**CASE REPORT**

**Pancreatic panniculitis in a pancreas–kidney transplant patient resolved after immunosuppression increase: Case report and review of literature**

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**Key words:** allograft rejection; pancreatic panniculitis; transplant patient.

**INTRODUCTION**

Panniculitides are a group of conditions characterized by inflammation of subcutaneous fat.1 Pancreatic panniculitis is a rare lobular panniculitis that appears in roughly 2% to 3% of patients with pancreatic diseases, such as pancreatitis and pancreatic carcinoma. Less commonly, pancreatic panniculitis has been reported in transplant patients in association with acute kidney or pancreas allograft rejection.2-5 Patients often present with tender erythematous nodules, which may drain an oily substance, on the distal lower extremities. Associated symptoms may include acute arthritis, necrosis of abdominal or bone marrow fat, pleural effusions, mesenteric thrombosis, leukemoid reaction, and eosinophilia. The pathogenesis is hypothesized to involve release of pancreatic enzymes, such as lipase, from the inflamed pancreas into the portal and lymphatic circulation and subsequently deposited in distant sites where they hydrolyze subcutaneous fat.

**CASE REPORT**

A 34-year-old African-American woman with a history of a simultaneous pancreas–kidney transplant 6 years prior for complications of type I diabetes mellitus and a rejected kidney allograft presented to dermatology clinic with painful nodules on her bilateral shins of 2 weeks’ duration. She denied taking new medications, fever, abdominal pain, arthralgia, or other systemic symptoms. She was on a stable immunosuppressive regimen of cyclosporine, 75 mg twice daily, and prednisone, 7.5 mg daily. On examination she was afebrile with normal vital signs. She had multiple violaceous, tender, deep 4- to 6-cm nodules scattered over the anterior portion of her shins bilaterally (Fig 1).

A deep 4-mm punch biopsy with ample subcutaneous tissue was performed from the center of a nodule on her left lateral shin. Histologic examination found septal panniculitis and an area of enzymatic fat necrosis with ghost cells and a neutrophilic infiltrate (Fig 2).

Based on clinicopathologic correlation, a diagnosis of pancreatic panniculitis in the setting of a pancreas transplant patient was made. The transplant team was immediately contacted, and laboratory data were ordered, which showed an elevated serum lipase of 2893 U/L (baseline, 130-300 U/L), elevated serum amylase of 650 U/L (baseline, 70-300 U/L), and undetectable cyclosporine level at less than 30 ng/mL (baseline, 40-100 ng/mL). Quantitative polymerase chain reaction result for serum cytomegalovirus (CMV) DNA was negative, ruling out a potential etiologic agent for acute allograft pancreatitis.6

The patient's cyclosporine was increased from 75 mg twice daily to 100 mg twice daily with close outpatient follow-up. After 1 week, her cyclosporine level was 131 ng/mL, and her lipase and amylase levels were down trending (Fig 3). By 8 weeks her lipase and cyclosporine levels were at baseline, and the shin nodules resolved without scarring.

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DISCUSSION

We present a case of pancreatic panniculitis in a female pancreas–kidney transplant recipient 6 years posttransplant on standard immunosuppressive medications. The diagnosis of allograft pancreatitis and rejection presenting with pancreatic panniculitis was supported clinically, histopathologically, and by laboratory data. Although biopsy of the patient’s pancreas allograft was not performed, acute allograft rejection is supported empirically by the patient’s dramatic increase in serum lipase and amylase coinciding with undetectable cyclosporine levels. In addition, increase of her immunosuppressive medications was correlated with rapid normalization of lipase and amylase levels, an elevation of cyclosporine serum level to the therapeutic range, and resolution of panniculitis.

A review of literature shows that this is the sixth reported case of pancreatic panniculitis occurring in a transplant recipient and the second in a simultaneous pancreas–kidney transplant recipient (Table I).2-5,7 The previous 5 cases occurred from 1996 to 2010, during which period on average more than 800 simultaneous kidney–pancreas, more than 10,000 kidney, and several hundred pancreas transplants were performed annually in the United States,8 illustrating the rarity of reported pancreatic panniculitis in a transplant patient. Furthermore, it is one of the first few cases associated with allograft rejection. In the 5 previously reported cases, all patients were 30 to 40 years of age, and 4 of the 5 patients were women. Similar to our patient, all 5 patients presented with classic painful, deep nodules on the legs, and all but one lacked significant abdominal symptoms at initial presentation. Reported timeframe of presentation of cutaneous symptoms ranged from 3 to 21 months posttransplant. Acute pancreatitis was diagnosed in all 5 patients, and all required hospitalization. The transplanted organ was biopsied in 3 patients, the results of which showed acute allograft organ rejection; the patients responded well to increased immunosuppression. One patient had pancreatitis diagnosed secondary to medication and improved after medication cessation. Imaging results corroborated clinicopathologic findings in 4 cases. In the earliest reported case, the patient died with a hemorrhagic and necrotic pancreas 1 month after admission. The other 4 patients survived, with normalization of laboratory values or imaging confirmation of resolved inflammation within 3 weeks to 6 months.

Our case is notable in 2 aspects. Our patient presented with pancreatic panniculitis 6 years after her organ transplant, which is the longest posttransplant presentation among the reported cases. Second, our patient was treated exclusively in the outpatient setting and responded rapidly to increased immunosuppression, negating the need for invasive or expensive testing; all 5 previously reported patients required hospitalization. Our case therefore illustrates that prompt diagnosis of cutaneous manifestations of pancreatic panniculitis in a transplant patient and coordination with the patient’s transplant team can lead to successful outpatient treatment.

Dermatologists should therefore be aware of characteristic painful erythematous nodules, elevated serum pancreatic enzyme levels, and possible associated symptoms such as arthralgias as important clinical clues for pancreatic panniculitis. Although abdominal symptoms and fever are present in most pancreas transplant patients presenting with acute graft pancreatitis,9 our case and
A review of literature shows that when transplant patients present with pancreatic panniculitis, abdominal symptoms are generally absent. Furthermore, cutaneous lesions may be the presenting symptoms in 40% of overall patients with pancreatic disease (acute and chronic pancreatitis, pancreatic carcinoma) and may precede abdominal symptoms by 1 to 7 months. Histopathologic findings of pancreatic panniculitis include a lobular panniculitis initially and septal panniculitis later in the course, with pathognomonic “ghost cells,” which represent coagulative necrosis of adipocytes resulting in anucleated adipocytes with thickened, shadowy cell membranes. Treatment for pancreatic panniculitis is mainly directed at managing the underlying pancreatic disease.

We present this case to highlight several important clinical aspects. First, when pancreatic panniculitis is seen in a pancreas transplant patient, organ rejection should be strongly considered as the underlying etiology. Second, dermatologic manifestations are often the first sign, and abdominal pain classically associated with pancreatitis is usually absent. Finally, close communication between subspecialties allowed this patient to be treated exclusively in the outpatient setting, which was advantageous to the patient and cost saving to the health care system.

**Fig 3.** Increase of cyclosporine was correlated with rapid normalization of lipase and amylase levels.

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| Case                  | Patient Details                        | Transplanted Organ(s) | Onset of symptoms posttransplant | Immunosuppression | Cutaneous findings | Abdominal symptoms before onset of lesions | Abdominal symptoms after onset of lesions | Serum pancreatic enzyme levels |
|-----------------------|---------------------------------------|-----------------------|----------------------------------|-------------------|-------------------|------------------------------------------|------------------------------------------|---------------------------------|
| Langeveld-Wildschut et al 1996 | 40 yo F, mesangiocapillary glomerulonephritis | K                     | AZA, CsA, PRED                   | Multiple erythematous nodes on lower legs | Right lower quadrant distension | Not reported                          | Elevated AMY, LIP               |
| Wang et al 2000       | 34 yo M, chronic glomerulonephritis   | K                     | AZA, CsA, CST                    | Painful nodules on legs | None              | Pain, vomiting                          | Elevated AMY, LIP               |
| Echeverria et al 2001 | 42 yo F, SLE                           | K                     | AZA, CsA, PRED                   | Painful nodules on legs | None              | None                                     | Elevated AMY, LIP               |
| Pike et al 2006       | 49 yo F, chronic kidney insufficiency, DM I | SPK                   | CsA, PRED, MMF                   | Painful nodules on knees and lower legs | None              | None                                     | Elevated AMY, LIP               |
| Prikis et al 2010     | 40 yo F, DMII                         | PAK                   | MMF, PRED, TAC                   | Painful nodules on legs and feet | None              | None                                     | Elevated AMY, LIP               |
| Current study         | 34 yo F, DMII                         | SPK                   | CsA, PRED                        | Painful nodules on legs | None              | None                                     | Elevated AMY, LIP               |

AMY, Amylase; AZA, azathioprine; CMV, cytomegalovirus; CsA, cyclosporine; CST, corticosteroid; CT, computed tomography; DMII, diabetes mellitus type II; K, kidney; LIP, lipase; MMF, mycophenolate mofetil; PAK, pancreas after kidney; PRED, prednisone; SLE, systemic lupus erythematosus; SPK, simultaneous pancreas—kidney; TAC, tacrolimus; U/S, ultrasound scan.
| Other findings                                      | Treatment setting | Prior transplanted organ history | Transplanted organ status during episode | CMV infection | Diagnosis                                      | Treatment                                      | Outcome                                                                                      |
|----------------------------------------------------|-------------------|--------------------------------|------------------------------------------|---------------|-----------------------------------------------|-----------------------------------------------|---------------------------------------------------------------------------------------------|
| Inpatient                                          |                   |                                |                                          |               |                                               |                                               | Patient died with hemorrhagic and necrotic pancreas 1 mo after admission                  |
| U/S and CT of kidney showed urinoma                | Inpatient         | Not reported                    | Biopsy proven acute renal allograft rejection | Acute CMV viremia | Acute pancreatitis possibly secondary to medication or CMV in setting of acute renal graft rejection and CMV infection | Ganciclovir, OKT3 | Lab values normalized after 3 weeks, commenced hemodialysis therapy for irreversible kidney graft failure |
| Fever, malar telangectasia, tender cervical lymphadenopathy, right lobe hepatomegaly, bilateral acute ankle arthritis, CT shows pancreatic enlargement | Inpatient         | History of chronic kidney rejection | Kidney not biopsed | History of CMV chorioretinitis, was not checked during episode | Acute pancreatitis secondary to medication (AZA and CsA) |                                      |                                                                                             |
| Elevated creatinine, CT evidence of allograft pancreatitis | Inpatient         | Not reported                    | Biopsy-proven moderate acute cellular renal allograft rejection | Not present during episode (negative pp65) | Acute pancreatitis in setting of biopsy proven kidney allograft rejection and presumed acute pancreas allograft rejection | Dexamethasone, switched CsA to TAC; MMF tripled; started thymoglobulin then OKT3 | MR imaging back to baseline after 2 months; allograft pancreatectomy after 17 months; no residual exocrine pancreas function; has foci of residual B-islets Good graft function 2 years later |
| CT evidence of allograft pancreatitis              | Inpatient         | Previously treated for acute renal and panc rejection, CMV viremia | Biopsy proven severe acute pancreas allograft rejection | Prior history but not present during episode (checked) | Acute pancreatitis in setting of pancreatic allograft rejection | Octreotide, high dose steroids, plasmapheresis, intravenous immunoglobulin, rituximab |                                                                                             |
| Undetectable CsA level                             | Outpatient        | Rejected kidney allograft s/p nephrectomy | Pancreas not biopsy | Not present (checked) | Acute pancreatitis in setting of presumed pancreatic allograft rejection | Increase CsA | Symptoms resolved over 2 months; allograft pancreas failure 5 months later                  |