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CASE REPORTS

ACUTE LIVER FAILURE IN A CHILD DUE TO EPSTEIN BARR VIRUS AND RESPONSE TO ANTIVIRALS

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ABSTRACT
Acute liver failure (ALF) with coagulopathy and encephalopathy is a dreaded condition and a medical emergency that occurs due to acute alteration of liver function in a previously healthy liver. Most common cause of ALF in the developing world are viral hepatitis A and E. Other causes are drugs, autoimmune disease, metabolic disorders and hypoperfusion. Rarely Epstein Barr virus (EBV) hepatitis can lead to ALF with high mortality. We present a 3-year-old boy with ALF due to EBV infection who responded to antivirals.

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Liver failure, coagulopathy, encephalopathy, Epstein Barr virus, mutism

Introduction

Epstein Barr virus (EBV) is a common human herpes virus which infects most of the world population. Though often asymptomatic, clinical manifestations ranging from infectious mononucleosis to lymphocytic cancers have been reported.[1] Serological diagnosis is done by immunofluorescence, ELISA, or western blot.[2] ALF is a rare clinical syndrome associated with EBV infection, but results in high case fatality.[3] We present a 3 years old boy who was diagnosed with EBV induced hepatitis with encephalopathy who responded to antivirals.

Case Report

A 3-year-old boy was hospitalized with cough and cold followed by fever on second day which increased gradually and responded incompletely to injectable medications in an outlay hospital. On day 5, the child complained of pain in abdomen, irritability and decreased oral intake which worsened over the next 24 hours leading to lethargy. The child was taken to a nearby hospital where abnormal movements were noticed, and the child was referred to our hospital. On admission, the child was incoherent, irritable with Glasgow coma scale (GCS) 8/15, had intermittent posturing, was febrile (temperature 99.5°F) with heart rate 170/min, blood pressure 60/44 mm of Hg, delayed capillary refill time & cold extremities. Liver and spleen were not palpable. There were no rash or lymphadenopathy. Other systems were normal. Initial investigations showed hypoglycemia (blood sugar 28 mg/dl) and venous blood gas showed metabolic acidosis (ph 7.2, bicarbonate 16 mEq/L). In view of poor GCS, the patient was intubated & ventilated. Hemodynamic monitoring was started, hypoglycemia was corrected and fluid resuscitation for shock was done. Initial reports showed neutrophilic leukocytosis (white cell count 18000 cells/cumm with neutrophils 83%) hemoglobin 8.3 gm/dl, platelet count 120,000/cumm, raised CRP (6.5 mg/dl), deranged liver function test (SGOT 25804 IU/L, SGPT 15572 IU/L, bilirubin 2.5 mg/dl, albumin 2.7 gm/dl), prothrombin time 46.8 sec (control 13.3 sec), INR 5.12, hyperammonemia (serum ammonia 357 mcg/dl), serum creatinine of 0.4 mg/dl, serum sodium 136 meq/L, potassium 3.7 meq/L. Serology for dengue NS1, malaria rapid antigen test and peripheral blood film, Hepatitis A IgM, Hepatitis B IgM, HIV ELISA and scrub typhus IgM were negative. Serum ferritin (168 ng/ml) and triglycerides (128 mg/dl) were normal. EBV viral capsid antigen (VCA) IgM was positive [4 ndx (normal <1ndx)]. Ultrasound (USG) abdomen showed gallbladder edema. Echocardiography was normal. EEG showed a diffuse 1-2 Hz delta rhythm with loss of anterior to posterior gradient with slowing on the right side suggestive of encephalopathy. Intravenous (IV) acyclovir (10 mg/kg/dose 8 hourly) was given for 10 days. With continued treatment (including IV fluids, multivitamins, L-ornithine- aspartate lactulose, levetiracetam, piperacillin- tazobactam), the patient's condition improved gradually, and he was weaned off the ventilator after 5 days. Coagulation parameters, liver function test and ammonia showed a gradual decline (Table 1). MRI brain showed subtle right frontal infarct. The child became hemodynamically and neurologically stable. But mutism and upper limb weakness persisted which showed gradual improvement on follow up.

Discussion

EBV induced infection can manifest from being asymptomatic to severe cancers. Common presentation is a triad of pharyngitis, lymphadenopathy and fatigue which is more common in adolescents than pediatric age group. In patients with solid organ transplant, EBV can lead to autoimmune as well as malignant manifestations.[2] Fatal complications are reported in the form of splenic rupture, encephalitis, and acute liver failure.[3]

Liver injury in EBV infection is postulated to be caused by dysregulation of the immune system with autoantibodies inhibiting antioxidative enzymes. Roles

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Table 1. Serial liver function tests and serum ammonia

	Day 1	Day 3	Day 5	Day 7	Day 9	Day 11	Day 13	Day 15	Day 22
SGOT (IU/L)	25804	23527	15498	6592	832	417	293	226	128
SGPT (IU/L)	15572	13512	8734	5945	2091	1083	471	428	173
Ammonia (mcg/dl)	357	231	157	64	60	42	27	31	26
INR	5.12	4.3	4.0	3.15	3.12	2.36	1.8	1.2	0.8
Bilirubin (mg/dl)	2.5	2.1	2.4	2.2	1.9	1.4	1.2	0.7	0.3

of NK cells, cytotoxic T cell, interleukin (IL)-2, tumor necrosis factor (TNF)-alpha has also been proposed but none of them are clearly elaborated.[4] In adults, EBV induced hepatitis is quite common but usually mild and self limiting with <1% cases landing into ALF.[3,5] Although splenomegaly is more common than hepatomegaly in EBV infection, it was not seen in our patient.[6] Feranchak et al reported 17 cases of EBV induced hepatic failure out of which 9 patients were below 15 years of age, with only 3 survivors.[7] US Acute Liver Failure Study Group studied 1,887 patients of ALF, EBV was as a cause in 4 of them and 2 of them survived.[3] ALF with EBV has been reported in a 2 years old boy with initial manifestation of fever, rash, anasarca, and high colored urine, but he gradually succumbed to complications like hypoglycemia, hypotension and encephalopathy.[8]

Supportive measures, steroids and liver transplant has been the frontline modalities of treatment.[3] Despite steroids like prednisolone[8], antivirals like acyclovir[8], immunomodulators like IL-2, interferon alpha and liver transplant being modalities for treatment of EBV induced ALF, none has been established as gold standard.[7] Various antivirals like nucleoside analogues (acyclovir), nucleotide analogue (cidofovir), pyrophosphate analogue (Foscarnet) have been tried for EBV treatment but none has proved to be the drug of choice probably due to the fact that the symptoms and signs of the disease are not the consequences of viral replication but the immunological response to EBV-infected B-cells that circulate in the blood and infiltrate the tissues of different organs.[9] Newer anti EBV compounds and modalities like inhibitors of EBV protein kinase BGLF4, inhibitors of EBV DNA polymerase, inhibitors of EBV nuclear antigen 1, antivirals targeting cellular events, lytic induction therapy are under trial.[9]

In our patient, conservative and symptomatic management with addition of acyclovir led to improvement.

Compliance with Ethical Standards

Funding None

Conflict of Interest None

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