-4362.1983.tb02128.x.

[3] Dieker W, Derer J, Henzler T, Schneider A, Rückert F, Wilhelm TJ, et al. Pancreatitis, panniculitis and polyarthritis (PPP-) syndrome caused by post-pancreatitis pseudocyst with mesenteric fistula. Diagnosis and successful surgical treatment. Case report and review of literature. Int J Surg Case Rep 2017;31:170–5. doi:10.1016/j.ijscr.2017.01.037.

[4] Francombe J, Kingsnorth AN, Tunn E. Panniculitis, arthritis and pancreatitis. Rheumatology 1995;34(7):680–3. doi:10.1093/rheumatology/34.7.680.

[5] Dahl R, Su WP, Cullimore C, Dicken H. Pancreatic panniculitis. J Am Acad Dermatol 1995;33:413–17. doi:10.1016/0190-9622(95)91385-8.

[6] Mourad FH, Hannoush HM, Bahlawan M, Uthman I, Uthman S. Panniculitis and arthritis as the presenting manifestation of chronic pancreatitis. J Clin Gastroenterol 2001;32(3):259–61. doi:10.1097/00004836-200103000-00019.

[7] Francombe J, Kingsnorth AN, Tunn E. Panniculitis, arthritis and pancreatitis. Br J Rheumatol 1995;34(7):680–3. doi:10.1093/rheumatology/34.7.680.