Transplant Int (1991) 4: 116–121

TRANSPLANT
International

Development of intrapancreatic abscess – a consequence of CMV pancreatitis?

Lars Bäckman[1], Christina Brattström[1], Finn P. Reinholt[2], Jan Andersson[3], and Gunnar Tydén[1]

[1] Department of Transplantation Surgery and [2] Department of Pathology, Huddinge Hospital, S-14186 Huddinge, Sweden
[3] Department of Infectious Diseases, Danderyd Hospital, Karolinska Institute, S-18288 Stockholm, Sweden

Received March 12, 1990/Received after revision December 5, 1990/Accepted January 14, 1991

Abstract. Cytomegalovirus (CMV) pancreatitis was diagnosed in eight out of 124 pancreatic transplant recipients. Five of the eight patients developed intrapancreatic abscesses and four of the grafts were lost, but one is still functioning. In the three additional cases of pancreatitis, antiviral treatment with foscarnet or ganciclovir was given as soon as signs of CMV pancreatitis were detected. No such grafts were lost during the acute phase. CMV infection was diagnosed in cells from pancreatic juice, by virus isolation, detection of CMV antigen in cells from pancreatic juice or by CMV serology. The signs and symptoms of CMV pancreatitis included fever, general malaise, abdominal pain, diarrhoea, localized peritonitis, hyperamylasaemia, leukopenia and hyperglycaemia. It is recommended that rapid diagnostic procedures for CMV should be carried out when early signs of pancreatitis develop in pancreatic graft recipients. Antiviral treatment should be given when CMV pancreatitis is suspected or diagnosed in order to prevent the development of intrapancreatic abscesses and graft loss.

Key words: Pancreas transplantation, CMV – Abscess, pancreas transplantation – CMV, pancreas abscess

Cytomegalovirus (CMV) infection is a major cause of morbidity and mortality after organ transplantation [17, 18, 20]. The incidence of CMV infections increases with increasing doses of immunosuppressive therapy and, in particular, with the use of antithymocyte globulin (ATG) or monoclonal T-cell antibodies [4, 10]. Gastrointestinal manifestations, including pancreatitis, have been reported during CMV infections in allograft recipients [18].

In order to avoid primary CMV infections after renal and/or pancreatic transplantation, grafts or blood products from CMV seropositive donors should not be given to CMV seronegative recipients [3, 21, 22]. The combination of giving a graft from a CMV seronegative donor to a seropositive recipient is also hazardous since the graft may be infected de novo by the recipient's CMV strain. We report the clinical outcome in eight cases of CMV pancreatitis in 124 pancreatic transplant recipients. In five patients intrapancreatic abscesses developed, four of these grafts were lost, but one was salvaged by removal of the abscess. In contrast, the grafts were saved in the three patients with evidence of CMV graft pancreatitis who were treated with antiviral agents in the acute phase.

Offprint requests to: G. Tydén

Patients and methods

Between April 1974 and August 1989, 124 pancreatic transplants were performed in our institution. The exocrine pancreatic secretion was managed by duct ligature in three cases, by diversion to the stomach in seven cases and by enteric diversion to the bowel in 114 cases [7]. The immunosuppressive therapy consisted of cyclosporin (CyA) (initial dose 8 mg/kg orally aiming at whole blood trough levels of 150 ng/ml at 3 months) and prednisolone (Pred) (100 mg daily, tapered to 20 mg at 1 month and 10 mg at 3 months) in eight cases; CyA, Pred and azathioprine (Aza, 2 mg/kg tapered to 1 mg/kg at 1 month) in seven cases; and a quadruple regimen consisting of ATG (3 mg/kg for 1 week), CyA, Aza and Pred in the remaining cases. All the recipients were patients with insulin-dependent diabetes mellitus of long standing. The majority had end-stage diabetic nephropathy and therefore underwent combined renal and pancreatic transplantation. Pancreatic transplantation alone was performed in a few cases where the patients had a pre-uraemic nephropathy, defective counter-regulation of hypoglycaemia or severe secondary complications, other than nephropathy.

Viral diagnosis

CMV serology. Serum was analysed for CMV-specific IgG and IgM antibodies by enzyme-linked immunosorbent assay (ELISA) prior to transplantation on recipient and donor sera (from 1986) [19]. Further analyses were carried out on recipient serum once a month for the first 6 months post-transplant (post-tx). Reactivated CMV infections were diagnosed by a twofold or more increase in ELISA absorbance between paired samples. Seroconversion for IgG and/or IgM was required for diagnosing a primary CMV infection.

CMV isolation. Cultures for CMV were performed on buffy coat, pancreatic biopsies, pancreatic juice and urine. Cells were seeded on human embryonic lung fibroblasts, which were cultured for 6 weeks. The isolates were further characterized by immunofluorescence (IF) [16].

CMV antigens. Cells obtained from pancreatic biopsies, pancreatic juice or buffy coat were analysed for evidence of CMV antigens by IF using monoclonal antibodies (CH 12 and CH 16) directed against late CMV antigens [16].

Results

In the whole series, 12 grafts were lost due to acute irreversible rejection and 18 due to chronic rejection. Serology for CMV antibodies had been performed from both donors and recipients since October 1986. Data were therefore available in only 49 donor-recipient pairs. When graft and patient survival rates were analysed according to CMV status in both the donors and the recipients no differences were found.

In 4 of 124 patients the grafts were lost because of strictly localized intrapancreatic abscesses. All these patients had been subjected to repeated antirejection treatments and were all CMV seropositive. The donor CMV serology was not known in one case, was positive in one and negative in two cases. In the last three patients, who also received extensive immunosuppressive therapy because of acute and chronic rejection and who were also CMV seropositive, antiviral therapy was instituted when signs of CMV pancreatitis were detected in order to prevent the development of intrapancreatic abscesses. The donor CMV serology in these cases was negative in two and positive in one. These eight cases are described below.

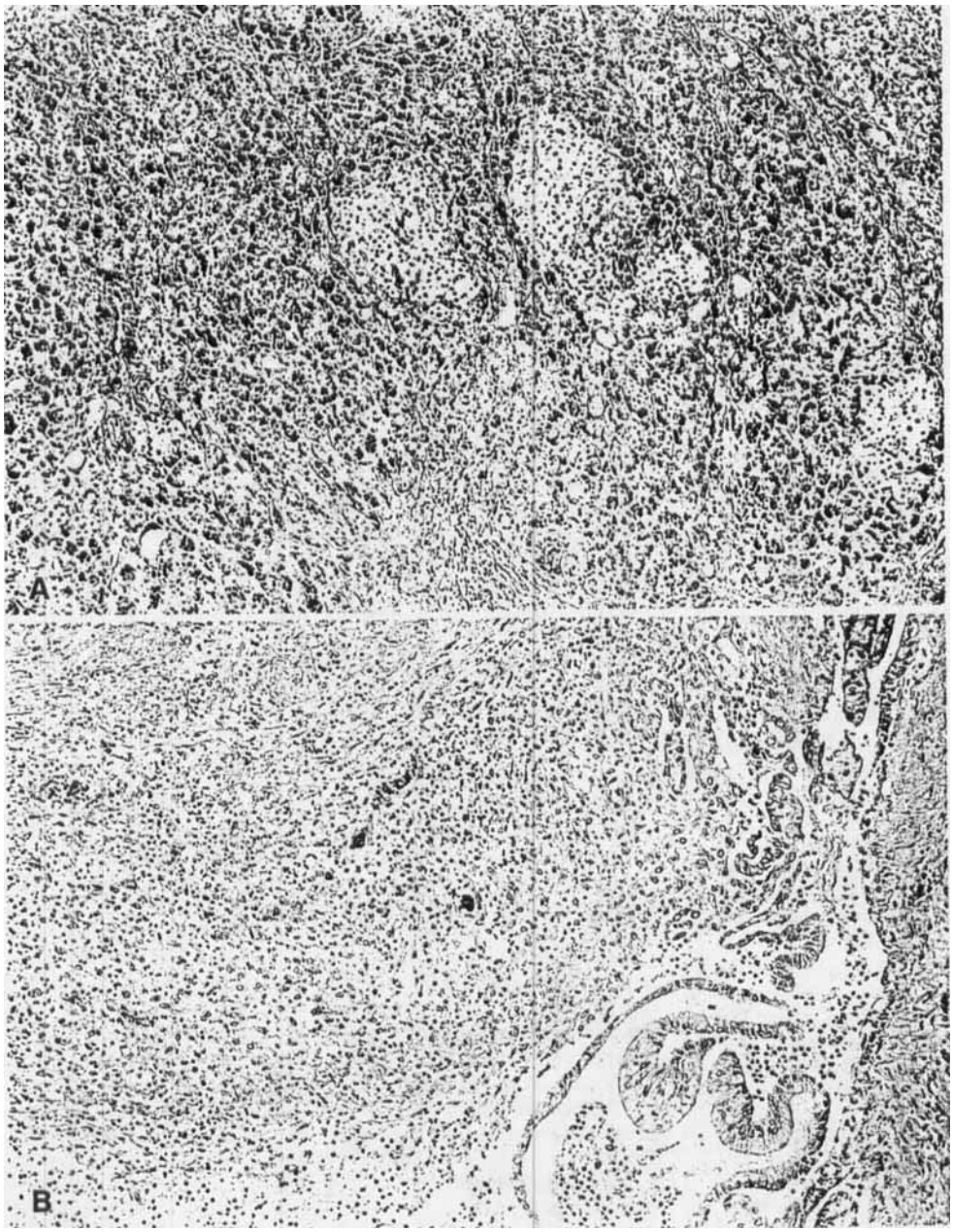

Fig. 1. A *Case no. I.* Histological section from the pancreas showing three well-preserved islets in an area adjacent to the abscess. Focal inflammation in a slightly fibrotic area is seen centrally at the lower end of the micrograph. H & E staining; × 110. **B** *Case no. II.* Non-specific abscess formation in the pancreas in continuity with a duct profile. Note the denuded duct epithelium with some reactive hyperplasia at the lower right side of the micrograph. H & E staining; × 110

Case reports

Case no. I. A CMV seropositive 27-year-old female underwent combined pancreatic and renal transplantation. The CMV serology of the donor was not known (Table 1). The immunosuppressive therapy consisted of CyA, Pred and Aza. Two pancreatic graft rejection episodes were treated with steroids (solumedrone 0.5 g i.v. for 1 day followed by 0.25 g for 3 days) on days 12 and 23 post-tx, respectively, for fever and decreasing pancreatic juice amylase levels [1]. The patient was discharged on day 29 with excellent blood glucose control, but was readmitted on day 39 because of an elevated fasting blood glucose level (11.3 mmol/l). The serum amylase level was normal and there were no abdominal symptoms or fever. Since acute rejection was suspected, a third antirejection treatment with steroids was given. After 1 week fever developed (38.9°C), together with headache, chest pain and general malaise. There was no abdominal pain and the serum amylase levels (s-amylase) remained normal. Serology revealed a significant rise in the anti-CMV IgG titres (from 1/5000 pretransplant to 1/25000), but attempts to isolate CMV from blood and urine were negative. Intravenous foscarnet (Foscavir 750–900 mg twice daily) was given over a 14-day period. The temperature remained elevated (38.5°C) but the s-amylase levels decreased gradually to subnormal levels. Because of deteriorating pancreatic endocrine function, exogenous insulin was administered. The immunosuppressive therapy was tapered, but the patient's condition did not improve. A transplantectomy was therefore performed on day 67 and an intrapancreatic abscess was found in the middle of the pancreatic tail. The abscess was strictly localized inside the pancreas and did not communicate with the surrounding structures or the peritoneal cavity. Viral cultures from the graft grew CMV. A histopathological examination revealed the development non-specific abscess formation. In addition, fat necrosis and focal inflammation with lymphocytic predominance were present. Arterial profiles displayed vascular rejection with intimal fibrosis and slight inflammation. In some profiles fresh thrombi were observed. Throughout the pancreas the parenchyma showed moderate interstitial fibrosis while the islets were well preserved (Fig. 1 A). Neither exocrine nor endocrine cells showed any nuclear inclusion bodies.

Case no. II. A 44-year-old male who was CMV seropositive received pancreas and kidney grafts from a CMV seropositive donor (Table 1). The immunosuppressive treatment consisted of CyA, Pred and Aza. However, CyA was stopped on day 3 post-tx because of poor renal graft function and a 7-day course of ATG was given. CyA was reinstituted on day 14 post-tx and Aza was discontinued because of leucopenia on day 71. Two days post-tx, the pancreatic juice amylase levels declined and a concomitant renal graft biopsy demonstrated hemorrhagic infarction and acute vascular rejection. A course of methylprednisolone was given. The pancreatic juice amylase increased, but the blood glucose levels remained high. Subsequently the endocrine pancreatic function improved, exogenous insulin treatment was stopped and the patient was discharged from hospital on day 26 with normal blood glucose levels. The patient was readmitted on day 46 because of fever and increasing blood glucose levels. Foscarnet (1000 mg twice daily) was commenced because a CMV infection was suspected. On day 60, the s-amylase increased, in the range 10.0–22.1 μcat/l (normal range 2.6–5.2 μcat/l). A laparatomy performed on day 90 demonstrated multiple intrapancreatic abscesses, and the graft was removed. Viral cultures from the graft showed growth of CMV. In addition alpha-haemolytic streptococci and *E. coli* were also isolated. Histological examination showed several abscesses of non-specific morphology, mostly located in the vicinity of the duct profiles (Fig. 1 B). The rest of the parenchyma was dominated by a mild interstitial fibrosis associated with mild inflammatory mixed infiltrate. No nuclear inclusion bodies were observed. Arterial profiles showed chronic vascular rejection with substantial fibrous thickening of the intima and, in some profiles, fresh thrombi.

Case no. III. This 32-year-old male underwent a single pancreatic transplantation (Table 1). He was CMV seropositive, but the donor was seronegative. The immunosuppressive therapy consisted of CyA, Pred and Aza, in combination with ATG during the first 4 days. A rejection episode was suspected on day 14 post-tx because of declining pancreatic juice amylase levels, and methylprednisolone was administered. The patient was discharged on day 27. On day 30, a series of abnormal liver function tests (increased ALAT, ASAT and bilirubin levels) was noted which normalized over a period of 3 weeks. During this period, there was also a significant rise in anti-CMV IgG titres. The patient was readmitted to hospital on day 83 post-tx with fever (38.5°C), abdominal pain and diarrhoea. On admission, the s-amylase was 9.9 μcat/l and blood glucose was 7.5 mmol/l. A laparatomy revealed no gross pathological changes in the graft. However, a biopsy was performed which showed signs of acute and chronic rejection, and a second course of methylprednisolone was given. The clinical condition improved, but s-amylase and blood glucose levels remained elevated. The patient was discharged on day 90 but was readmitted on day 102 with fever, abdominal pain and hyperamylasaemia (15.4 μcat/l). A third course of methylprednisolone was given. However, 1 week later, fever and hyperamylasaemia recurred. A second laparotomy was performed on day 140 post-tx. The graft contained an abscess with a wedge-shaped infarct, and it was removed. A histopathological examination revealed a 1.5 cm abscess in the distal part of the pancreatic tail. The abscess was attached to the main pancreatic duct. Other parts of the parenchyma showed severe focal fibrosis with only mild, mainly lymphocytic, inflammation. No nuclear inclusion bodies were observed. The arterial profiles showed severe stenosis due to a fibrous intimal thickening typical of chronic vascular rejection.

Case no. IV. This 34-year-old male underwent combined pancreatic and renal transplantation (Table 1). He was CMV seropositive but the donor was seronegative. The initial immunosuppressive therapy consisted of CyA, Pred, Aza and an initial 1-week course of ATG. However, Aza was given only once because of a suspected allergic reaction with skin rashes and respiratory obstruction. A course of methylprednisolone was given on day 3 post-tx because of fever and deteriorating renal function. A second course of methylprednisolone was given on day 9. On day 11 post-tx, a laparotomy was performed because of abdominal pain, fever and rising s-amylase levels. Necrotic tissue was removed from the pancreatic graft and continuous peritoneal dialysis treatment was commenced in order to rinse the peritoneal cavity. At a second laparotomy 2 days later, an intrapancreatic abscess was found and the graft was removed. A histopathological examination showed the development of a non-specific abscess. In addition, small scattered areas of fat necrosis were found. Nuclear inclusion bodies typical of CMV infection were not seen. No signs of vascular rejection were found, but in small arterial profiles, adjacent to the abscess and areas of fat necrosis, fresh and organizing thrombi were seen. In general, the parenchyma and in particular the islets were well preserved. CMV serology from the day of pancreatectomy showed a significant CMV IgG-titre elevation (from 1/10000 to 1/100000), suggesting reactivation.

Case no. V. A 35-year-old CMV seropositive female received a pancreas from a CMV seronegative donor (Table 1). The immunosuppressive treatment included CyA, Pred and Aza in combination with an 8-day course of ATG started on the day of transplantation. Six days post-tx, CMV antigen was detected in the pancreatic juice by IF staining and later by virus isolation, but no antiviral treatment was given at that time. A course of methylprednisolone treatment was given on days 10–16 post-tx because of fever, abdominal discomfort, and the appearance of lymphoblasts in the pancreatic juice. On day 17, hyperamylasaemia and subfebrility developed and activated lymphoblasts appeared again in the pancreatic juice. A second course of methylprednisolone was given and the patient improved. CMV antigen was again identified in the pancreatic juice on day 31 by IF. Because of this, 4 days of foscarnet (850 mg twice daily) treatment was given and the patient was then discharged from hospital. On day 42, she was readmitted because of hyperamylasaemia and a third antirejection treatment was given. However, hyperamylasaemia persisted, and a second course of foscarnet was therefore given for 14 days (1650 mg/day which was increased to

Table 1. Patient and donor characteristics

Case	Grafts	CMV status (recipient/donor)	No. of rejections	Signs of CMV infection	Outcome
I	Pancreas and kidney	Positive/unknown	3	Increasing IgG CMV titres; CMV cultured from graft at transplantectomy	Intrapancreatic abscess day 67; chronic vascular rejection
II	Pancreas and kidney	Positive/positive	1	CMV cultured from the graft at transplantectomy	Intrapancreatic abscess day 100; chronic vascular rejection
III	Pancreas	Positive/negative	3	Increasing IgG CMV titres; CMV isolated from urine	Intrapancreatic abscess day 140; chronic vascular rejection
IV	Pancreas and kidney	Positive/negative	2	Increased IgG CMV titres	Intrapancreatic abscess day 13
V	Pancreas	Positive/negative	3	Increased IgG CMV titres; CMV identified in pancreatic juice	Chronic rejection
VI	Pancreas and kidney	Positive/positive	1	CMV isolated from blood; increasing IgG CMV titres	Chronic rejection
VII	Pancreas and kidney	Positive/negative	2	CMV identified in pancreatic juice and from pancreatic biopsy specimen	Still functioning
VIII	Pancreas	Positive/negative	1	CMV identified in pancreatic juice and isolated from blood	Intrapancreatic abscess; still functioning.

5000 mg/day). The endocrine function was largely unaffected and the s-amylase levels normalized. During the treatment, the anti-CMV titres increased. Subsequently, a biopsy was performed because of increasing s-amylase levels. The biopsy showed no signs of intrapancreatic abscess formation or acute rejection, but the specimen showed severe fibrotic changes.

Case no. VI. A 42-year-old male received a combined pancreatic and renal transplant (Table 1). Both the recipient and the donor were CMV seropositive. The immunosuppression consisted of CyA, Pred, Aza and an 8-day course of ATG. On day 9 a rejection episode was diagnosed by pancreatic juice cytology and fine-needle aspiration biopsy of the kidney, and he was treated with methylprednisolone for 6 days. The patient's renal function improved and he was discharged from hospital on day 26 with excellent graft function. He was readmitted on day 30 because of fever and hyperamylasaemia. CMV was isolated from the buffy coat and the anti-CMV IgG titre had increased. DHPG (350 mg twice daily) was given for 10 days, and the s-amylase levels returned to baseline levels. The pancreatic and renal grafts were lost 6 months post-tx due to chronic vascular rejection, but there were no signs of intrapancreatic abscess formation.

Case no. VII. This CMV seropositive 40-year-old male received pancreatic and renal allografts from a CMV seronegative donor (Table 1). The immunosuppressive therapy consisted of CyA, Pred and Aza. S-amylase levels remained moderately elevated for the first 14 days post-tx (peak level 18.4 μcat/l on day 8). Lymphoblasts were noted in the pancreatic juice on day 10 post-tx, and methylprednisolone therapy was instituted on day 12 because of increasing s-creatinine levels. The rejection episode did not respond to steroids, and a 7-day course of OKT-3 was started on day 16. CMV antigens were detected in the pancreatic juice by IF on day 23, and on day 26 DHPG (140 mg three times daily) was commenced. A pancreatic biopsy on day 28 showed interstitial and vascular rejection, and a second antirejection treatment was given with steroids. In addition, CMV antigen was detected by IF in the same specimen. The patient was treated with DHPG for a total of 27 days, and required no exogenous insulin 50 days after the transplantation.

Case no. VIII. This 40-year-old male recipient of a pancreatic graft was also CMV seropositive prior to transplantation and received a graft from a CMV seronegative donor (Table 1). The indication for transplantation was defective counterregulation to hypoglycaemia. The immunosuppression consisted of Pred and Aza in combination with OKT-3 for the first 11 days. CyA was added on day 9 post-tx. The immediate postoperative course was uneventful. However, the patient received antirejection treatment on day 11 post-tx because of the presence of lymphoblasts in the pancreatic juice. CMV antigen was identified in the pancreatic juice on day 22 post-tx, but no antiviral therapy was given. He was readmitted to hospital on day 67 because of nausea and vomiting, without abdominal pain or fever. The blood glucose and serum amylase levels were normal but CMV was isolated from the buffy coat. Because of increasing s-amylase levels he was readmitted to hospital on day 221 post-tx. A needle biopsy showed interstitial inflammation and interstitial fibrosis. A second antirejection treatment was given but the amylase levels remained elevated. On laparatomy, performed in order to obtain an open graft biopsy, the tail of the pancreas was found to contain an intrapancreatic abscess, which was then drained. The graft was left in situ and the abdomen was closed. The patient requires no exogenous insulin and the s-amylase levels are normal 245 days after transplantation.

Discussion

In the present study, 8 of 124 recipients of pancreatic grafts developed signs of pancreatitis concomitant with ongoing CMV infections. In five patients strictly intrapancreatic abscesses developed and four such grafts had to be removed. In three patients who received antiviral treatment at an early stage, i.e. within 10 days of evidence of CMV replication in the pancreas, the grafts were retained. There are several reasons why it seems likely that the intrapancreatic abscesses were a consequence of CMV pancreatitis, particularly when the patients were receiving massive immunosuppression. First, all the patients showed evidence of ongoing, active CMV infection with increasing IgG titres, positive virus isolation from

the blood or pancreatic juice and/or growth of CMV from transplantectomy specimens or biopsies. Second, from the histological point of view, although no inclusion bodies were found, the absence of inclusion bodies does not exclude an ongoing or recent CMV infection [5]. Third, although all the patients were heavily immunosuppressed, it seems unlikely that the abscesses were due solely to repeated acute rejection episodes and the ensuing antirejection treatment. Thus, in our series of 124 pancreatic transplantations, of which the majority suffered at least one rejection episode and all received ATG as prophylaxis or as treatment for rejection, we saw intrapancreatic abscesses only in the patients with CMV disease described above. All of the patients were CMV seropositive prior to transplantation. In five cases where the donor serology was negative, a possible explanation of the CMV pancreatitis may be a de novo CMV infection in the graft from the recipient. In the cases where both the donor and the recipient serologies were positive, an infection with a different CMV strain may have occurred in the graft. However, the combination of a CMV seropositive recipient and a seronegative donor does not in itself lead to CMV pancreatitis and intrapancreatic abscesses. Thus, our series includes seven additional CMV-positive patients who received pancreatic grafts from negative donors, none of whom developed intrapancreatic abscesses.

A similar case of large cystic duct structures within a rejecting pancreatic graft was recently reported [15]. The patient had previously been treated for multiple episodes of rejection. No data on the CMV status in the patient or donor were given, but it is possible that these cystic structures, later found to contain necrotic tissue, had the same aetiology as the abscesses observed by us. CMV pancreatitis has also been reported by Margreiter et al. in four highly immunosuppressed patients after combined pancreatic-renal transplantation [13].

The explanation for the development of CMV pancreatitis and intrapancreatic abscess may be twofold. In vitro studies show that CMV induces a depression of monocyte function. It has been suggested that this is due to CMV inhibition of IL-1 production [2]. However, more recent data suggest that the monocyte dysfunction (down-regulation of class II molecules and antigen presentation) is induced by another monokine [11, 14]. A local CMV infection may thereby induce local impairment of the cellular immune response which increases the risk of secondary bacterial infections in the pancreas. Another explanation for the development of an abscess may be CMV-induced ischaemic damage of the pancreatic tissue. It has recently been shown that CMV can infect endothelial cells and cause tissue necrosis due to arteritis [9]. Thus, local virus replication in the intima of the pancreatic vessels may cause vascular damage and necrosis which predispose to secondary bacterial infections. The finding that six of the patients also had signs of chronic rejection is interesting since CMV infections have been shown to correlate with the occurrence of chronic graft-versus-host disease after bone marrow transplantation [12]. A correlation between atherosclerotic vascular changes and CMV infections in heart-transplant recipients has also been reported [6].

Unfortunately, the clinical symptoms of CMV pancreatitis are similar to those of acute rejection, and many probably unnecessary antirejection treatments were given to these patients and contributed to the unfavourable outcome. It seems, therefore, that the combination of extensive antirejection therapy and 'CMV incompatibility' was responsible for the development of the abscesses. In the three patients treated with foscarnet or DHPG after rapid CMV antigen detection, the pancreatic grafts were not lost in the acute phase. The virostatic effect of these two drugs in vivo necessitates their early introduction before extensive CMV replication causes irreversible tissue damage [8]. This is exemplified by the three patients with acute pancreatitis and ongoing CMV infections who did not develop abscesses or lose their grafts in the acute phase.

This was a study with limited material and further prospective studies need to be done in order to evaluate the origin, cause, pathogenesis and treatment of CMV graft pancreatitis. However, CMV infection in combination with heavy immunosuppression and rejection seems to be of importance for the development of an intrapancreatic abscess. We suggest that aggressive antiviral therapy should be instituted on the basis of rapid CMV antigen or DNA/RNA detection in the pancreatic juice when CMV pancreatitis is suspected, in order to prevent the development of intrapancreatic abscesses and resultant loss of the graft.

Acknowledgements. This study was supported by the Swedish Medical Research Council Project no. 07501, the Swedish Cancer Foundation, the Karolinska Institute and the Swedish Diabetes Association.

References

1. Brattström C, Tydén G, Reinholt FP, Bohman SO, Borgström A, Bäckman L, Bolinder J, Groth CG (1989) Markers for pancreas graft rejection in humans. Diabetes 38 [Suppl 1]: 57–62
2. Buchmeier N, Cooper NR (1989) Suppression of monocyte functions by human cytomegalovirus. Immunology 66: 278–283
3. Chou S (1986) Acquisition of donor strains of cytomegalovirus by renal transplant recipients. N Engl J Med 314: 1418–1423
4. Fox AS, Tolpin MD, Baker AL, Brolesch CE, Whittington PF, Jackson T, Thistle Hiwaite JR, Stuart FP (1988) Seropositivity in liver transplant recipients as a predictor of cytomegalovirus disease. J Infect Dis 157: 383–385
5. Gnann JW, Ahlmén J, Svalander C, Olding L, Oldstone MBA, Nelson JA (1988) Inflammatory cells in transplanted kidneys are infected by human cytomegalovirus. Am J Pathol 132: 239–248
6. Grattan MT, Moreno-Cabral CE, Starnes VA, Oyer PE, Stinson ED, Shumway NE (1989) Cytomegalovirus infection is associated with cardiac allograft rejection and atherosclerosis. JAMA 261: 3561–3566
7. Groth CG, Tydén G, Östman J (1989) Fifteen years' experience with pancreas transplantation with pancreaticoenterostomy. Diabetes 38 [Suppl 1]: 13–15
8. Hecht DW, Snydman DR, Crumpacker CS, Warner BG, Heinze-Lacey B (1988) Ganciclovir for treatment of renal transplant associated primary cytomegalovirus pneumonia. J Infect Dis 157: 187–189
9. Ho DD, Rota TR, Andrews CA, Hirsch MS (1984) Replication of human cytomegalovirus in endothelial cells. N Engl J Med 150: 956–957

10. Johnson Bia M, Andiman W, Gaudio K, Kliger A, Siegel N, Smith D, Flye W (1985) Effect of treatment with cyclosporine versus azathioprine on incidence and severity of cytomegalovirus infection posttransplantation. Transplantation 40: 610–614
11. Kapasi K, Rice GP (1988) Cytomegalovirus infection of peripheral blood mononuclear cells; effects on interleukin-1 and -2 production and responsiveness. J Virol 62: 3603–3607
12. Lönnqvist B, Ringdén O, Wahren B, Gahrton G, Lundgren G (1984) Cytomegalovirus infection associated with and preceding chronic graft-versus-host disease. Transplantation 38: 465–468
13. Margreiter R, Then P, Schmid T, Bosmuller C, Konigsrainer A (1991) Cytomegalovirus (CMV) pancreatitis: a rare complication after pancreas transplantation. Transplant Proc 23: 1619–1622
14. Moore K, Vieira P, Fiorentino M, Kahn T, Mosman T (1990) Homology of cytokine synthesis inhibitor factor IL-10 to the Epstein-Barr virus gene BCRF1. Science 248: 1230–1234
15. Nobrega J, Halvorsen RA, Letourneau JG, Snover D, Sutherland D (1990) Cystic central necrosis of transplanted pancreas. Gastrointest Radiol 15: 202–204
16. Pereria L, Hoffman M, Gallo D, Cremer N (1982) Monoclonal antibodies to human cytomegalovirus three surface membrane proteins with unique immunological and electrophoretic properties specify cross-reactive determinants. Infect Immunol 36: 924–932
17. Rubin RH (1988) Infection in the renal and liver transplant patient. In: Rubin RH, Young LS (eds) Clinical approach to infection in the compromised host, 2nd edn. Plenum, New York, pp 557–621
18. Son WJ van, The TH (1989) Cytomegalovirus infection after organ transplantation: an update with special emphasis on renal transplantation. Transplant Int 2: 147–164
19. Sundqvist VA, Wahren B (1982) An interchangeable Elisa for cytomegalovirus antigen and antibody. J Virol Methods 2: 301–312
20. Tolkoff-Rubin NE, Rubin RH (1986) The impact of cyclosporine therapy on the occurence of infection in the renal transplant recipient. Transplant Proc 18: 168–173
21. Weir MR, Irwin BC, Maters AW, Genemans G, Shen S, Charache P, Williams GM (1987) Incidence of cytomegalovirus disease in cyclosporin-treated renal transplant recipients based on donor/recipient pretransplant immunity. Transplantation 43: 187–193
22. Weir MR, Henry ML, Blackmore M, Smith J, First MR, Irwin B, Shen S, Genemans G, Alexander JW, Corry RJ, Nghiem DD, Ferguson RM, Kittur D, Shield CF, Sommer BG, Williams GM (1988) Incidence and morbidity of cytomegalovirus disease associated with a seronegative recipient receiving seropositive donor-specific transfusion and living related donor transplantation. Transplantation 45: 111–116