Case Report

Acute allograft pancreatitis associated with renal allograft rejection

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Introduction

Acute allograft pancreatitis is common following simultaneous pancreas and kidney (SPK) transplantation with either bladder or enteric drainage [1,2]. Allograft pancreatitis may be caused by infection, bladder drainage problems, alcohol, drugs and diet [1]. Pancreatic allograft rejection, usually occurring in the context of renal allograft rejection, may cause a syndrome similar to acute allograft pancreatitis but with certain important differences [3]. This report describes the coincidence of graft pancreatitis and acute renal allograft rejection. We suggest that graft pancreatitis in this case heralded the occurrence of renal allograft rejection. Acute renal allograft rejection should therefore be considered in the differential diagnosis of acute graft pancreatitis.

Case

A 20-year-old lady was admitted to hospital with a 3-day history of lower abdominal pain. This was worse after micturition though she had neither dysuria nor haematuria. The pain was cramping in nature and she had had one loose bowel motion on the day of admission. She had been started on oral antibiotics for a presumed urinary tract infection 2 days previously. She had had a combined kidney–pancreas transplant 10 months previously. She had been diagnosed with insulin-dependent diabetes mellitus 7 years ago and subsequently developed meningococcal septicaemia with acute renal failure 4 years later. A renal biopsy at the time revealed acute cortical necrosis. She required 4 months of dialysis initially but then regained sufficient renal function to become dialysis independent. Two years later, however, renal function had deteriorated to such a level that she again required dialysis and she commenced continuous ambulatory peritoneal dialysis (CAPD). Five months after starting CAPD, she underwent a cadaveric SPK transplant with the portal vein anastomosed to the iliac vein and the duodenum anastomosed to the dome of the bladder. Her course post-transplantation was complicated by two episodes of cellular rejection and by an episode of post-transplant lymphoproliferative disorder (PTLD) related to acute Epstein–Barr virus (EBV) infection. The PTLD was managed with a reduction in the immunosuppression regime, oral valaciclovir (for the EBV) and by monitoring the antiviral response. She made an excellent recovery from her PTLD that occurred 4 months prior to this admission. Medications she was taking included tacrolimus, prednisolone and sodium bicarbonate. She was a non-smoker and drank < 5 units of alcohol per week. Examination revealed a young lady who was comfortable at rest. Pulse rate was 90 beats per min and her blood pressure was 140/70 mmHg. Heart sounds were normal and the chest clear to auscultation. The abdomen was soft and distended. There was tenderness in the lower half of the abdomen (over both the renal and pancreatic grafts) and bowel sounds were present.

A full blood count showed a haemoglobin 13.7 g/dl [normal range (NR) 11–15 g/dl] with an MCV of 84 (NR 80–100), white cell count 9.7 × 10⁹/l (NR 4–11 × 10⁹/l) and platelet count 387 × 10⁹/l (NR 150–400 × 10⁹/l). Blood chemistry revealed a normal sodium [141 mEq/l (NR 135–145 mEq/l)], potassium [4.8 mEq/l (NR 3.5–5.0 mEq/l)] and urea [13.2 mg/dl (NR < 22.4 mg/dl)] and elevated serum creatinine [1.4 mg/dl (NR 0.6–1.2 mg/dl)]. Baseline creatinine was 0.9–1.1 mg/dl. A random blood glucose was 124 mg/dl, bicarbonate was 28 mmol/l (NR 22–32 mmol/l), liver function tests were normal and corrected calcium was 9.7 mg/dl (NR 8.8–10.2 mg/dl). The tacrolimus level was 7 (having been between 4 and 5 for the
previous 4 weeks). The serum amylase was 880 U/l (NR <110 U/l), having been 497 U/l the previous day (baseline amylase 105–180). A plain abdominal X-ray was normal. An ultrasound of the abdomen showed normal renal and pancreatic allografts. A small amount of free intraperitoneal fluid was seen. An 8-h urine collection was sent for a urinary amylase measurement. A cytomegalovirus (CMV) direct antigen test was negative. The following day, the amylase had almost doubled to 1607 U/l whereas her creatinine had risen to 1.5 mg/dl. A biopsy of her renal graft was performed, which revealed acute cellular rejection with significant numbers of plasma cells (Figure 1). There was also some chronic damage present but no evidence of PTLD.

The patient was treated with three doses of i.v. methylprednisolone on three consecutive days and with a 20% increase in her tacrolimus dosage. Her abdominal pain worsened and was accompanied by increasing abdominal distension. She developed a low-grade temperature (37.5 °C) and her white cell count rose to 21.8 × 10^9/l (with a neutrophilia 19.4 × 10^9/l). Both her amylase (to 1730 U/l) and her creatinine (to 2.2 mg/dl) continued to increase and her bicarbonate dropped to 21 mmol/l. An abdominal ultrasound showed normal renal and pancreatic grafts but also a large amount of ascites in addition. A computed tomography (CT) scan of the abdomen showed a perfused pancreatic allograft, free intraperitoneal fluid and no intra-abdominal lymphadenopathy (Figure 2). The native pancreas appeared normal. Aspiration of the ascites revealed straw-coloured fluid, which on microscopy contained 270 × 10^5 red blood cells/l, 240 × 10^6 white blood cells/l and moderate numbers of pus cells. There were no organisms on Gram stain and no growth on subsequent culture. The patient’s urinary amylase level (8 h collection) had dropped by almost 50%, to 14 537 U/l having been 28 945 U/l 6 days previously. The clinical and biochemical results suggested acute graft pancreatitis consequent to acute renal allograft rejection. The patient was commenced on i.v. antibiotics, kept nil by mouth and she was managed using the same guidelines as for acute pancreatitis, with her immunosuppression being given intravenously. An ascitic drain was inserted under ultrasound guidance to help relieve the abdominal distension.

Subsequently her pain settled and the drain was removed. She made a good recovery and she started to eat and drink again. The amylase fell rapidly to normal levels and the creatinine reached its original baseline of 0.9 mg/dl. Her current immunosuppression is prednisolone and tacrolimus (levels in the region of 8–9).

Discussion

There is an increased incidence of rejection in SPK recipients compared with those who receive kidney transplants alone [4]. This occurs despite the use of more potent immunosuppressive therapy in SPK patients [5]. In SPK recipients, combined pancreas and kidney rejection is the most common rejection pattern, followed by kidney-only rejections and occasionally pancreas-only rejections [4,6]. The reasons for this are unclear. Pancreatic rejection is associated with falling urinary amylase levels or increasing alkalosis (as the pancreatic graft’s bicarbonate excretion decreases) [7] and usually occurs in the context of renal allograft rejection. Stratta et al. showed that pancreatic allograft rejection was an early process (generally occurring within 40 days of transplantation) that was gradual in both onset and recovery [3]. Hyperamylasaemia occurs in 17% of cases of pancreatic allograft rejection and usually precedes rejection by ~10 days [3]. Graft pancreatitis may cause a syndrome similar to pancreatic allograft rejection but with certain important differences. Allograft pancreatitis is typically abrupt in both onset and hyperamylasaemia, and recovery generally is rapid [3]. It occurs late after SPK transplantation usually 3–51 months post-allograft [1–3]. Graft pancreatitis has been described previously in association with infections such as CMV, problems with bladder drainage and secondary to other precipitants

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**Fig. 1.** Renal biopsy showing acute cellular rejection and chronic damage (Banff 97 Category 4 Type IA, Category 5 Grade III).

**Fig. 2.** CT of the abdomen showing ascites and perfused pancreatic and renal allografts.
including alcohol, stress and diet [1]. The clinical presentation in this case therefore best fits the pattern of graft pancreatitis.

A rise in serum creatinine may be associated with graft pancreatitis due to non-specific effects, such as changes in fluid status or infection. A rise in serum creatinine in this context may not, therefore, appear to require a renal biopsy. In the described case, however, a renal biopsy clearly demonstrated that graft dysfunction was due to acute cellular rejection. There was a significant cellular infiltrate, and tubular destruction was clearly demonstrated. This was unlikely to be a coincidental finding as the degree of chronic damage argued against the long-standing presence of a silent cellular infiltrate. No pancreatic biopsy was performed as there was no indication on clinical grounds, but pancreatic rejection was unlikely given the time course of the hyperamylasaemia and the rapidity of clinical recovery. We suggest that graft pancreatitis in this case heralded the occurrence of renal allograft rejection. Therefore, in the absence of other recognized causes of graft pancreatitis, renal allograft rejection should be considered in the differential diagnosis of hyperamylasaemia in SPK recipients.

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References

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