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Case Report
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A Potentially Preventable Case of *Cytomegalovirus* Esophagitis and Colitis after a Liver Transplantation

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Abstract

A *Cytomegalovirus* (CMV) infection after a liver transplantation is a known complication; however, positive serology in the donor liver confers an increased risk of CMV infection in the recipient, in addition to further complications, bacterial infections, and even transplant rejection. This case report discusses a 56-year-old male who presents with one month of diarrhea, approximately three months after a CMV-positive donor liver transplantation. For unclear reasons, he was not started on antiretroviral prophylaxis after transplantation. This report will review diagnostic tests for CMV, treatment recommendations, and suggestions for anti-retroviral prophylaxis after liver transplantation.

Keywords: *Cytomegalovirus*; Esophagitis; Colitis; Prophylaxis; Liver transplant

Introduction

In liver transplantation patients, mortality has generally improved, but viral infections cause many complications [1]. *Cytomegalovirus* (CMV) is the most common infection in the first six months after liver transplantation. These patients can be asymptomatic or present as tissue invasive disease [2]. CMV, a member of the Human Herpesvirus family, is common and is present in 50% to 100% of all people [3]. Most immunocompetent patients with CMV infections have a self-limiting course and rarely seek medical attention. It is mostly seen in immunocompromised individuals, such as those with HIV or solid organ transplantation [3]. Regarding those with liver transplantation, patients who are seronegative with seropositive donors (D+R-) are at highest risk of complications [2]. CMV infections most commonly present in liver transplantation patients with fever, malaise, arthralgia, leukopenia, and thrombocytopenia and it can lead to hepatitis, retinitis, pneumonitis, esophagitis and colitis [2]. For CMV colitis, symptoms are typically non-specific and can include diarrhea, abdominal pain, fever, rectal bleeding, weight loss, and malaise [3]. CMV esophagitis can present as odynophagia, substernal chest pain, and gastrointestinal bleeding [4]. Although one must suspect a CMV infection in immunocompromised patients, some patients are at higher risk than others because of donor seropositivity, making prophylaxis an important consideration.

Case Presentation

Informed consent was obtained for this case. A 56-year-old male with past medical history significant for treated Chronic Hepatitis C (HCV), alcoholic cirrhosis complicated by refractory ascites and hepatic encephalopathy which improved after liver transplantation, which was three months prior to presentation, and splenectomy secondary to an intraoperative laceration presented with a 4-day history of fatigue and fever (101.5 F). He reported multiple, daily episodes of non-bloody diarrhea for the last month, along with subjective chills, anorexia, dyspnea on exertion and a productive cough.

The patient's donor liver was high risk due to polysubstance abuse and incarceration. The donor liver was HCV antibody positive and nucleic acid test positive (Ab+ NAT+), and also CMV positive. Our patient was started on HCV treatment one month after transplantation with glecaprevir/pibrentasvir for a planned 12 weeks. Our patient's CMV status was negative, and, after transplantation, his CMV titers were negative on three separate occasions. His medications included antibiotic prophylaxis (amoxicillin), *Pneumocystis jirovecii* prophylaxis (trimethoprim/sulfamethoxazole), mycophenolate, tacrolimus, and glecaprevir/pibrentasvir. For unknown reasons, he was not started on CMV prophylaxis. At presentation, his vitals were 99.1F, 69 beats/min, 135/81 mmHg, and 18 breaths/min. His physical examination was significant for healed, abdominal

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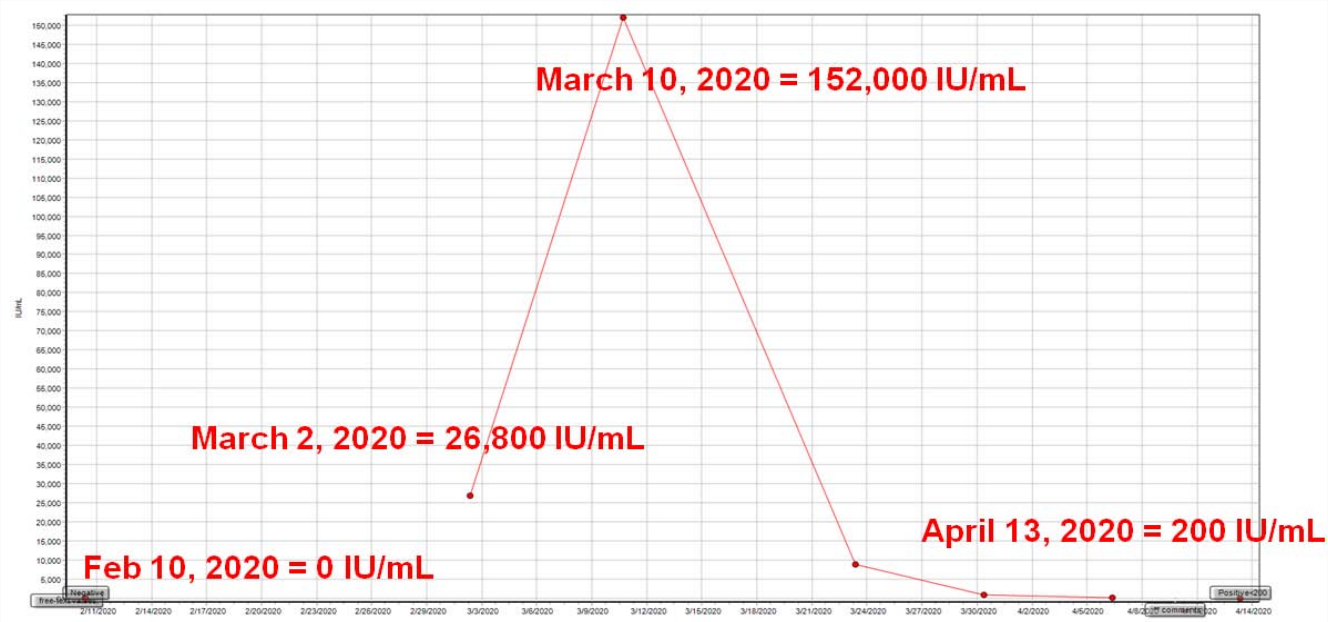

Figure 1: CMV PCR over the course of diagnosis and treatment.

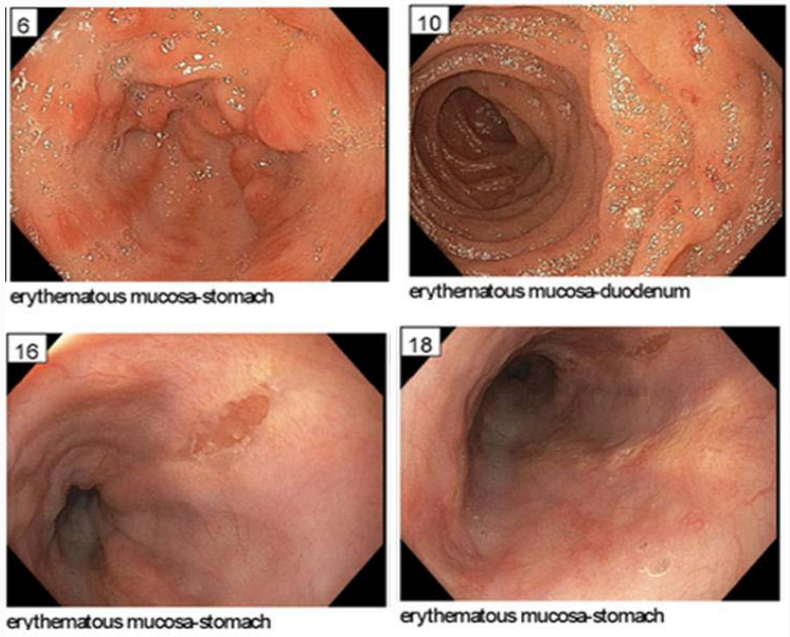

Figure 2: Selected photos from patient's EGD.

scars related to his transplantation, but otherwise unremarkable. Significant admission laboratory data included a creatinine of 2 mg/dL, with a baseline of 1.2 mg/dL, bicarbonate of 14 meq/L, albumin of 2.9 g/dL, tacrolimus level of 17.2 ng/mL. The remainders of his labs were unremarkable. A chest X-ray demonstrated a left lower lobe infiltrate. He was started on vancomycin, piperacillin/tazobactam, valganciclovir and oseltamivir. Antibiotics were subsequently narrowed to amoxicillin/clavulanate and azithromycin after clinical improvement. He required bicarbonate supplementation for worsening metabolic acidosis and acute tubular necrosis secondary to diarrhea and nephrotoxic medication.

His CMV PCR viral load collected a prior to admission, was 26,800 IU/mL, which resulted during his hospitalization. A repeat CMV PCR, while admitted, demonstrated a fivefold increase in the viral load, at 152,000 IU/mL (Figure 1).

While admitted, he developed worsening diarrhea and had one episode of hematemesis. An Esophagogastroduodenoscopy (EGD) and colonoscopy were performed with biopsies. His colonoscopy did not demonstrate significant findings. The EGD demonstrated an erosion and erythematous mucosa in the fundus, body, and pylorus of the stomach and the duodenum (Figure 2).

He was diagnosed with suspected CMV colitis and esophagitis and was started on valganciclovir. His viral load decreased with treatment and his symptoms resolved (Figure 1). After discharge, his pathology

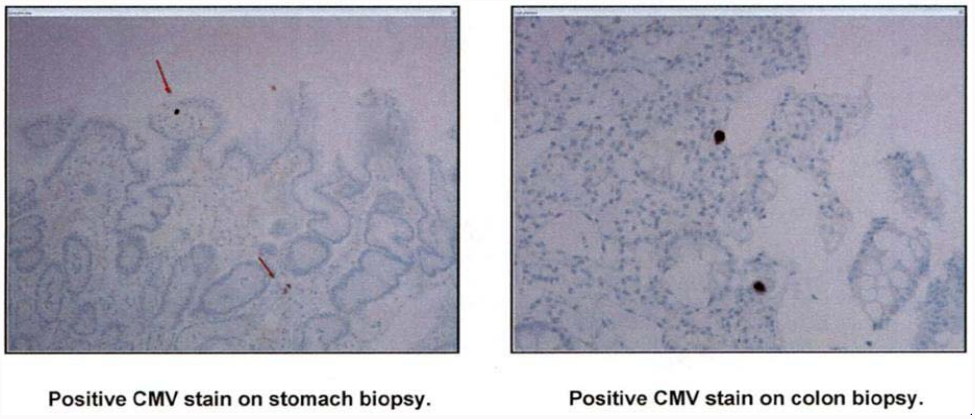

Figure 3: Immunohistochemistry stains for patient's biopsy.

report demonstrated gastric mucosa with reactive gastropathy, gastric and esophageal focal erosions, and chronic inflammation in the small and large intestines. Immunohistochemistry biopsies were positive for CMV in the esophagus, stomach, duodenum, and colon (Figure 3).

Discussion

In cases of suspected CMV infections, PCR and CMV pp65, an antigenemia assay, are available tests [3]. CMV viral load directly correlates to the patient's symptoms and disease state. Histopathology of the affected area can also confirm diagnosis; however, biopsies of multiple sites are required as the disease has patchy involvement. CMV specific immunohistochemistry is considered "gold standard" for diagnosis [3].

According to recent review articles on CMV donor-positive, recipient-negative (D+R-) liver transplantation patients, it is both acceptable to give antiviral prophylaxis for 3 to 6 months after transplantation or to initiate preemptive therapy based upon weekly nucleic acid testing [6,8]. Preemptive therapy entails weekly monitoring of CMV nucleic acid tests. Shared decision making is necessary as prophylactic medications have side effects, incur patient costs, and require frequent lab monitoring [6]. CMV prophylaxis does not guarantee prevention of infection. A study of 67 CMV D+R- liver transplantation patients, who despite receiving CMV prophylaxis with oral ganciclovir or valganciclovir, has demonstrated that 29% still developed CMV infections [7]. CMV prophylaxis still has benefits. A retrospective study with 192 liver transplantation recipients has shown that 14 days of CMV prophylaxis with ganciclovir decreased the risk of bacteremia especially in seropositive donors [9].

For treatment of CMV infections, oral valganciclovir is often given for at least two consecutive weeks until the viral load undetectable and there is clinical resolution [8]. Based upon the CMV half-life, CMV PCR is often measured every five to seven days to monitor viral replication and to determine treatment response [5]. Interestingly, in a study of 267 patients, it has been demonstrated that symptomatic patients with a pretreatment viral load of less than 18,200 IU/mL have a significant faster time to disease resolution [6]. If there is persistently high CMV viral loads within six weeks of treatment, it may indicate relapse [8,9]. The key learning point is that CMV PCR is essential for diagnosis, prognosis, and response to treatment.

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