

TWO AIDS PATIENTS WITH LIFE-THREATENING PANCREATITIS SUCCESSFULLY TREATED, ONE WITH GANCICLOVIR THE OTHER WITH FOSCARNET

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SUMMARY

Two AIDS patients, clinically suspected to have cytomegalovirus (CMV) pancreatitis are described. The first patient was successfully treated with ganciclovir 10 mg/kg/day. This patient refused ganciclovir maintenance treatment and developed 3 other episodes of pancreatitis which responded each time to ganciclovir. The second patient was successfully treated with foscarnet 200 mg/kg/day followed by maintenance foscarnet treatment 100 mg/kg/day. No pancreatitis relapse was observed.

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INTRODUCTION

Most persons with human immunodeficiency virus (HIV) infection have also been infected with cytomegalovirus (CMV) (1). If a person with HIV infection develops severe immunodeficiency (CD4 lymphocyte counts $< 100/\text{mm}^3$), reactivation of the CMV infection may occur (2). In persons with the acquired immunodeficiency syndrome (AIDS), CMV is known to be able to cause retinitis, oesophagitis, colitis, gastritis, encephalitis, polyradiculomyelitis, hepatitis, pancreatitis and adrenalitis (2). Moreover, CMV infection is a major cause of death in patients with AIDS (3).

Nearly all reported cases of CMV pancreatitis have been diagnosed in post-mortem studies (4-6). Joe et al made a pre-mortem diagnosis of CMV pancreatitis using a CT-guided needle aspiration of a pancreatic mass (7). Cella and

Gupta established a diagnosis of CMV pancreatitis on the basis of a positive CMV culture of pancreatic duct fluid obtained through pancreatic duct washing during an endoscopic retrograde cholangiography (8). Because of the difficulties to diagnose CMV pancreatitis clinically this condition probably often remains undiagnosed. A systematic necropsy of 113 AIDS patients in Italy revealed cytomegalic inclusion cells in pancreas tissue in 10 (9%) of them.

Two drugs are currently used in the treatment of CMV infection: ganciclovir and foscarnet (9). In a study of AIDS patients with CMV retinitis, foscarnet treatment offered a survival advantage over ganciclovir treatment (10). Little is known about the usefulness of ganciclovir or foscarnet treatment in HIV infected individuals with CMV pancreatitis (4). An AIDS patient with CMV pancreatitis who was successfully treated with ganciclovir was recently reported (8). Foscarnet was shown to be successful in the treatment of CMV pancreatitis in pancreatic transplant recipients (11). We describe 2 AIDS patients with life-threatening pancreatitis who were successfully treated, one with ganciclovir, the other with foscarnet.

CASE REPORTS

Case 1

In November 1990, a 30-year-old HIV seropositive caucasian heterosexual woman was admitted with severe abdominal pain and vomiting.

Her medical history revealed an herpes zoster infection in 1987 and 1989 and an episode of

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facialis paralysis in 1987. HIV infection was diagnosed in April 1989. Since April 1990 she developed recurrent episodes of otitis, sinusitis and oral candidiasis. Since August 1989 she was treated with zidovudine. In July 1990 she developed polyneuritis. There was no drug or alcohol abuse.

Physical examination on admission revealed the following findings : a cachectic anaemic woman in poor general condition, blood pressure 105/85 mmHg, pulse 80/min, temperature 37.7°C, body weight 49 kg, abdominal defence, rebound tenderness and poor peristalsis.

Laboratory values on admission included : haemoglobin 9.8 g/dl, haematocrit 28.5%, leucocytes $3.2 \times 10^9/l$, lymphocytes $0.3 \times 10^9/l$, CD4 lymphocyte count $10/mm^3$, amylase 1156 U/l (normal 24-75 U/l), lipase 13670 U/l (normal 23-208 U/l), LDH 506 U/l (normal 120-220 U/l), alkaline phosphatase 1448 U/l (normal 63-166 U/l), AST 423 U/l (normal 2-17 U/l), ALT 159 U/l (normal 5-22 U/l), GGT 291 U/l (normal 6-20 U/l), total bilirubin 0.6 mg/dl (normal 0.2-1.0 mg/dl), direct bilirubin 0.39 mg/dl (normal 0-0.2 mg/dl), hepatitis B serology: absence of hepatitis B antigens and antibodies.

A chest and abdominal X-ray was normal. An abdominal ultrasound examination showed free liquid in the abdominal cavity and a normal appearance of the pancreas. Funduscopy showed cotton wool spots on the retina of the left eye, but no signs of CMV retinitis.

Because the consulting surgeon suspected an intestinal perforation a laparotomy was performed. During surgery only an oedematous pancreatitis was found.

Treatment consisted of gastric aspiration, cimetidine intravenously, ganciclovir (10 mg/kg/day) and rehydration with intravenous saline followed by parenteral nutrition. The abdominal pain regressed progressively. One week after starting the ganciclovir there was still free liquid present in the abdominal cavity. Treatment with ceftazidime intravenously was started.

After a culture of this liquid revealed a *Streptococcus faecalis* infection, cotrimoxazole intravenously was given. Two weeks after admission the abdominal pain had disappeared and she started eating normally. The serum amylase-lipase levels and the liver tests remained slightly abnormal. The ganciclovir was continued for 17 days, but was then stopped because of serious leucopenia ($0.8 \times 10^9/l$). Four weeks after admission she left the hospital in quite good condition. In December 1990, she developed a new episode of pancreatitis which was again successfully treated with ganciclovir. She refused to continue ganciclovir maintenance treatment. In January 1991, she developed two other episodes of pancreatitis, each again responding to ganciclovir. She never accepted ganciclovir maintenance treatment and finally died in February 1991. No autopsy was performed.

Case 2

In November 1992, a 29-year-old HIV seropositive caucasian homosexual man was admitted because of explosive vomiting and epigastric pain. Since several weeks he complained of fatigue, anorexia, weight loss and episodes of diarrhoea.

HIV infection had been diagnosed in 1988. In June and September 1992 he had been treated for a *Streptococcus pneumoniae* pneumonia. There was no drug or alcohol abuse.

Physical examination on admission revealed the following findings: a cachectic anaemic and icteric man. Temperature 37°C, blood pressure 120/70 mmHg and pulse 74/min. Body weight 53 kg. Abdomen: tympanism on percussion, defence, rebound tenderness and poor peristalsis.

Laboratory values on admission included : haemoglobin 10.2 g/dl, haematocrit 32%, leucocytes $1.1 \times 10^9/l$, lymphocytes $0.4 \times 10^9/l$, CD4 lymphocyte count $40/mm^3$, serum sodium 129 mEq/l (normal 135-140 mmol/l), LDH 666 U/l (normal 120-220 U/l), AST 1299 U/l (normal 2-17 U/l), ALT 388 U/l (normal 5-22 U/l), amy-

lipase 654 U/l (normal 24-75 U/l), lipase 11160 U/l (normal 23-208 U/l), GGT 4471 U/l (normal 6-20 U/l). Hepatitis B serology: absence of hepatitis B antigens and antibodies.

An abdominal X-ray showed liquid and air levels, but without free air under the diaphragm. An abdominal ultrasound examination revealed: hepatosplenomegaly and an enlarged pancreatic head with fluid around the pancreas. At funduscopy no signs of CMV retinitis were found.

Treatment included gastric aspiration, foscarnet intravenously (200 mg/kg/daily) through a Port-A-Cath system and rehydration with intravenous saline.

The abdominal pain and icterus disappeared after 3 days. Serum amylase and lipase levels and liver tests normalised over a period of 30 days. Because a stool culture grew *Campylobacter jejuni*, erythromycin 2 g daily was added. After 7 weeks of foscarnet treatment the patient developed a *Staphylococcus aureus* septicemia because of an infected Port-A-Cath system. In February 1993, he died because of this *Staphylococcus* endocarditis. At autopsy, serious destruction of the heart valves was found, but histopathologic signs of pancreatitis were no longer present.

DISCUSSION

In AIDS patients a diagnosis of CMV disease is made either clinically (e.g. CMV retinitis, most cases of CMV polyradiculo-myelitis) or by histology (e.g. CMV colitis)(1). A positive CMV culture of a body fluid is not a proof of CMV disease and AIDS patients may have CMV disease in the absence of a positive CMV culture from blood or urine (1,9,12). Because performing an endoscopic retrograde cholangiography or obtaining a biopsy from the pancreas in an AIDS patient with pancreatitis may be associated with certain risks for the patient and cause considerable discomfort we propose that certainly for patients in advanced stage of HIV disease and with a strong clinical suspicion of

CMV pancreatitis empiric treatment with ganciclovir or foscarnet should be given for at least one week. A rapid improvement of the patients clinical condition during ganciclovir or foscarnet treatment strongly suggests that the patient indeed has CMV pancreatitis. If within one week no clinical improvement is seen then the anti-CMV treatment should be stopped. With careful monitoring of the patients, the potential toxicity caused by a short course of ganciclovir or foscarnet treatment is minimal. These two case reports suggest that maintenance treatment with either ganciclovir or foscarnet is indicated to avoid relapse of CMV pancreatitis. CMV pancreatitis should be suspected in a person with HIV infection, in the presence of a CD4 count < 100/mm³, abdominal pain, high serum amylase-lipase levels, ultrasound findings suggesting pancreatitis and in the absence of other risk factors able to cause pancreatitis such as e.g. cholelithiasis, alcoholism, use of ddI or pentamidine.

SAMENVATTING

Twee AIDS patiënten met een klinisch vermoeden van cytomegaal virus (CMV) pancreatitis worden beschreven. De eerste patiënt werd succesvol behandeld met ganciclovir 10 mg/kg/dag. Deze patiënt weigerde echter ganciclovir onderhoudsbehandeling en ontwikkelde 3 andere episoden van pancreatitis, die telkens opnieuw onderdrukt werden door ganciclovir behandeling. De tweede patiënt werd succesvol behandeld met foscarnet 200 mg/kg/dag gevolgd door onderhoudsbehandeling met foscarnet 100 mg/kg/dag. Geen herval van pancreatitis werd getoond.

RESUME

Deux patients SIDA avec un diagnostic présomptif de pancréatite à cytomegalovirus (CMV) sont décrits. Le premier patient a été traité avec succès par le ganciclovir à la dose de 10mg/kg/jour. Ce patient a refusé un traitement d'entretien par le ganciclovir et a développé 3 autres épisodes de pancréatite, qui ont chaque fois répondu au traitement par le ganciclovir. Le second patient a été traité avec succès par le

foscarnet à la dose de 200 mg/kg/jour, suivi d'un traitement d'entretien de foscarnet (100 mg/kg/jour). Aucune récurrence de pancréatite n'a été observée.

REFERENCES

1. Schooley RT. Cytomegalovirus in the setting of infection with human immunodeficiency virus. *Rev Infect Dis.* 1990; 12: 5811-19.
2. Gallant JC, Moore RD, Richman DD, Keruly J, Chaisson RE and the Zidovudine Epidemiology Group. Incidence and natural history of cytomegalovirus disease in patients with advanced human immunodeficiency virus disease treated with zidovudine. *J Infect Dis.* 1992; 166: 1223-27.
3. Macher AM, Reichert CM, Strauss SE et al. Death in the AIDS patient: role of cytomegalovirus. *N Engl J Med.* 1983; 309: 1454.
4. Wilcox CM, Forsmark CE, Grendell JH, Darragh TM. Cytomegalovirus associated acute pancreatic disease in patients with acquired immunodeficiency syndrome. Report of two patients. *Gastroenterology.* 1990; 99: 263-7.
5. Brivet F, Coffin B, Bedossa P et al. Pancreatic lesions in AIDS. *Lancet.* 1987; ii: 570-1.
6. Bricaire F, Marche C, Zoubi D, Saimot AG, Regnier B. HIV and the pancreas. *Lancet.* 1988; i: 65-6.
7. Joe L, Ansher AF, Gordin FM. Severe pancreatitis in an AIDS patient in association with cytomegalovirus infection. *South Med J.* 1989; 82: 1444-45.
8. Cella P, Gupta S. Diagnosis of cytomegalovirus pancreatitis in AIDS by endoscopic retrograde cholangiopancreatography. *N Engl J Med.* 1991; 326: 204.
9. Connolly GM, Nelson MR, Barton SE, Gassman BG. Problems in the management of cytomegalovirus in patients with AIDS. *Int J STD & AIDS.* 1991; 2: 405-10.
10. Studies of ocular complications of AIDS research group, AIDS clinical trials group. Mortality in patients with the acquired immunodeficiency syndrome treated with either foscarnet or ganciclovir for cytomegalovirus retinitis. *N Engl J Med.* 1991; 326: 213-9.
11. Backman L, Brattstrom C, Reinhold FP, Andersson J, Tyden G. Development of intrapancreatic abscess - a consequence of CMV pancreatitis? *Transpl Int (Germany).* 1991; 4: 116-21.
12. Zurlo JJ, O'Neill D, Polis MA et al. Lack of clinical utility of cytomegalovirus blood and urine cultures in patients with HIV infection. *Ann Intern Med.* 1993; 118: 12-7.