Case Report

Fatal hepatitis B reactivation in a patient with islet cell tumor on octreotide and sirolimus

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Abstract: Reactivation of hepatitis B viral infection (HBVr) is a known risk in cancer patients with a history of chronic hepatitis B infection receiving cytotoxic or immunosuppressive therapies. Patients with hematologic malignancies or those who have received stem cell transplantation seem to be most at risk but reactivation has been reported with various malignancies. Reactivation can present as asymptomatic liver function test abnormalities (LFTs), with symptoms of abdominal pain, encephalopathy, or as fulminant hepatitis and liver failure. Here we report the first case of a patient with islet cell tumor on octreotide and sirolimus who developed hepatitis B reactivation with fulminant liver failure and death.

Keywords: Hepatitis B; islet cell; octreotide; sirolimus; antiviral agents

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Introduction

Reactivation of hepatitis B viral infection (HBVr) is a well-recognized complication and concern for patients with chronic hepatitis B viral (HBV) infection undergoing cytotoxic chemotherapy (1-5). Patients most at risk are those who have undergone hematopoetic stem cell transplantation and/or treatment with rituximab (4,6). Here we describe the fatal case of a patient with islet cell tumor on octreotide and sirolimus who developed HBVr with fulminant liver failure and death. We believe this is the first report of HBVr in a patient treated with octreotide and sirolimus.

Case report

A 51-year-old Caucasian man from Albania with a history of islet cell tumor metastatic to the liver and spleen requiring multiple embolization procedures, most recently 2 years earlier, on treatment with octreotide and sirolimus presented to our institution with worsening fatigue, altered mental status, and 1 month of increasing liver function tests (LFTs).

The patient was first diagnosed with a pancreatic islet cell tumor 5 years prior to presentation at which time he was started on sandostatin. He had no known prior history of viral hepatitis infection. Approximately 7 months prior to presentation, he was started on sirolimus and octreotide. He was seen by his oncologist at the outpatient clinic 11 days prior to admission. At that time, his laboratory values were notable for an aspartate transaminase (AST) of 949 IU/L, alanine transaminase (ALT) of 1,217 IU/L, alkaline phosphatase of 235 IU/L, and total bilirubin of 2.0 mg/dL. His last dose of octreotide was administered 3 days later, 1 week prior to admission.

On the day of admission, he was confused and complaining of nausea and vomiting as well as weakness. He presented to the emergency department and on examination, he was alert and oriented to person, place, and time. His blood pressure was 155/78 mmHg. His LFTs were found to be AST of 670 IU/L, ALT of 1337 IU/L, alkaline phosphatase of 198 IU/L, total bilirubin of 6.4 mg/dL, and international normalized ratio (INR) of 1.9 with an ammonia level of 201 mg/dL (*Table 1*). Serologies revealed that the patient was hepatitis B surface antigen positive, surface antibody negative, core antibody positive, with a hepatitis B PCR viral load of greater than 200,000,000 copies/mL. On hospital day 2, gastroenterology was consulted and the

Table 1 LFTs results by hospital day

Lab value	Admission (HD 0)	HD 1	HD 5	HD 12	HD 14
AST (IU/L)	670	563	595	266	468
ALT (IU/L)	1,337	1,126	1,020	**	**
Alkaline phosphatase (IU/L)	198	189	188	146	172
Total bilirubin (mg/dL)	6.4	6.2	9.2	8.6	13.2
INR	1.9	2.03	1.95	1.70	1.54
Ammonia (mg/dL)	201	201	205	217	279

**, not available. LFTs, liver function tests; HD, hospital day; AST, aspartate transaminase; ALT, alanine transaminase; INR, international normalized ratio.

patient was started on 100 mg of lamivudine daily. Adefovir 10 mg daily was added on hospital day 4 because of persistent liver dysfunction.

The patient's mental status declined and he was treated with lactulose and rifaximin. Despite this intervention, his encephalopathy worsened, and he required admission to the intensive care unit. Increased dosage of lactulose and the addition of neomycin were ineffective; the patient continued to have neurologic deterioration. An emergent computerized tomography (CT) scan of the head was negative for acute pathology. A liver transplant team was contacted at another institution for consideration for orthotopic or heterotopic liver transplant. Due to the patient's active malignancy, he could not be considered as a transplant candidate. The patient developed worsening hypoxemia requiring intubation as well as hypotension and oliguria. Given his poor prognosis and multiorgan failure, the patient's family elected to pursue comfort care. A do not resuscitate (DNR) order was placed, and the patient expired on hospital day 14.

Discussion

We believe this is the first reported case of hepatitis B reactivation in a patient treated with sirolimus and octreotide.

HBVr is a known risk in cancer patients with a history of chronic HBV infection receiving cytotoxic or immunosuppressive therapies (7). HBVr can present as asymptomatic ALT elevation, or with sequelae of hepatitis including abdominal pain, encephalopathy, or fulminant hepatitis and liver failure (2). Without adequate immunosurveillance, latent virus replicates in hepatocytes leading to the clinical signs and symptoms of reactivation (7).

The risk of HBVr is well described in the literature with rituximab and bone marrow transplant where rates of reactivation may range from 38.5% to 54% (1,2,5,8-15). However, the risk still exists in patients with solid tumor malignancies or on other immunomodulators such as tumor necrosis factor α inhibitors (7,16-20). Despite this variation in risk, the morbidity and mortality associated with HBVr may be significant, as was the case in this patient.

Antiviral prophylaxis in seropositive patients results in a lower incidence of hepatitis and HBV reactivation (8,21,22). The available data suggests that had this patient been screened, effective antiviral prophylaxis would have prevented HBVr and the subsequent unfortunate clinical course. Although antiviral therapy was administered in this patient day 2 of presentation, therapy likely was initiated too late to change the outcome.

In 2008, the US Centers for Disease Control recommended HBV screening for all patients prior to beginning immunosuppressive therapy (2,23,24). Universal screening for hepatitis B would allow patients such as this one to be effectively prophylaxed against HBVr prior to treatment with immunosuppressive therapy (4,25,26).

This case suggests that a wide range of chemotherapy regimens and malignancies carry a risk of hepatitis B reactivation. Universal screening and appropriate prophylaxis should be considered by oncologists regardless of the primary malignancy or planned immunosuppressive regimen in order to prevent morbidity and mortality associated with fulminant liver failure.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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