Cytomegalovirus Gastritis in Renal Graft: Case Report

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Abstract

Introduction: Cytomegalovirus (CMV) is an important pathogen, and its infection develops in 70% to 90% of transplant patients. Upper gastrointestinal (GI) symptoms in the solid organ recipient are common (20%) and clinical signs are more serious in 10% of cases.

Case Presentation: This study reports on a 30-year-old male with end-stage renal disease that had undergone kidney transplantation from a CMV negative donor at Imam Khomeini hospital, Urmia, Iran during June 2013. After 1.5 months, he was admitted with fever, generalized body pain, oral aphthous ulcers, and epigastric pain accompanied by malaise. Endoscopic examination and clinicopathological investigations revealed multiple antral erosions with surrounding erythema.

Management and Outcome: The patient was started on Intravenous (IV) ganciclovir 5mg/kg per day, every 12 hours initially for 3 weeks. Afterwards, the general condition of the patient improved.

Discussion: The colon and stomach were the most common sites of the gastrointestinal infection, yet localization to the gastric antrum is not common.

Keywords: Cytomegalovirus (CMV), Renal Transplantation, Gastritis, Infection

1. Introduction

Cytomegalovirus (CMV) is a Herpes virus family member and also a common cause of infection in immunocompromised hosts, including patients with acquired immune deficiency syndrome (HIV/AIDS), neonates, and transplant recipients (1). Overall, 50% to 90% of American and European adults have CMV infection (2, 3). The virus remains latent during life and it is characterized by its ability to become reactivate periodically (4, 5). In solid organ transplantation, common sites of gastrointestinal (GI) infection are colon and stomach, yet infection of the stomach with antral involvement is rare (6). Cytomegalovirus is the main reason of morbidity in immunocompromised patients' upper GI (7, 8). Patients with CMV gastritis have nonspecific symptoms, including epigastric pain, nausea, vomiting, high-grade fever, and GI bleeding (9). Endoscopic features are quite variable and include normal mucosa, diffuse erythema, nodules, pseudo-tumors, and erosions yet characteristic findings on upper endoscopy are punched-out gastric ulcers (10). Most CMV gastrointestinal infections respond well to Ganciclovir (11). This report describes a renal transplant recipient with dyspeptic complains presentation, whose principal sign was multiple antral erosions, which have rarely been reported so far.

2. Case Report

A 30-year-old male with end-stage renal disease underwent kidney transplantation from a CMV negative donor at Imam Khomeini Hospital, Urmia, Iran in June 2013. Serologic determination for CMV IgM and IgG antibodies were done before transplantation and both antibodies were negative. The patient received an induction therapy of anti-thymocyte globulin (ATG) for 14 days, Ganciclovir for 21 days, and Methyl-prednisolone for 3 days. Renal function improved, and the postoperative was uneventful. Patient was discharged on day 15. One and a half months later, he presented fever, generalized body pain, oral aphthous ulcers, and epigastric pain accompanied by malaise. Clinical examination revealed epigastric tenderness. The laboratory findings were as following: hemoglobin: 10.5 mg/dL (NI: 43-51), white blood count (WBC): 7100 (NI: 4,000 - 10,000), Platelet: 38000 (NI: 150,000 - 400,000). Liver enzyme tests and serum amylase levels were normal. Blood, urine and stool cultures were negative. Tests for CMV antigen and anti-CMV antibody (IgM) were positive. The abdominal-pelvic ultrasonography was normal. The upper gastrointestinal endoscopic revealed multiple antral erosions with erythema, yet no deep ulcer was seen. Histopathological examination of lesions showed large ep-

ithelial cells with intranuclear inclusion body called Owl's eye appearance, which is highly specific for CMV infection (Figure 1A and 1B). No evidence of *Helicobacter pylori* infection was seen. The patient was started on Ganciclovir IV 5mg/kg/day every 12 hours, initially for 3 weeks. The fever subsided afterwards; blood cell count returns to normal ranges and clinical status improved (Table 1).

3. Discussion

Infection with CMV develops in 70% to 90% of the transplant patients (6). Some of these infections represent a reactivation of the latent virus, while some may be primary infection transmitted from a donor to the recipient (12). One of the most important sites of latent infection is the GI tract. The CMV infection of GI tract occurs within the 6th and 12th months after the transplantation depending on the type of transplantation and the serologic status of the donor and recipient. The colon and stomach are common sites of gastrointestinal infection. The rate of GI involvement by CMV is high and gastric CMV infections are usually located in the fundus with adjacent involvement of the gastro-esophageal junction, and the gastric antrum is not common (6). However, in the study of Gupta et al. (6), all five reported patients had lesions in the antrum (6). Symptoms of CMV gastritis are nonspecific, including epigastric pain, nausea, vomiting, fever, and bleeding (9). There are only a few references in the literature to postural epigastric pain as a symptom of CMV gastritis (13, 14). Although endoscopic features are variable, frequent endoscopic findings in patients with gastric involvement by CMV are punched out gastric ulceration or mild erosion. The ulcer base is the site of most intense inflammations. These histologic alterations may be patchy, therefore 8 to 10 biopsies of suspicious lesions are recommended (6, 13). Pyloric stenosis, bleeding, and perforation are all potential complications of CMV gastritis. It has been suggested that there is an association between the use of Mycophenolate mofetil and cytomegalovirus, especially in the GI tract (15). Treatment of an active disease includes reduction in the immunosuppressive regimen, and administration of intravenous Ganciclovir. Remission occurs in the majority of the patients with one course of treatment. However, an additional period of treatment is not infrequent. Cytomegalovirus antigenemia and clinical symptoms resolved in the patient with a course of 21 days of Ganciclovir IV 5mg/kg/day treatment (16).

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Footnotes

Ethical Approval: All procedures performed in studies involving human participants were in accordance with ethical standards of Ethics Committee, Urmia University of Medical Sciences and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflict of Interest: No conflict of interest.

References

- Bhadauria D, Sharma RK, Kaul A, Prasad N, Gupta A, Gupta A, et al. Cytomegalovirus disease in renal transplant recipients: a single-center experience. *Indian J Microbiol.* 2012;**52**(3):510-5. doi: [10.1007/s12088-012-0268-9](#). [PubMed: [23997350](#)].
- Staras SA, Dollard SC, Radford KW, Flanders WD, Pass RF, Cannon MJ. Seroprevalence of cytomegalovirus infection in the United States, 1988-1994. *Clin Infect Dis.* 2006;**43**(9):1143-51. doi: [10.1086/508173](#). [PubMed: [17029132](#)].
- Lopo S, Vinagre E, Palminha P, Paixao MT, Nogueira P, Freitas MG. Seroprevalence to cytomegalovirus in the Portuguese population, 2002-2003. *Euro Surveill.* 2011;**16**(25). [PubMed: [21722611](#)].
- Reeves MB, MacAry PA, Lehner PJ, Sissons JG, Sinclair JH. Latency, chromatin remodeling, and reactivation of human cytomegalovirus in the dendritic cells of healthy carriers. *Proc Natl Acad Sci U S A.* 2005;**102**(11):4140-5. doi: [10.1073/pnas.0408994102](#). [PubMed: [15738399](#)].
- Reeves M, Sinclair J. Aspects of human cytomegalovirus latency and reactivation. *Curr Top Microbiol Immunol.* 2008;**325**:297-313. [PubMed: [18637513](#)].
- Gupta T, Agarwal D, Mandot A, Desai D, Joshi A, Abraham P. Cytomegalovirus involving gastric antrum in immunocompromised hosts: a report of 5 cases. *Indian J Gastroenterol.* 2005;**24**(6):258-60. [PubMed: [16424624](#)].
- Halme L, Hockerstedt K, Lautenschlager I. Cytomegalovirus infection and development of biliary complications after liver transplantation. *Transplantation.* 2003;**75**(11):1853-8. doi: [10.1097/01.TP.0000064620.08328.E5](#). [PubMed: [12811245](#)].
- Helderman JH, Goral S. Gastrointestinal complications of transplant immunosuppression. *J Am Soc Nephrol.* 2002;**13**(1):277-87. [PubMed: [11752050](#)].
- Zuluaga Quintero M, Aristizábal Alzate A, Nieto Ríos JF, Ocampo Kohn C, Serna Higuera LM, Pérez Cadavid JC, et al. Epigastric Pain related to Posture as a Possible Symptom of Gastritis due to Cytomegalovirus in a Renal Transplant Patient: A Case Report. *Revista Colombiana de Gastroenterología.* 2015;**30**(3):356-9.
- Ebisutani C, Kawamura A, Shibata N, Nasu M, Ueno R, Mimura K, et al. Gastric ulcer associated with cytomegalovirus in an immunocompetent patient: method for diagnosis. *Case Rep Gastroenterol.* 2012;**6**(2):365-8. doi: [10.1159/000339714](#). [PubMed: [22740812](#)].
- Hokama A, Taira K, Yamamoto Y, Kinjo N, Kinjo F, Takahashi K, et al. Cytomegalovirus gastritis. *World J Gastrointest Endoscop.* 2010;**2**(11):379.
- Boeckh M, Bowden RA, Goodrich JM, Pettinger M, Meyers JD. Cytomegalovirus antigen detection in peripheral blood leukocytes after allogeneic marrow transplantation. *Blood.* 1992;**80**(5):1358-64. [PubMed: [1325214](#)].

Figure 1. Photomicrography of the gastric biopsy showing in A, Large epithelial cells with eosinophilic intranuclear inclusions (x10 H&E), in B, Large epithelial cells with characteristic owl's eye eosinophilic intranuclear inclusion body surrounded by a clear halo (x 40 H&E).

Table 1. Paraclinical Test Results of the Patients^a

	Hemoglobin, mg/dL	WBC	Platelet	Liver Enzyme Tests and Serum Amylase Levels	Blood, Urine and Stool cultures	Helicobacter Pylori Infection	abdominal- Pelvic Ultrasonogra- phy	CMV Antigen and Anti-CMV antibody (IgM)
Results	10.5	7,100	38,000	Normal	Negative	Negative	Normal	Positive

^aThe results of complete blood count (CBC), liver function tests, and abdominal pelvic ultrasonography were normal. Blood, urine, and stool cultures and *H. pylori* test results were negative. Both CMV antigen and anti-CMV antibody test results were positive.

13. Crespo P, Dias N, Marques N, Saraiva da Cunha J. Gastritis as a manifestation of primary CMV infection in an immunocompetent host. *BMJ Case Rep.* 2015;2015. doi: [10.1136/bcr-2014-206991](https://doi.org/10.1136/bcr-2014-206991). [PubMed: [26150611](https://pubmed.ncbi.nlm.nih.gov/26150611/)].
14. Giladi M, Lembo A, Johnson BJ. Postural epigastric pain: a unique symptom of primary cytomegalovirus gastritis?. *Infection.* 1998;26(4):234-5. [PubMed: [9717682](https://pubmed.ncbi.nlm.nih.gov/9717682/)].
15. Gallagher H, Andrews PA. Cytomegalovirus infection and abdominal pain with mycophenolate mofetil: is there a link?. *Drug Saf.* 2001;24(6):405-12. [PubMed: [11368249](https://pubmed.ncbi.nlm.nih.gov/11368249/)].
16. Franzin G, Muolo A, Griminelli T. Cytomegalovirus inclusions in the gastroduodenal mucosa of patients after renal transplantation. *Gut.* 1981;22(9):698-701. [PubMed: [6271652](https://pubmed.ncbi.nlm.nih.gov/6271652/)].