

Early Presentation of CMV Gastritis in Renal Transplant Recipients: Case Reports

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Abstract

Upper gastrointestinal (GI) tract symptoms in solid organ recipients are common. There are various factors predisposing to GI symptoms. Cytomegalovirus (CMV) is considered to be the major viral cause of upper GI symptoms in organ transplant recipients. Gastrointestinal CMV infection occurs within the 6th and 12th months of transplantation. It was worth describing the two renal transplant recipients who presented with dyspeptic complaints in the post transplant 2nd month, and diagnosed for CMV gastritis. Treatment was successful with the administration of intravenous ganciclovir.

Key Words: CMV, CMV gastritis, renal transplantation, abdominal pain, ganciclovir

Gastrointestinal (GI) complications of solid organ transplantation are common. Nausea and vomiting may simply be related to the multiple medications these patients require, but more serious conditions, such as oral lesions (aphthous ulcer, cyclosporine induced gingival hyperplasia), fungal esophagitis, peptic ulcer, infectious gastritis, diarrhoea [bacterial, viral or due to mycophenolate mofetil (MMF)], GI bleeding and perforation may occur.

Cytomegalovirus (CMV) is considered to be an implicated cause of GI symptoms in organ transplant recipients. Considered it as uncommon; it was worth describing the two renal transplant recipients who presented with dyspeptic complaints and were diagnosed for CMV gastritis.

Case 1 :

A 49-year old male patient with end stage renal failure (ESRD) secondary to a chronic pyelonephritis, underwent cadaveric renal transplantation in March 2005 while he was on hemodialysis. Serologic detection of CMV IgM and IgG was done prior transplantation and CMV IgM was negative while CMV IgG was positive (66 IU). He received an induction therapy of a total dose of 900mg Anti-thymocyte globulin (ATG) and was further treated for an acute rejection episode by 3 times pulse of 750 mg methyl-prednisolone. The patient presented with an epigastric pain, nausea and loss of appetite within the second month of transplantation. The epigastric pain decreased in a supine position and increased while sitting and further increased when standing or walking. His blood pressure and heart rate was 130/80mmHg and 80/min, respectively. He had no fever. The physical

examination revealed an epigastric tenderness. The laboratory findings were as following: hemoglobine:11.5 gr/dl (N:13.5-17.5), hematocrit: 34% (N: 43-51.5), WBC: 7000/mm³ (N: 4000-10000), platelet: 160000/mm³ (N: 150000-400000). Liver function and serum amilase levels were normal, however creatinine was 2.7 mg/dl (the baseline level was 1.7 mg/dl and N: 0.6-1.4 mg/dl). CMV antigenemia assay by indirect immunofluorescent method detected 280 CMV antigen positive white blood cells through 200000 cells. Intravenous ganciclovir was administered at a dose of 5mg/kg/day. Moreover a reduction of MMF was done from 1500mg/day to 1000mg/day while the doses of steroid and cyclosporine were continued as 15mg/day and 300mg/ day respectively. Abdominopelvic ultrasound (USG) was normal. Diagnostic upper GI endoscopy revealed erythematous gastritis, multiple antral 2 to 4 mm sized polypoid lesions bulging from the mucosa. Histopathological examination revealed reactive epithelial changes and chronic inflammation of the lamina propria admittted with polynuclear leucocytes.

Intestinal metaplasia and helicobacter pylori were negative. Glandular epithelial and endothelial intranuclear inclusion bodies were detected in the mucosal biopsy materials and the immunohistochemical staining with CMV specific-labeled antibody was positive. (Figure 1) Histopathological diagnosis was CMV gastritis. The patient was discharged from the hospital after the completion of treatment that lasted for 21 days.

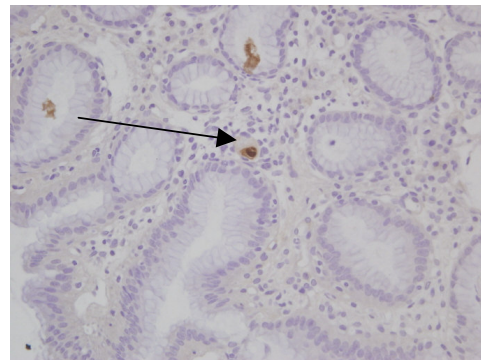


Figure 1. The arrow shows the intranuclear inclusion body in the tissue biopsy materials of the first and second case, respectively

Case 2 :

A 43-year old male patient with ESRD secondary to chronic glomerulonephritis underwent kidney transplantation from a living unrelated donor in February 2005. Serologic detection of CMV IgM and IgG was done prior transplantation and CMV IgM was negative while CMV IgG was positive (86 IU). The patient received a total dose of 900 mg ATG for induction therapy. He presented with a positional epigastric pain and a loss of appetite in the second month of transplantation. The laboratory findings were as following: hemoglobine:14.6 gr/dl, hematocrit: 43%, WBC: 9700/mm³, platelet: 268000 mm³, serum amilase: 74 IU (N:25-70), creatinine: 1.35 mg/dl. The liver function was normal. CMV antigenemia was positive in 400/200000 white blood cells. A treatment of 5mg/kg/day intravenous ganciclovir was initiated and the immunosuppressive regimen was continued as 20mg/day prednisolone, 1440mg/day mycophenolic acid and 450mg/day cyclosporine. The abdominopelvic USG was normal while the upper GI endoscopy revealed hiatal hernia, grade A esophagitis, erithematous gastritis and antral edematous polypoid lesion. Histopathological examination from the biopsy of the polypoid lesion revealed a chronic inflammation at the lamina propria. Intestinal metaplasia and helicobacter pylori were negative. Glandular epithelial and endothelial intranuclear inclusion bodies and the immunohistochemical staining with CMV specific-labelled antibody were positive (Figure 2). Histopathological diagnosis was CMV gastritis. CMV antigenemia and the symptoms resolved during the follow-up and the patient was discharged after 21 days while the treatment was completed.

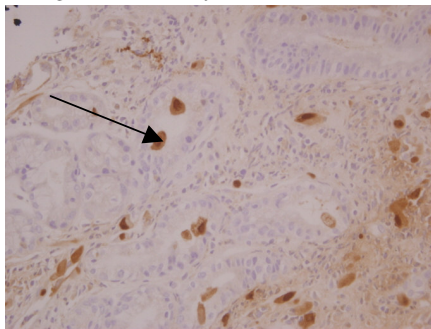


Figure 1. The arrow shows the intranuclear inclusion body in the tissue biopsy materials of the first and second case, respectively

Discussion

Upper GI tract symptoms in solid organ recipients are common (20%) and clinical signs are more serious in 10 % of cases (1,11,13). There are various factors predisposing to GI symptoms; the GI irritation and inflammation caused by immunosuppressive and other medications, as well as bacterial, viral and fungal infections are the most common culprits (2). CMV is considered to be the major viral cause of upper GI symptoms in organ transplant recipients (2,3). Although this complication is a significant source of morbidity and mortality in patients with advanced HIV infection or malignancy, solid organ and bone marrow transplant recipients and in patients under steroid treatment, the immunocompetent individuals are also at risk (8). CMV infection of GI system occurs within the 6th and 12th months of transplantation depending on the type of

transplantation and the serological status of the donor and recipient (4). It is significant that CMV infection occurred in the second month of transplantation in both of our recipients. GI CMV infection occurs more often with immunosuppressive regimens including MMF. Symptomatic CMV infection may be further differentiated into the CMV syndrome (fever, leukopenia and increased CMV antigen titer) and invasive CMV disease. Invasive CMV disease has also been implicated as a cause of symptomatic esophagitis, gastritis, duodenitis, ileitis or colitis. The patients presented with a variety of clinical symptoms such as diarrhoea, abdominal pain, loss of appetite, malaise, nausea and vomiting according to the organ involved (5). The unique type of abdominal pain is a sharp epigastric pain that decreases in a supine position, increases while sitting and further increases when standing or walking (14). The clinical presentation in both of our patients was a similar epigastric pain. Diagnostic endoscopy can reveal solitary or multiple ulcerations and haemorrhage, gastritis, duodenitis and pseudotumors; but is not specific (6). We demonstrated mucosal bulging polipoids in both of our recipients. Endoscopic pseudotumors are more significant in AIDS related CMV gastritis (9).

For the diagnosis of CMV infection, tissue biopsy or cytology materials should be examined by immunohistochemical methods or cytology for CMV antigens or inclusion bodies. Histologic diagnosis requires the demonstration of cellular PAS (periodic acid shift) (+) stained cytoplasmic inclusions and intranuclear inclusion bodies (7). The microscopic pathological findings are mucosal ulcerations, erosions and mucosal haemorrhage. Other pathologic findings include acute and chronic inflammatory changes, tissue necrosis, crypt abscesses and vascular thrombosis. CMV DNA detection by PCR has an enhanced sensitivity (100%) (10,12). CMV antigenemia, features of chronic gastritis and histological inclusion bodies were demonstrated in both of our patients.

Pyloric stenosis, bleeding and perforation are all potential complications of CMV gastritis. Treatment of an active disease includes reduction in the immunosuppressive regimen, as tolerable, and the administration of intravenous ganciclovir. Remission occurs in majority of the patients with an appropriately initiated treatment. However, an additional period of treatment may be necessary in a selected group of patients. CMV antigenemia and clinical symptoms resolved in both of our patients with a course of 21 day treatment of 5mg/kg/day ganciclovir.

Conclusion

In conclusion, renal transplant recipients who receive antilymphotic medications and MMF should be evaluated for CMV gastritis when they present with epigastric pain especially after the first month of transplantation.

References

- Hardinger K, Brennan DC, Lowell J. Long term outcome of gastrointestinal complications in renal transplant patients with mycophenolate mofetil. *Transpl Int.* 2004; 17 (10): 609-16
- Peter A, Telkes G, Varga M, Sarvary E, Kovalszky I. Endoscopic diagnosis of cytomegalovirus infection of

- upper gastrointestinal tract in solid organ transplant recipients. *Clin Transplant* 2004; 18: 580-84
3. Goodgame RW. Gastrointestinal cytomegalovirus disease. *Ann Intern Med.* 1993; 105 (6): 1769-75
4. Helderman JH, Goral S. Gastrointestinal complications of transplant immunosuppression. *J Am Soc Nephrol* 2002; 13(1): 277-87
5. Kaplan B, Meier-Kriesche HU, Jacobs MG et al. Prevalance of cytomegalovirus in the gastrointestinal tract of renal transplant recipients with persistent abdominal pain. *Am J Kidney Dis.* 1999; 34 (1): 65-8
6. Graham SM, Flowers JL. Oppurtunistic upper gastrointestinal infection in transplant recipients. *Surg Endosc* 1995; 9 (2): 146-150
7. Shrestha BM, Parton D, Gray A et al. Cytomegalovirus involving gastrointestinal tract in renal transplant recipients. *Clin Transplant.* 1996; 10 (2): 170-5
8. Buckner FS, Pomeroy C. Cytomegalovirus disease of the gastrointestinal tract in patients without AIDS. *Clin Infect Dis.* 1993; 17 (4): 644-56
9. Laguna F, Garcia J, Alonso MJ. Pseudotumoral appearance of cytomegalovirus esophagitis and gastritis in AIDS patients. *Am J Gastroenterol.* 1993; 88 (7): 1108-11
10. Kusne S, Manez R, Frye B, StGeorge K et al. Use of DNA amplification for diagnosis of cytomegalovirus enteritis after intestinal transplantation. *Gastroenterology* 1997; 112: 1121-8
11. Ponticelli C, Passerini P. Gastrointestinal complications in renal transplant recipients. *Transpl Int.* 2005; 18 (6): 643-50
12. Abecassis MM, Koffron AJ, Kaplan B. The role of PCR in the diagnosis and management of CMV in solid organ recipients: what is the predictive value for the development of disease and should PCR be used to guide antiviral therapy? *Transplantation* 1997; 63 (2): 275-9
13. Sarkio S, Halme L, Kyllonen L, Salmela K. Severe gastrointestinal complications after 1515 adult kidney transplantations. *Transpl Int.* 2004; 17 (9): 505-10
14. Giladi M, Lembo A, Johnson BL. Postural epigastric pain: a unique symptom of primary cytomegalovirus gastritis? *Infection* 1998; 26 (4): 234-5