CASE REPORT

Pancreatic panniculitis and polyarthropathy due to undifferentiated pleomorphic sarcoma

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Key words: pancreatic panniculitis; pancreatic panniculitis with polyarthritis; pancreatic sarcoma; PPP syndrome; soft tissue sarcoma; undifferentiated pleomorphic sarcoma.

INTRODUCTION

Pancreatic panniculitis is a rare cutaneous manifestation occurring in 0.3%-3% of patients with pancreatic diseases.1 The most common underlying etiology is pancreatitis, making up approximately 88% of cases, while pancreatic neoplasms account for the remaining 12%.2 Tender erythematous nodules localized to the lower extremities is the most common presentation. Extracutaneous findings include arthropathy, eosinophilia, osteolytic bone lesions, and serositis.3 When pancreatitis, panniculitis, and polyarthritis occur simultaneously (PPP), this triad is termed PPP syndrome. Herein, we present a patient with pancreatic panniculitis with polyarthropathy secondary to primary pancreatic undifferentiated pleomorphic sarcoma (UPS).

CASE REPORT

An 18-year-old male presented with a 2-week history of intermittent fever, arthralgias, lower extremity edema, and pretibial violaceous subcutaneous nodules. Past medical history was significant for childhood asthma. He denied any pertinent sexual activity, recent travel, or associated upper respiratory, gastrointestinal, or urinary symptoms. All immunizations were up to date. Previous treatment included a 5-day course of oral prednisone.

Physical examination revealed joint tenderness involving the upper and lower extremities without warmth, erythema, weakness, or reduced range of motion. Multiple tender dusky subcutaneous nodules were present along the bilateral anterolateral lower extremities (Fig 1) with pitting edema. Laboratory evaluation revealed an elevated white blood cell count without eosinophilia, erythrocyte sedimentation rate, C-reactive protein, aspartate aminotransferase, alanine transaminase, total bilirubin, and lipase (9754 U/L; 11-82 U/L). Rheumatologic workup was notable for positive antinuclear antibodies and immunoglobulin G subclass 4 and negative rheumatoid factor, antineutrophil cytoplasmic antibodies, angiotensin converting enzyme, anti-cyclic citrullinated peptide, carcinoembryonic antigen, smooth muscle, antimitochondrial, and double stranded-DNA antibodies. Extensive infectious workup was negative.

A punch biopsy of a lower extremity nodule revealed an unremarkable epidermis and superficial dermis and a mixed inflammatory cell infiltrate with fibrosis within the deeper dermis. Within the subcutaneous fat, ghosts of lipocytes within adipose lobules surrounded by basophilic material and a mixed inflammatory cell infiltrate are present, consistent with pancreatic panniculitis (Fig 2).

Chest x-ray and computed tomography angiography of the chest and neck were negative. Abdominal computed tomography identified a pancreatic mass while magnetic resonance...
cholangiopancreatography confirmed a 5.1 cm × 6.8 cm complex lesion within the mid-pancreatic body. Ultrasound guided fine needle aspiration of the pancreatic mass demonstrated spindle cells with marked nuclear pleomorphism and mitotic figures. Immunohistochemistry was positive for S100 with patchy CD34 positivity and negative for SOX10, c-KIT, SMA, and desmin. Additionally, SARM1-NTRK1 gene fusion was identified. These findings were consistent with a high-grade undifferentiated pleomorphic pancreatic sarcoma. The patient was initiated on chemotherapy with doxorubicin-phosphate and pazopanib in addition to targeted larotrectinib therapy. Surgical resection was unable to be performed due to local inflammation and surrounding vasculature. No metastasis was present at 6 months.

**DISCUSSION**

Pancreatic panniculitis presents as firm, tender nodules that may be more easily palpated than visualized. In nearly half of cases, cutaneous findings precede abdominal or pancreatic symptoms, underscoring the importance of cutaneous recognition.2 PPP syndrome can occur at any age but is most associated with middle-aged men with a history of alcohol abuse.1 This case is uncharacteristic in that our patient was younger and PPP syndrome was associated with primary pancreatic UPS. The mortality rate of PPP syndrome when associated with pancreatic cancer is 74%.5,6 Fortunately, our patient has no observed metastasis and continues to undergo chemotherapy.

The etiology of pancreatic panniculitis and PPP syndrome remains unclear; however, it is believed that pancreatic damage leads to the release of pancreatic enzymes, which increases the permeability of the microcirculation within lymphatic vessels.2,4 It is important to note that the degree of lipase elevation does not necessarily indicate disease severity, but may correlate with the degree of extra-pancreatic symptoms. Arthritis in PPP syndrome may be caused by hydrolysis of triglycerides by pancreatic enzymes, which releases free fatty acids into joint spaces.7 As observed in our patient, about 70% of pancreatic panniculitis and PPP syndrome cases demonstrate mild or absent abdominal symptoms.6 In comparison, polyarthralgia when present may be severe and debilitating.2 Joint involvement presents as symmetric or asymmetric polyarthritis, most commonly involving the ankles, knees, wrists, and metacarpophalangeals.4,5 The clinical differential diagnosis of pancreatic panniculitis and PPP syndrome includes erythema nodosum, which is associated with arthralgias in half of all cases, nodular vasculitis, Weber–Christian disease, alpha 1-antitrypsin deficiency, lupus profundus, erythema induratum, infection, and other panniculitides.1,3 Pancreatic panniculitis can be differentiated from these histologically, displaying the characteristic ghost-like necrotic adipocytes, which are absent in other forms of panniculitis.

The treatment of pancreatic panniculitis is supportive, with resolution observed upon treatment of the underlying pancreatic process. Corticosteroids,

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**Fig 1.** Multiple violaceous subcutaneous nodules can be seen on the bilateral shins.

**Fig 2.** Hematoxylin–eosin staining shows sections of basket-weave stratum corneum with an inflammatory dermal infiltrate (A, magnification ×4), and characteristic ghosts of lipocytes within adipose lobules surrounded by basophilic material and a mixed inflammatory cell infiltrate (B, magnification ×20), shown in higher power in (C, magnification ×40).
non-steroidal anti-inflammatory drugs, and immunosuppressive agents are often utilized but are ineffective at treating the skin nodules and arthritis associated with PPP syndrome.4

Pancreatic sarcomas account for less than 1% of all tumors arising from the pancreas, with primary pancreatic UPS being exceptionally rare. There have only been 22 reported cases of primary pancreatic UPS in the medical literature, including this case. Among the previously reported cases, there was a strong male predominance with an average age of diagnosis of around 55 years.8 To our knowledge, this patient is the youngest reported case.

The most common presenting symptom of pancreatic UPS is epigastric pain, in addition to nausea, vomiting, weight loss, and abdominal mass.8,9 Diagnostic workup for primary pancreatic UPS typically involves an abdominal computed tomography revealing a heterogeneous mass with calcifications and necrosis.9 Histopathology evaluation is essential for diagnosing UPS and reveals atypical pleomorphic spindle cells.8-10 Definitive diagnosis requires immunohistochemical exams to exclude other malignancies.10 Radical resection is the mainstay of treatment for retroperitoneal sarcomas, including primary pancreatic UPS. Adjuvant therapeutic options include radiotherapy and chemotherapy with doxorubicin and ifosfamide.9

This case represents a rare neoplasm associated with pancreatic panniculitis and PPP syndrome uncharacteristically occurring in a young patient with pancreatic UPS. Minimal presenting symptomatology underscores the importance of awareness for early diagnosis.

Conflicts of interest
None disclosed.

REFERENCES
1. Preiss JC, Fais S, Loddenkemper C, et al. Pancreatic panniculitis in an 88-year-old man with neuroendocrine carcinoma. Diges- tion. 2002;66(3):193-196. https://doi.org/10.1159/000066758
2. Zundler S, Strobel D, Manger B, et al. Pancreatic panniculitis and polyarthritis. Curr Rheumatol Rep. 2017;19(10):62. https://doi.org/10.1007/s11926-017-0690-4
3. Curtan RT, Wesche WA, Jenkins JJ 3rd, et al. A fatal case of pancreatic panniculitis presenting in a young patient with systemic lupus. J Cutan Pathol. 2000;27(9):466-471. https://doi.org/10.1034/j.1600-0560.2000.027009466.x
4. García-Romero D, Vanaclocha F. Pancreatic panniculitis. Dermatol Clin. 2008;26(4):465-470. vi. https://doi.org/10.1016/j.det.2008.05.009
5. Narváez J, Bianchi MM, Santo P, et al. Pancreatitis, panniculitis, and polyarthritis. Semin Arthritis Rheum. 2010;39(5):417-423. https://doi.org/10.1016/j.semarthrit.2008.10.001
6. Arbeláez-Cortés A, Vanegas-García AL, Restrepo-Escobar M, et al. Polyarthritis and pancreatic panniculitis associated with pancreatic carcinoma: review of the literature. J Clin Rheumatol. 2014;20(8):433-436. https://doi.org/10.1097/RHU.0000000000000181
7. Dieker W, Derer J, Henzlter T, 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;31:170-175. https://doi.org/10.1016/j.jscr.2017.01.037
8. Sanei B, Kefayat A, Samadi M, et al. Undifferentiated pleomorphic sarcoma of pancreas: a case report and review of the literature for the last updates. Case Rep Med. 2018;2018: 1510759. https://doi.org/10.1155/2018/1510759
9. Liang Z, Han J, Tuo H, et al. Undifferentiated pleomorphic sarcoma of the pancreas: a rare case report and literature review. World J Surg Oncol. 2022;20(1):55. https://doi.org/10.1186/s12957-022-02525-1
10. Robles-Tenorio A, Solis-Ledesma G. Undifferentiated pleomorphic sarcoma. In: StatPearls. StatPearls Publishing; 2022.