

Epstein-Barr Viral Hepatitis: An Unusual Case of Scleral Icterus in an Adolescent

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OBJECTIVE

To present a case of liver disease with cholestatic features secondary to Epstein-Barr virus

INTRODUCTION

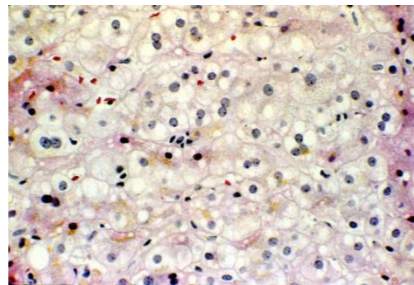
Primary Epstein-Barr virus (EBV) infection in children is typically asymptomatic with seroconversion. If primary infection occurs in adolescence or adulthood, the most common manifestation is infectious mononucleosis, with symptoms of fever, lymphadenopathy, hepatosplenomegaly, and pharyngitis. Although mild and transient elevation of serum aminotransferases is common, jaundice is uncommon and complete recovery is the rule. Cholestatic liver disease presenting with an elevation of serum alkaline phosphatase and bilirubin is rare, with the mechanism unclear. EBV has no direct cytotoxic effect on hepatic cells, yet destruction is caused by the toxic action of free radicals through lipid peroxidation. Patients with Epstein-Barr virus have autoantibodies directed against enzyme superoxide-dismutase which neutralizes the enzyme's antioxidant action. As a result, free radicals accumulate in hepatic cells and cause damage. Rarely, this results in hepatic failure and severe jaundice.

CASE PRESENTATION

An 18-year-old Latino male with no significant past medical history presented with diffuse abdominal pain and fever of 8 days duration. He had no history of smoking or alcohol abuse, and no family history of liver disease. He noted recent sexual intercourse with a new partner. He had no recent travel, with travel to Mexico one year prior. His family had recently acquired a stray dog. On admission, he demonstrated scleral icterus, mild jaundice, left anterior cervical lymphadenopathy and inguinal lymphadenopathy, hepatomegaly, and right upper quadrant tenderness. The liver function tests reported aspartate aminotransferase 253 IU/L, alanine aminotransferase 373 IU/L, alkaline phosphatase 181, and total bilirubin 3.7. Abdominal ultrasound demonstrated splenomegaly. A hepatitis panel with serology for hepatitis A, B, and C was negative. Flow cytometry for leukemia and lymphoma was negative. Serology for Epstein-Barr virus and parvovirus were positive. Serum PCR for EBV was 10,500 copies/mL and parvovirus PCR was negative. A liver biopsy demonstrated lymphocytic inflammation consistent with EBV hepatitis.

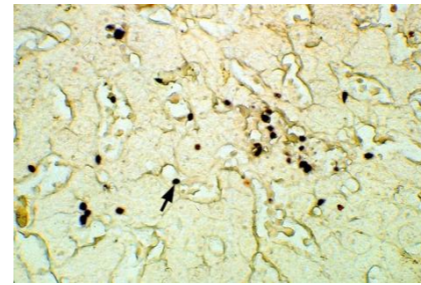
DIAGNOSIS

EBV is not commonly confirmed as an etiologic agent of acute hepatitis, with infection confirmed via serology (heterophile or specific antibodies) or immunofluorescence and molecular biologic techniques to confirm the presence in biopsy specimen. The EBV-specific serology can initially be negative in patients who have been ill for only a few days. However, within 1-2 weeks, antibodies to EBV-specific antigens appear at the expected titers.



(A)

(A) Low grade mononuclear lobular inflammation, typical of EBV-related hepatitis, like that seen in the general population with hepatitis related to infectious mononucleosis. Note the slight increase in sinusoidal lymphocytes and "indian-filing" along the sinusoids.

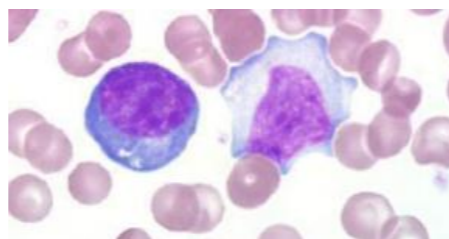


(B)

(B) In situ hybridization for EBV EBER RNA. In this photomicrograph, note the nuclear staining of the lymphocytes scattered within the sinusoids [arrow].

TREATMENT

Treatment for primary Epstein-Barr viral hepatitis is usually supportive as it is generally self-limiting. Steroids and antiviral medications have been utilized to treat cases of severe viral hepatitis. Acyclovir has not been shown to be efficacious in the treatment of severe EBV hepatitis. There are case reports on the use of ganciclovir in immunocompetent patients with severe viral hepatitis. However, randomized studies have not been performed for these treatments. In our case, our patient soon recovered with only conservative treatment.



REFERENCES

Kang, M et al. Infectious Mononucleosis Hepatitis in Young Adults: Two case Reports. The Korean Journal of Int Med. Vol 24, Num 4, December 2009: 381-387

Kofteridis, D et. al. European Journal on Int Med. 22, 2011" 73-76

DISCUSSION

We should consider Epstein-Barr viral hepatitis in differentiating patients presenting with liver abnormality, fever, pharyngitis, and lymphadenopathy.

HISTORY

The classic presentation is that of fever, oropharyngitis, and lymphadenitis. Hepatosplenomegaly may also be present. In a small percentage of patients, jaundice and scleral icterus occur.

PHYSICAL EXAM

Physical exam frequently reveals lymphadenopathy, most common in the cervical chain as well as axilla. Frequently, there is tonsillar enlargement with injection. Splenomegaly is also present. Rarely, patients will present with jaundice as well as scleral icterus due to the presence of increased levels of bilirubin.

DIAGNOSTIC TESTS

Diagnosis primarily relies on the clinical presentation with a high index of clinical suspicion, supported by laboratory findings:

- Atypical lymphocytes
- Aminotransferases
- Bilirubin
- EBV IgM antibodies
- Heterophile antibody test
- Negative serology for
 - Hepatitis A, B, C
 - HIV
 - CMV
 - Varicella zoster
 - Herpes simplex virus
- Serum PCR
- Pathology
- Immunofluorescence
- Molecular techniques, e.g. in situ hybridization

TREATMENT

- Supportive
- Steroids
- Antiviral medications
 - Acyclovir without proven efficacy
 - Case reports of ganciclovir
- Transplantation if fulminant hepatic failure