

Acute Liver Failure: due to Epstein Barr Virus infection- A Case Report

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Abstract

Acute Liver failure (ALF) can be defined as recent and acute (<8 weeks) onset alteration of liver function in a previous healthy liver with coagulopathy with or without the presence encephalopathy. Prominent causes world wide includes drug induced ALF, viral hepatitis, autoimmune liver disease, shock and hypoperfusion. Most common cause of ALF in developing world is viral hepatitis (A,E) either alone or in combination but rarely infection with other hepatotropic virus like Epstein Bar Virus(EBV) can present with acute liver failure. Here, we present a case of 2 years old boy admitted with acute liver failure due to complication of EB Virus infection.

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Introduction

EBV, a DNA virus of herpes family is the cause of infectious mononucleosis (glandular fever) with typical manifestation of fever, exudative pharyngitis, lymphadenopathy, hepatosplenomegaly and atypical lymphocytosis. EBV infection is common world wide and is often asymptomatic with mild self limited hepatitis in 80-90% cases. Less commonly, complications such as hemolytic anemia, aplastic anemia, splenic rupture, encephalitis and acute liver failure can occur [1]. It mainly causes symptomatic illness in the adolescents and young adults. ALF as a complication of EBV in pediatric population is extremely rare [1]. Our proband, a 2 year old immunocompetent boy presented with features of fever, rash, lymphadenopathy and ultimately developed ALF and succumbed.

Case Report

A 2 year old boy was admitted with h/o fever for 10 days, progressive maculopapular erythematous rash from day 2 of fever with anasarca for 3 days and high coloured urine for 3 days. There was no h/o drug intake including natural supplements or bleeding from any orifices.

On admission, he was toxic, irritable, GCS 11/15, H/R -120/min, R/R-35/min. BP-90/60 mmHg. He had marked icterus with bilateral cervical lymphadenopathy with generalized pitting edema (Figure 1).

There was 5cm hepatomegaly in right MCL. There was no neurological deficit & DTRs were normal. Initial reports showed Hb -9.6gm/dl ,TLC-16,200/cmm , -2,64,000/cmm, CRP-15.5 mg/

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L(normal <6), normal RFT, deranged LFT with Bil (T)-6.02 mg/dl, Bil (D)- 5.14mg/dl, Bil (I)-0.88 mg/dl, SGOT-46 IU/L, SGPT-569 IU/L, PT-22.4 seconds and INR-2.10. Peripheral smear showed atypical lymphocytes (42%). Tests for malarial antigen, HBsAg, Widal, Anti HAV IgM, Anti HCV IgM, Anti HEV IgM, HLH profile were negative. Autoimmune profile, A1AT were also negative. Serology for EBV was sent which came out to be positive with EBV VCA IgM >1:20 and EBV VCA IgG 1:600. PCR was done which revealed viral load of >100,000. He was shifted to PICU and managed conservatively with fluids, vitamin K, antibiotics, N-Acetyl Cysteine infusion, blood product transfusion. Liver biopsy could not be done as coagulation profile was abnormal and remained so even after giving vitamin K and FFP.

But even after all the measures taken, he gradually deteriorated, liver function further worsened. Eventually he developed refractory hypoglycemia, hypotension, grade IV encephalopathy, uncontrollable bleeding and expired after 7 days of PICU stay.

Discussion

The classic triad of EBV infection i.e fatigue, lymphadenopathy, and pharyngitis as seen in 30-50% cases of adolescents and adults may not be much apparent in children as primary infection



Figure 1 He had marked icterus with bilateral cervical lymphadenopathy with generalized pitting edema.

with EBV during childhood is usually asymptomatic or mild and indistinguishable from other viral infections of childhood. The most dreaded but less common complications of EBV are splenic rupture, encephalitis and ALF. Primary EBV infection accounts for <1% ALF but is associated with high case fatality rate [1].

In adults, EBV induced hepatitis is quite common but is mild and self limiting, although ALF has been reported world wide with an overall mortality of 85% [2].

The pathogenesis of EBV infection associated with ALF is not clearly known but 2 proteins (BRF1 and BARF1) may help the virus to evade the host's immune system. It has also been postulated that high concentrations of enzyme inhibiting auto-antibodies against the antioxidative enzymes, manganese superoxide dismutase (MSD) may play a role in the pathogenesis. Once this virus enters the host it causes liver injury which is primarily caused by the intense host response elicited by virus. This cellular response is composed of NK cell activity, cytotoxic /suppressor cells, and antibody dependent cellular cytotoxicity (ADCC) [3].

In the index case, all the classic pictures of EBV-IM with ALF were present. The initial clinical picture of persistent fever, rash and lymphadenopathy was complicated by progressing jaundice, coagulopathy and encephalopathy was suggestive of a fulminant ALF caused by EBV that was further substantiated by a positive EBV serology and a huge viral load. CNS involvement in the form

of encephalopathy may be due to EBV infection or secondary to hepatic encephalopathy. The exact reason of encephalopathy is very difficult to make out but whatever may be the reason, it carries a poor prognosis.

Feranchak et al. in their article reported 17 cases of hepatic failure with EBV infection before 1998 in all age groups including 9 cases in children below 15 years of age, with only 3 survivors [4]. Among these most of them were treated with steroids and one with liver transplantation (OLT). Another case series from 1998-2012 done by USALFSG in adults ALF patients showed among 1,887 patients, four were diagnosed with EBV related ALF, out of which two died, one survived with supportive measures and one underwent liver transplant [1]. All other series and case reports also revealed very high mortality in EBV associated ALF with all sorts of conservative therapy and here comes the option of liver transplant if the patient has poor liver function and not responding to conservative management but it has its own hazards. Firstly, it has to be done in expertise hands, secondly post transplantation serious complications like lymphoproliferative disease (common in children) and B-cell lymphoma can occur. Therefore, outcome even after transplantation cannot be explained and reported cases are few. Thirdly, a long follow up has to be done which is cumbersome and we may lose patient especially in developing countries like, India and the most important is that the proper infrastructure is definitely lacking. There has been a case report of a ten year old girl in Iran in the year 2012 with EBV-related secondary HLH where prognosis remain uncertain but Rituximab may be a useful treatment for decreasing mortality [5]. Another case report from Brazil showed that EBV related HLH all had very severe initial clinical presentations and required immunochemotherapy to control signs and symptoms [6].

As already mentioned, liver injury in EBV is immune mediated and stimulated T cells results in increased serum levels of IL-2, TNF- α , IFN- γ , but role of immunomodulators is still unknown. A study has revealed that even with remission of symptoms recurrences are very common as sudden withdrawal of these agents results in immunological rebound and carry a poor prognosis. Even role of antiviral agents is doubtful as it decreases viral replication and oropharyngeal shedding during the administration but does not reduce the severity or duration of symptoms or alter the eventual outcome. Steroid use is of unproven benefit and there are reports of encephalitis and myocarditis and secondary bacterial infections can occur. We were not able to save our patient despite all the efforts but a transplant might have changed the outcome.

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