A Man with Painful Lower Extremity Nodules, Pancreatitis and Polyarthritis

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Introduction
A triad composed of panniculitis, pancreatitis, and polyarthritis is termed in the literature as PPP syndrome. Pancreatic panniculitis is a rare form of subcutaneous fat necrosis associated with underlying pancreatic disease. The etiology of PPP syndrome remains unclear; however, it has been hypothesized that serum trypsin released from the damaged pancreas is responsible for enzymatic destruction of the surrounding subcutis and bone marrow. Patients typically present with mild to absent abdominal symptoms and coexisting joint pain, pitting edema, and subcutaneous nodules.

History
A 69-year-old Caucasian man presented with exquisitely painful nodules and marked edema of his bilateral lower legs. The nodules first appeared nine months ago and exhibited a waxing and waning course. His past medical history was significant for chronic pancreatitis of unknown origin, hypertension, gastroesophageal reflux disease, inflammatory arthritis, and hypercholesterolemia.

Examination
Physical examination revealed multiple 1-3 cm ill-defined, red to brown subcutaneous nodules on the bilateral lower legs and the right interomedial thigh. Marked erythema and edema of MCP and MTP joints, and bilateral ankles were observed. Diffuse 2+ pitting edema was present in the bilateral lower extremities.

Laboratory and Diagnostic Imaging
Laboratory results revealed increased amylase (5,250 U/L), lipase (9,197 U/L), ESR (94 mm/h), and CRP (93.5 mg/L). Triglycerides, ANA, and RF were within normal limits. CT scan of the left ankle revealed cortical bony erosion of the calcaneus. Abdominal ultrasound revealed a solitary pseudocyst with coexisting pancreatic ductal dilation.

Histopathology
Punch biopsy of a nodule on the right leg revealed extensive lobular and septal liquefactive adipocyte necrosis with scattered neutrophils and lymphocytes. Aggregates of fine granular basophilic material were observed with prominent adipocyte degeneration and calcification.

Course and Therapy
The patient underwent a pancreaticoduodenectomy (Whipple procedure) with significant improvement in his pancreatic enzymes, lower extremity subcutaneous nodules, and arthritis. He is currently being followed by rheumatology and internal medicine.

Discussion
A triad of pancreatic panniculitis, pancreatitis, and polyarthritis describes an extremely rare entity known as PPP syndrome. Currently, only 25 well-documented cases exist in the literature. Pancreatic panniculitis is a rare form of subcutaneous fat necrosis associated with underlying pancreatic disease. Pancreatic panniculitis has been found in roughly 2-3% of patients with acute or chronic pancreatitis, and pancreatic carcinoma (acinic cell type). Joint disease has been reported in 54-80% of cases, most commonly involving the ankles, knees, wrists, and MTP joints of the hands.

Pancreatic panniculitis in the setting of PPP syndrome commonly presents with ill-defined, red-brown, exquisitely tender, edematous subcutaneous nodules on the lower legs. The subcutaneous nodules may spontaneously ulcerate and exude oily, viscous material as a result of the liquefactive necrosis of adipocytes. Patients with PPP syndrome typically present with mild to absent abdominal symptoms and coexisting joint pain, pitting edema, and subcutaneous nodules.

The exact pathogenesis of PPP syndrome remains unclear. It has been hypothesized that serum trypsin released from the damaged pancreas is responsible for damage to the surrounding subcutis and bone marrow. Intramuscular fat necrosis is responsible for the development of multiple osteolytic bone lesions and endosteal erosions seen on plain radiographs and CT scans. Needle aspiration of the arthritic joints often yields yellow, viscous, purulent fluid with lipid crystals and elevated lipase levels.

Histopathologic findings of pancreatic panniculitis demonstrate lobular subcutaneous inflammation with liquefactive necrosis of adipocytes in the subcutis, leading to the characteristic appearance of “ghost adipocytes”. Ghost adipocytes are cells with absent nuclei containing fine basophilic homogenous material in the presence of fat saponification.

Treatment of PPP syndrome is largely supportive, with a focus on correcting the underlying pancreatic disease. NSAIDs, corticosteroids, and octreotide have been utilized with minimal effectiveness. Plasmapheresis is an effective treatment option in patients with persistent hyperamylasemia and hyperlipasemia. Often reserved for severe rectoracy disease, a cholecystectomy and/or a pancreatic duct removal have demonstrated success in the management of chronic pancreatitis and panniculitis.

Conclusion
PPP syndrome is an extremely rare diagnosis composed of a triad of pancreatic panniculitis, pancreatitis, and polyarthritis. Adjuvant therapies for PPP syndrome, such as NSAIDs, corticosteroids, plasmapheresis and octreotide, have been used, but definitive treatment requires correction of the primary pancreatic disorder. More importantly, the diagnosis of pancreatic panniculitis could be an early indicator of an occult pancreatic malignancy and should prompt early evaluation with a multidisciplinary approach.

References