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CASE REPORT | LIVER

A Case of Non-Cirrhotic Portal Hypertension Associated With Chronic Didanosine Therapy

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Abstract

A 66-year-old man with HIV and recurrent thromboembolism presented with new-onset ascites with an extensive diagnostic work-up that was unremarkable. He was diagnosed with non-cirrhotic portal hypertension after a liver biopsy revealed mild fibrosis and hepatic venography revealed an elevated hepatic venous pressure gradient. The etiology of portal hypertension was attributed to didanosine therapy, a rare but noted side effect.

Introduction

Portal hypertension is typically attributed to the presence of underlying cirrhosis, though, in rare cases, may result from alternate pathologies. This phenomenon, known as non-cirrhotic portal hypertension (NCPH) can arise from idiopathic portal hypertension, extrahepatic portal venous thrombosis, schistosomiasis, veno-occlusive disease, and congenital hepatic fibrosis.

Case Report

A 66-year-old white man with HIV, on treatment for 20 years, presented with several months of progressive abdominal distention and early satiety. He suffered from recurrent deep venous thromboembolism and pulmonary embolism for which an inferior vena cava (IVC) filter had been placed. His medications included tenofovir, didanosine, and nevirapine for several years, and chronic anticoagulation with coumadin. He had no significant alcohol use.

His examination showed a protuberant abdomen with a fluid wave, shifting dullness, and a palpable spleen. Laboratory values revealed normal electrolytes, renal function, hemoglobin, and white blood cell count. His platelet count was 110,000 U/mL. His hepatic panel revealed an alanine aminotransferase (ALT) 24 U/L, aspartate aminotransferase (AST) 43 U/L, bilirubin 0.4 mg/dL, alkaline phosphatase 157 U/L, total protein 5.9 g/dL, and albumin 3.3 g/dL. His international normalized ratio (INR) was 1.8 (on coumadin therapy). His CD4 count was 278 cells per mm^3 and HIV viral load was undetectable.

A Doppler ultrasound and abdominal computed tomography (CT) revealed ascites, but was otherwise normal. A diagnostic paracentesis revealed a serum ascites–albumin gradient of 1.5 g/dL with a total protein of 2.7 g/dL. Chest

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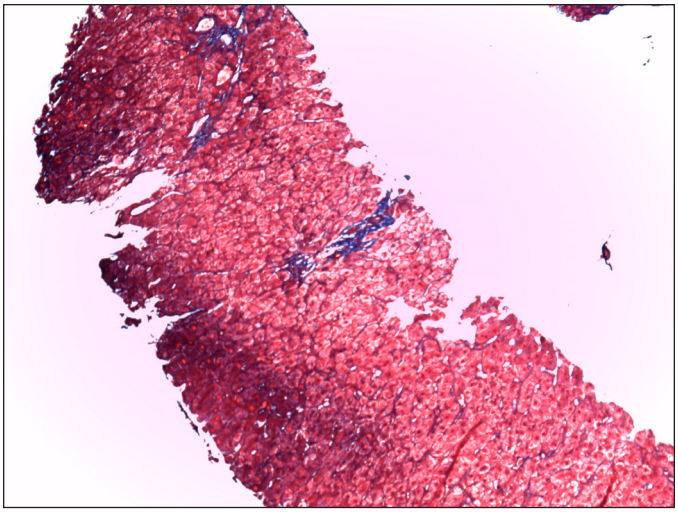

Figure 1. Liver biopsy with portal hypertension. Histology with trichrome staining revealed mild fibrosis (seen in blue) around the edges of the portal tracts, without evidence of bridging fibrosis or cirrhosis.

radiograph and echocardiogram were normal. A chronic liver disease work-up was negative, including hepatitis B surface antigen, hepatitis B surface antibody, hepatitis B core antibody, anti-hepatitis C virus antibody, antinuclear antibody, anti-mitochondrial antibody, anti-smooth muscle antibody, iron studies, α-1 antitryspin phenotype, and ceruloplasmin. Stool examination did not show evidence of schistosomiasis. Acid-fast bacilli culture and smear of the peritoneal fluid and quantiferon-gold testing was negative.

A transjugular liver biopsy revealed a hepatic wedge pressure of 26 mm Hg, free hepatic vein pressure of 12 mm Hg, hepatic venous pressure gradient (HVPG) of 14 mm Hg, and mild perisinusoidal fibrosis without bridging fibrosis, confirming the diagnosis of NCPH (Figure 1).

Discussion

In the United States, cirrhosis accounts for 85% of cases of ascites.[1] Multiple etiologies, including heart failure, peritoneal carcinomatosis, nephrotic syndrome, tuberculosis peritonitis, and Budd-Chiari syndrome, comprise the remaining 15%, with NCPH being quite uncommon. This case was unique given the variety of risk factors that made alternative etiologies of ascites possible (i.e., history of recurrent blood clots, presence of IVC filter, and history of HIV). To confirm NCPH, one must have clinical signs of portal hypertension with patent hepatic vasculature on imaging, the exclusion of cirrhosis on biopsy, and exclusion of other causes of liver disease on laboratory work-up.[2]

Didanosine is an antiretroviral agent frequently used as part of highly active antiretroviral therapy (HAART). NCPH is an increasingly seen complication associated with didanosine exposure,[3-6] which has led the Food and Drug Administration to update the labeling of the drug. While the mechanism by which didanosine causes NCPH is not known, it may be caused by depletion of intracellular glutathione with subsequent death of sinusoidal endothelial cells. A potential genetic predisposition and causal effect of duration of didanosine therapy have been implicated in its pathogenesis. A large case-control study performed in the Netherlands has implicated tenofovir when issued concomitantly with didanosine to an increased risk of NCPH.[4] Management involves cessation of the causative drug and treatment of portal hypertension-related sequela.[5-6]

Disclosures

Author contributions: M. Stotts wrote and edited the manuscript. P. Chisholm assisted with data collection, including images. D. Nurutdinova provided writing and editing assistance. H. Maddur wrote and edited the manuscript, and is the article guarantor.

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