An unreported case of pancreatic panniculitis in a liver transplant patient

María Anders,1 Virginia Mariana González,2 Juan Ruiz,3 Gabriel Casas,4 Nicolás Goldaracena,1 Federico Orozco,1 Florencia Antinucci,1 Margarita Larralde,2 Hugo Catalano,3 Emilio Quiñonez,1 Lucas McCormack,1 Ricardo Mastai1

1Liver Transplant Unit.
2Department of Medicine, Dermatological Division.
3Department of Medicine, Internal Medicine Division.
4Department of Pathology.
Hospital Alemán, Ciudad Autónoma de Buenos Aires, Argentina.

Acta Gastroenterol Latinoam 2014;44:239-242

Correspondencia:
Ricardo Mastai
Unidad de Trasplante – Hospital Alemán
Tel: (0054-11) 4827-7000 / Fax: (0054-11) 4827-7014
E-mail: rmastai@hospitalaleman.com

Summary
Pancreatic panniculitis is an uncommon condition that can occur in association with pancreatic disease. Most of the cases reported to date were associated with acute or chronic pancreatitis and pancreas cancer. Recently, development has been described in kidney transplant patients and secondarily to allograft pancreatitis in a pancreas-kidney transplant recipient. Both findings suggest that immunological processes may be involved in the pathogenesis of this entity. We report for the first time a case of acute pancreatitis associated with pancreatic panniculitis in a patient who underwent a liver transplant 10 months before. A 69-year-old man with a history of epigastric pain of a few days of evolution was presented with painful subcutaneous nodules on both legs. Blood chemistry showed raised serum amylase and lipase levels. Ultrasoundography and multislice CT scan were suggestive of an acute pancreatitis. A skin biopsy showed typical features of pancreatic panniculitis which included lobular panniculitis with lipocyte degeneration and ghost cells. The administration of octreotide resulted in both a rapid improvement of symptoms and a disappearance of skin lesions. Liver transplant specialists should be aware that the pancreatic panniculitis could be a manifestation of pancreas disease in patients who have undergone liver transplantation.

Key words. Pancreatic panniculitis, liver transplant, acute pancreatitis, ghost cells, lipocyte degeneration.

Paniculitis pancreática: reporte de un caso en un paciente trasplantado hepático

Resumen
La pancitulitis pancreática es una condición poco frecuente que puede presentarse en asociación con enfermedades pancreáticas. La mayoría de los casos reportados a la fecha se asociaron con pancitulitis aguda o crónica, o cáncer. Recientemente, se ha descrito la enfermedad en el contexto del trasplante renal y en forma secundaria a pancitulitis del injerto en receptores de trasplante renao-pancreático. Ambos hallazgos sugieren que podrían estar involucrados procesos inmunológicos en la patogénesis de esta entidad. Se presenta por primera vez un caso de pancitulitis aguda asociada a pancitulitis pancreática en un paciente trasplantado hepático diez meses antes del diagnóstico. Se trata de un hombre de 69 años de edad, con una historia de dolor epigástrico de unos pocos días de evolución que se presentó a la guardia con nódulos subcutáneos dolorosos en ambas piernas. Los estudios de laboratorio demostraron elevación de amilasa y lipasa en sangre. La ecografía y la tomografía computarizada multislice fueron sugestivos de pancitulitis aguda. Se realizó una biopsia de piel que demostró lesiones típicas de pancitulitis pancreática como pancitulitis lobular, degeneración lipócítica y células fantasma. Con la administración de octreotide el paciente presentó mejoría de los síntomas con desaparición de las lesiones cutáneas. Se sugiere que los médicos especialistas en trasplante hepático deben ser conscientes de que la pancitulitis puede ser una manifestación dermatológica de enfermedad pancreática.

Palabras claves. Pancitulitis pancreática, trasplante hepático, pancitulitis aguda, células fantasma, degeneración lipócítica.
Panniculitis, a group of diseases whose hallmark is inflammation of subcutaneous adipose tissue, is a rare complication in the setting of pancreatic disease.\(^1\)\(^,\)\(^2\) The exact pathogenic mechanism of pancreatic panniculitis is still unknown, but release of pancreatic enzymes, such as lipase, trypsin and amylase may be involved.\(^2\)\(^,\)\(^3\)

Few cases of pancreatic panniculitis in renal and pancreas-kidney transplant recipients have been reported in the literature.\(^4\)\(^-\)\(^6\) However, to our knowledge, this is the first reported case after liver transplantation. We describe the case of a 69-year-old man who underwent liver transplantation with pancreatic panniculitis which we believe was secondary to acute pancreatitis. Recent literature is reviewed to further familiarize the transplant specialist with this unique presentation.

**Case report**

A 69-year-old man with a longstanding history of chronic liver disease received a liver transplant in July 2010. The patient’s postoperative course was normal and he was discharged on the 9th day of transplantation. In May 2011, 10 months post-transplantation, he was admitted to our hospital because of a few days history of a pain in the right knee and ankle, associated with painful erythematous nodules (Figure 1). The patient had a severe discomfort, which made him unable to walk. He also noticed the appearance of red elevated skin lesions over both legs. He gave a history of a mild, nonspecific epigastric pain. His abdomen was soft and non-distended, and he had no abdominal pain. A complete blood count was within normal limits and his blood chemistry revealed a moderate increase in aspartate aminotransferase levels (111 U/L) and alanine aminotransferase levels (95 U/L).

The patient’s amylase and lipase levels were both significantly elevated at hospital admission.

A marked deterioration of renal function was also observed. At the time of admission, the patient’s immunosuppressive medications included tacrolimus and sodyc mycofenolic acid. Ultrasound of the abdomen ruled out biliary compromise. Computed tomography scan of the abdomen showed stranding around the pancreas consistent with acute pancreatitis. The magnetic resonance cholangiopancreatography was normal. One week after, some subcutaneous nodules became fluctuant and drained a brown, viscous, sterile fluid (Figure 2). A skin biopsy of a right medial ankle nodule was taken demonstrating lobular panniculitis with prominent fat necrosis, neutrophilic cell infiltration and the presence of leukocytoclastic granular basophilic debris and numerous ghost cells (Figure 3). Based on previous studies suggesting that octreotide may have a role in the treatment of pancreatitis, a single dose of 20 mg of long-acting octreotide was used.\(^7\)

Since pain was the predominant and disabling symptom of the patient, pain intensity was assessed daily before and during the treatment with octreotide. A scale of 0 to 10 was employed in the medical history. Criteria for maximal scoring\(^10\) was pain that interfered with sleep, inability to evaluate the damaged area and need to increase the amount of analgesics. A full response to treatment was defined as the complete lack of pain, and a partial response as 50% reduction in the pain score. The onset of beneficial effect was two days, a partial response was observed between day three and seven, and the pain disappeared completely after this period. The skin lesions were improved in parallel,
disappearing within the first month after starting specific treatment. The administration of octreotide was well tolerated and not associated with serious adverse effects.

**Discussion**

Pancreatic panniculitis is a rare condition occurring in 0.3% to 3% of patients in the setting of pancreatic disease, in which fat necrosis occurs in subcutaneous tissue and elsewhere.1-3 The pancreatic disorders most commonly associated with pancreatic panniculitis are alcohol-related acute and chronic pancreatitis. It is also associated with cancers of the pancreas, usually of acinar cell type.9 Moreover, pancreatic panniculitis can be associated with pancreas divisum, pancreatic pseudocysts, vesiculo-pancreatic fistula and COX-2 inhibitor intake.10 Our case is relevant for two reasons: the development of a dermatological complication first described in a patient with liver transplantation as well as the excellent response to treatment with octreotide, a long-acting analogue of somatostatin.

The exact pathogenic mechanism of pancreatic panniculitis is still unclear, but release of pancreatic enzymes, such as lipase, phosphorylase, trypsin and amylase, may be involved. Moreover, the activity of these enzymes may cause a syndrome called lobular panniculitis with focal necrosis of lipids and a concomitant inflammatory reaction. In the skin, it is characterized by inflamed-appearing nodules and pustules on an erythematous base.1-3 Despite the high frequency, about 50% of the development of acute arthritis was not observed in our patient, and neither serositis (ascites, pleural effusion or pericardial effusion).

At the time of patient admission to hospital the main differential diagnosis to consider at the onset of erythematous nodules on the lower extremities of an immunocompromised patient included erythema nodosum, erythema induratum of Bazin or infectious panniculitis. Therefore, a skin biopsy was performed immediately. The histopathological findings were found pathognomic of pancreatic panniculitis. A particularly unique aspect was the foci of anucleated adipocytes with thickened, shadowy cell membranes known as “ghost cells” within the affected fat lobules. Surrounding these groups of clusters was observed a polymorphus inflammatory cell infiltrate consisting of neutrophils, lymphocytes, macrophages and foreign-body giant cells.

Until now, there is no particular treatment for pancreatic panniculitis other than treatment of the underlying pancreatic disease.1-3 Symptomatic treatment may include support stockings, leg elevation and bed rest since the subcutaneous nodules tend to develop on the lower extremities most commonly.1-3 In our patient, the evidence for pancreatic enzyme release inducing panniculitis is further reinforced by the beneficial effect of the somatostatin analogue octreotide, a drug that shows mixed results. In a patient with pancreatic carcinoma a rapid improvement of symptoms after octreotide was observed.13 However, these positive results have not been reproduced in other patients.14-15 When this treatment was administered, a significant resolution of symptoms was observed in a few days. Moreover, the clinical picture in our case was correlated with pancreatic enzyme levels. In this case, resolution of the panniculitis occurred concomitantly with transplantation.12 In this regard, cases of pancreatic panniculitis in renal transplant alone have been reported in the literature.4 None of these patients were undergoing acute renal allograft rejection at the time of the presentation. On the contrary, the development of pancreatic panniculitis secondary to allograft pancreatitis in a pancreas-kidney transplant recipient has been more recently shown.4,6 In both cases the allograft pancreatitis was associated with acute pancreas rejection. These findings are important for clinicians to recognize in these events an expression of dermatological manifestations of pancreas disease including allograft pancreatitis and acute rejection.

Our patient presented with pancreatic panniculitis with tender and erythematous nodules. Nodules have also been reported on the buttocks, trunk, and upper extremities and scalp.1-3 As previously described, in the patient nodules ulcerate and drain a sterile, oily material.1-3
disease regression during the pharmacological treatment, suggesting that effective management of acute pancreatitis induces regression of panniculitis.

In conclusion, we present a unique case of pancreatic panniculitis in a liver transplant patient. Although exceptional, the development of panniculitis should alert us of the presence of some type of pancreatic damage. This case also illustrates the diagnostic challenges of such cases and the need for clinical and pathologic correlation in order to facilitate timely and accurate diagnosis and initiate appropriate treatment.

Disclosure. The authors of this manuscript have no conflicts of interest to disclose and no funding.

References