



Successful Treatment of Herpes Esophagitis With Ganciclovir in a Liver Transplant Patient

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Abstract

The presence of Herpes Simplex Virüs-1 (HSV-1) esophagitis in patients with liver transplantation has been reported rarely. Among the reports that are accessible in the literature, none could have shown tissue positivity for Herpes virus-1 DNA via Polymerase Chain Reaction (PCR) in patients with liver transplantation. This case is presented as the patient was diagnosed with herpes esophagitis based on the histopathological findings and HSV-1 DNA positivity (detected by PCR) in the biopsy material and was treated with Ganciclovir. Due to the specific action of Ganciclovir against CMV infections, it is natural that the drug cannot use in the treatment of HSV infections. However it is reported that ganciclovir has been reduced the incidence of symptomatic HSV infections after liver transplantation. We report on a patient after liver transplantation with HSV-1 esophagitis, who was successfully treated with Ganciclovir. We assume that most transplant centers according to their protocols use ganciclovir for CMV prophylaxis, which may contribute to avoid HSV infection.

Key words: Herpes Simplex Virüs-1 (HSV-1); Liver transplantation; Ganciclovir; Polymerase Chain Reaction (PCR); Esophagitis

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INTRODUCTION

The presence of Herpes Simplex Virus-1 (HSV-1) esophagitis in the patients with the solid organ transplantation has been reported by some case reports in the literature^[1-3]. The clinical diagnosis of mucosal HSV infection is uncertainty, laboratory diagnosis essential to guide therapy. HSV infection is best confirmed by isolation of virus or demonstration of HSV DNA in tissue culture and histopathological findings^[4]. However, among the reports that are accessible in the literature, none could have shown tissue positivity for HSV-1 Deoxyribonucleic acid (DNA) via Polymerase Chain Reaction (PCR) in liver transplant recipients. Only one publication in a patient after renal transplantation reported about HSV-1 DNA presence detected by in situ hybridization^[3]. It is known that acyclovir is the first line therapy in HSV infection. Due to the specific action of Ganciclovir against CMV infections, it is natural that the drug is not used in the treatment of HSV infections. However it is reported that ganciclovir has been reduced the incidence of symptomatic HSV infections after liver transplantation from 23.5% to 3.5%^[5]. We report on a patient after liver transplantation with HSV-1 esophagitis, who was successfully treated with Ganciclovir. The HSV-1 diagnosis was established by HSV-1 PCR from esophagus tissue sample.

CASE REPORT

A 24-year-old female patient applied to the Emergency Department of our hospital in August 2011 with

complaints of nausea, vomiting, fever, acholic feces and darkened urine color. The patient's history revealed that she had undergone left hepatectomy+cyst excision (12 cm) + partial right lobe resection+ Roux-en-Y high hilar ductojejunostomy in February 2011 due to her complaint of a palpable mass located on the right side of the abdomen and the preliminary diagnosis of hydatid cyst and that she had been using antibiotics due to cholangitis attacks, which had been recurring over a period of 6 months. The patient was hospitalized in the gastroenterology department where anastomotic stenosis was detected in her via MRCP (Magnetic Resonance Cholangiopancreatography). On September 2011, the patient underwent PTC (Percutaneous Transhepatic Cholangiography) which revealed severe stenosis in bilioenteric anastomosis. An external drainage catheter was placed. Repeated attempts by interventional radiology failed to pass through the stenotic site. Although reanastomosis was considered, no appropriate intrahepatic bile duct on PTC could be identified for enteric drainage. We also wanted to redo ductojejunostomy but in case of non dilated biliary system there would be chance of not finding anything to anastomose. What we did, we schedule him for conventional hepatobiliary surgery but at the same time in case we fail to do appropriate anastomosis we prepared his relative for living related liver transplant (as liver donor). After we found that it is impossible to save her liver because of damaged, fibrotic strictured biliary system we pursued and switch to liver transplant procedure for her living donor. We tried but we couldn't help her with conventional hepatobiliary surgery principles. Living related liver transplantation from her brother was decided and performed. Her induction immunosuppressive regimen was consisted tacrolimus (0.1mg/kg/day BID), myophenolate mofetil (750 mg BID) and steroid (1gr methylprednisolone IV bolus during reperfusion and tapered down to 15 mg/day starting from 100 mg/day on POD day 1). Ceftriaxone (2x1gr/day) was used for antibacterial prophylaxis for 3 days while antiviral and antifungal prophylaxes were not used. Due to muscular defense and rebound tenderness detected during the physical examination of the patient performed on the 2nd postoperative day and the increase in the hemorrhagic fluid released from the drainage tubes, the patient was reoperated for intraabdominal hemorrhage. The bleeding and biliary leakage was brought under control. Since the patient complained of nausea and vomiting during the follow-up, endoscopy was performed and a gastric biopsy sample was collected. Since macroscopic investigation revealed exudative ulcers in the esophagus, Cytomegalovirus (CMV) antigenemia and CMV DNA tests were scheduled and Ganciclovir (2x5mg/kg/day) treatment was initiated (Figure 1A). On the 7th day of the Ganciclovir treatment, on microscopic examination of the esophageal biopsy, superficial

squamous epithelium demonstrating area of ulceration and discohesive squamous epithelial cells, some of which were multinucleated and containing prominent ground-glass nuclei (consistent with Cowdry Type B intranuclear inclusions) with margination of nuclear chromatin was revealed. These findings were found to be consistent with HSV esophagitis (Figure 1B). HSV-1 DNA was determined by PCR from biopsy material.^[6] CMV antigenemia and CMV DNA tests were negative. At that time the patient was already treated for 7 days ganciclovir. According to clinical improvement of the patient, we did not change our regime. After 14 days of ganciclovir treatment a control endoscopy was done. All ulcers were regressed significantly (Figure 2). PCR for HSV DNA was negative. The patient is still alive in a good clinical condition. The follow-up is done by our outpatient clinic.

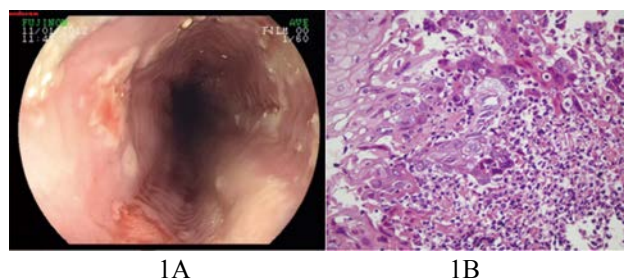


Figure 1
A. Endoscopic View of Esophagus Showing Multiple Ulcers and Erosions (Thin Arrows) Before Treatment. IB: Esophageal Mucosa With Area of Ulceration and Squamous Cells With Cowdry Type B Intranuclear inclusions, 400X, H&E.



Figure 2
Endoscopic View of Esophagus After Ganciclovir Treatment

DISCUSSION

Patients following liver transplantation are at major risk to develop both, bacterial and viral infections. HSV esophagitis may result from direct extension of oropharyngeal HSV infection into the esophagus or may occur by reactivation of HSV and spread of the virus to the esophageal mucosa via vagus nerve^[4]. Although Anti HSV IgM and IgG levels were not checked before the

transplantation, the lack of oropharyngeal lesions and the occasional detection of herpes labialis lesions before the transplantation suggested that HSV reactivation resulted from immunosuppression. It has been reported that, in the first 2-3 postoperative weeks, HSV-1 may be detected in the saliva of patients who undergo kidney, liver and bone marrow transplantations^[4]. Even if these patients are asymptomatic, mucocutaneous lesions may develop. Since the patient introduced in the present study was asymptomatic, her saliva was not investigated for the presence of HSV. The abdominal surgery that the patient had undergone due to reasons other than transplantation surgery and the reoperation that were performed due to intraabdominal hemorrhage might have facilitated vagus nerve stimulation.

If antiviral prophylaxis is used for patients who undergo liver transplantation (in order to prevent CMV infection, this prophylaxis is used together with ganciclovir or valganciclovir), the lesions can be treated without even making the diagnosis of herpes esophagitis. Our patient was already empirically treated with Ganciclovir for 7 days when we obtained the positive histopathological results for HSV. In order of the clinical improvement we did not change the treatment. The repeated endoscopy 14 days after start of treatment was clear and confirmed our proceeding. Although, it is known that acyclovir is the first line therapy in HSV, our patient was treated with Ganciclovir which was initiated for possible CMV infection. Both acyclovir and ganciclovir are deoxyquanosine analogue but ganciclovir has an additional hydroxymethyl group on the acyclic side chain. Both of drugs are also effective in HSV infection. Acyclovir is approximately 10 times more potent against HSV-1, HSV-2 than against Varicella-zoster virus and it is even less active against CMV^[7]. But ganciclovir is more toxic than acyclovir, it is generally not recommended for treatment of HSV-1 infection. Due to the specific action of Ganciclovir against CMV infections, it is natural that the drug is used in the treatment of CMV infections. However it is reported that ganciclovir has been reduced the incidence of symptomatic HSV infections after liver transplantation from 23.5% to 3.5%^[5]. The review of the literature did not reveal any previous case of a herpes esophagitis patient treated with ganciclovir. We assume that most transplant centers according to their

protocols use ganciclovir for CMV prophylaxis, which may contribute to avoid HSV infection. Subsequently it is supposed that there are no reports about HSV esophagitis in the literature. Since different transplantation centers follow different prophylaxis recommendations, an increase in *the potential prevalence of* some rare opportunistic infections occurs and some infections cannot be diagnosed. In conclusion, viral infections such as HSV esophagitis, may affect immunosuppressed patients like liver transplant recipients. This should be encountered it in term of nausea, vomiting and dysphagia after liver transplantation.

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