Interferon Therapy for Chronic Hepatitis Delta Viral Infection

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Introduction

Hepatitis delta virus (HDV) is an RNA deltavirus that infects human hepatocytes, causing significant damage to the liver. The replication of HDV depends upon a simultaneous infection with the Hepatitis B virus (HBV), and thus, HDV is a much more severe infection than HBV alone.[1,2] HDV infections can be of the acute or chronic form; acute infections are rare and manifest from a coinfection with HBV, while chronic HDV develops as a result of superinfection of HDV with a hepatitis B surface antigen carrier (HBsAg).[2] Chronic HDV infections manifest as a rapidly progressing form of viral hepatitis which can lead to cirrhosis with an increased risk of hepatocellular carcinoma.[3] Currently, HDV has no approved treatment options from the United States Food and Drug Administration, and the recommended therapy of pegylated interferon alpha has yielded only fractionally effective results.[3] We present a patient that undergoes interferon therapy for chronic hepatitis delta infection with an emphasis on efficacy and side effects of treatment.

Features of Hepatitis B & Hepatitis Delta Viruses[4]

Hepatitis B Virus	Hepatitis Delta Virus
• Partially double stranded, circular DNA virus • Parenteral, sexual, and perinatal transmission • Long incubation period (months) • Cytotoxic T cell mediated hepatocyte damage • Increases risk for hepatocellular carcinoma • Carrier state is common	• RNA deltavirus • Parenteral, sexual, and perinatal transmission • Short incubation period for superinfection, long incubation period for coinfection • Cytotoxic T cell mediated hepatocyte damage • Increases risk for hepatocellular carcinoma • Depends upon HBsAg coat for infectivity

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Case Description

A 20 year old previously healthy African male presents with progressive fatigue. Bloodwork demonstrates elevated liver enzymes, thrombocytopenia, positive Hepatitis B surface antigen and core antibody, and is negative for hepatitis B e-antigen. HBV DNA levels are 30 IU/mL (reference range <10 IU/mL).

Six months later, liver enzymes remain elevated (AST 100 U/L, ALT 186 U/L). Liver biopsy confirms chronic hepatitis and moderate fibrosis with Metavir grade A3, stage F2, and is consistent with viral hepatitis infection. The biopsy also reveals schistosomiasis of the liver, for which the patient is treated with two series of Praziquantel 1800 mg, three times daily. Schistosomiasis resolve following treatment, yet liver enzymes remain elevated. Subsequent bloodwork is positive for HDV, with very high levels of HDV RNA at 14,000,000 IU/mL.

The patient is started on tenofovir 300mg/day and peginterferon 180 mcg/week. This therapy is maintained for over 4 years, with limited side effects of headache and fatigue noted during the 48 hours post injection. Liver biopsy near the end of treatment course reveals mild portal inflammatory infiltrate composed predominantly of lymphocytes with scattered foci of lobular inflammation; Metavir grade 1, stage 0. Bloodwork at this time shows improvement in liver enzymes with AST 57 U/L and ALT 39 U/L. Patient stopped interferon due to side effects after four years of suppressive treatment. The most recent bloodwork shows HBV and HDV viral suppression via PCR, and negative Hepatitis B surface antigen. Liver surveillance via ultrasound reveals no evidence of hepatocellular carcinoma during the duration of therapy.

Discussion

Hepatitis delta virus (HDV) is a blood-borne virus that infects human hepatocytes; the replication of HDV depends upon a simultaneous infection with Hepatitis B virus (HBV). Chronic HDV infections manifest as a rapidly progressing form of viral hepatitis which can lead to cirrhosis with an increased risk of hepatocellular carcinoma. Hepatitis Delta Virus is estimated to affect 42-78 million people worldwide, and yet, is still without an efficacious treatment option.[3,5] Currently, pegylated interferon alpha is the only recommended treatment for HDV infections, but has been found to be fractionally effective with a host of adverse side effects including hematologic changes, neuropsychiatric disturbance, and influenza-like symptoms.[3,5]. Even with the potential for low efficacy and many side effects, patients may choose to undergo interferon treatment to prevent the severe liver damage caused by HDV. On the contrary to the trends in the current literature, the patient in this case report had an effective course of treatment with pegylated interferon alpha therapy with a mild side effect profile, including only headaches and fatigue noted in the first 48h post injection. Moreover, the combination of treatments that this patient received resulted in HBV and HDV viral suppression. This suppression was sustained over at least two months following the original suppression in viral DNA. Our case provides unique insight into the efficacy and side effect profile of pegylated interferon alpha treatment for chronic HDV infection.

References

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