Case Report

Liver Abscesses and Hyper IgM Syndrome

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Abstract

Hyper IgM (HIGM) syndrome is an immunodeficiency that can lead to liver disease in more than 80% of affected males by an age of 20 years. Hepatitis, sclerosing cholangitis, and hepatocellular malignancies are common among them. We encountered two cases in children of less than 12 years who presented with typical manifestations of liver abscess and were later detected to have a concomitant underlying HIGM syndrome.

Key words: Children, hyper IgM, liver abscess

Introduction

Liver abscesses are frequently observed in pediatric clinical practice in tropics and subtropics especially in developing countries. Children with liver abscesses constitute more than 79 per 1 lakh pediatric admission in India.[1] Most of the liver abscesses in children are pyogenic in nature with amebic liver abscesses constituting 21-30% of cases.[2] Among cases of pyogenic liver abscesses, staphylococcus is a leading cause in most series.[3] Fungal hepatic microabscesses either alone or in association with splenic microabscesses may occur in children with leukemia and immunodeficiency.[2] Tubercular[1] and typhoid[4] liver abscesses are also known.

Chronic granulomatous disease, hyper IgE syndrome, and C1 complements deficiencies are also known to be associated with liver abscesses.[5] Hyper IgM syndrome (HIGM) can present with recurrent staphylococcal abscesses of skin, lungs, joints, bones, and viscera. There are case reports available showing associations of HIGM syndrome with sclerosing cholangitis but none with liver abscesses.[6,7] Here, we have reported two cases presented to us with liver abscesses and later on found to have underlying HIGM syndrome.

Case Reports

Case 1

A 5-year-old boy presented with recurrent fever for 1.5 months and intermittent pain in right hypochondrium along with vomiting for 1 month. On examination, he had tender hepatomegaly and pallor. Investigations showed multiple small hypodense lesions in the liver suggestive of microabscesses. His investigations showed hemoglobin 8.8 gm/dL, WBC count 17,400/mm^3, platelet count 438,000/mm^3, bilirubin 0.8 mg/dL, SGOT 102 IU/L, SGPT 68 IU/L, total proteins 5.5 gm/dL, and albumin 2.4 gm/dL. Stool showed cysts of *E. histolytica* and blood culture did not grow any organism. HIV ELISA was negative. He was treated with IV piperacillin/metronidazole and oral chloroquine for 10 days but had no response. He subsequently had a drop in hemoglobin level along with leukocytosis (34,500/mm^3) and thrombocytopenia for which he received 5 units of blood transfusion and antibiotics were changed to vancomycin and ceftazidime. He also developed ascitis and ascitic fluid showed 1920 cells/mm^3 (80% polymorphs, 20% lymphocytes). Urine examination showed presence of fungal hyphae and child was treated with amphotericin B. In view of severe infections, he was tested for immunodeficiencies. His HIV ELISA was negative and serum immunoglobulins showed low serum IgG (530 mg/dL (normal = 971-1746 mg/dL)), normal IgA (104 mg/dL (normal = 75-178 mg/dL)), and high serum IgM (183 mg/dL (normal = 66-153 mg/dL)). Nitroblue tetrazolium (NBT) test was normal. Patient responded to above therapy and is currently asymptomatic.

Case 2

A 6-year-old girl presented with fever for 5 days and pain in right hypochondrium for 3 days. There was no jaundice or vomiting. On examination, she had a tender hepatomegaly. Other systems were normal. Investigations showed hemoglobin 6.9 gm/dL, WBC count 57,300/mm^3, platelets 290,000/mm^3,

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SGOT 39 IU/L, SGPT 28 IU/L, total proteins 7.9 gm/dL, albumin 2.9 gm/dL, and deranged prothrombin time and partial thromboplastin time. Ultrasound of abdomen showed abscess (size 6 × 5 × 4 cm) in right lobe of liver. Blood culture was negative. Child was treated with IV antibiotics: Ceftraixone and cloxacillin for 1 month and surgical drainage of abscess was done; subsequently, patient was given oral cloxacillin and cotrimoxazole for another 2 months and ultrasound showed complete resolution of abscess. Her HIV ELISA was negative and serum IgG was low (620 mg/dL (normal = 971-1746 mg/dL)), serum IgA was normal (118 mg/dL (normal = 75-178 mg/dL)), and serum IGM was elevated (229 mg/dL (normal = 66-153 mg/dL)). Her Nitroblue tetrazolium (NBT) was normal.

Discussion

HIGM syndrome is a primary immunodeficiency characterized by normal or elevated serum IgM levels associated with low or absent IgG, IgA, and IgE serum level; indicating a defect in class-switch recombination (CSR) process.[8] Causative mutation have been identified in two genes on the X-chromosomes; the CD40 ligand[9] localized on Xq26 which causes HIGM type 1 (HIGM1); and NEMO (nuclear factor KB (NF-KB) essential modulator)[10] genes and 3 genes on autosomal chromosomes – the AICDA (activation-induced cytidine deaminase) genes on chromosome 12, the uracil DNA glycosylase (UNG) gene on chromosome 12, and CD40 gene (HIGM type 3 - HIGM3) on chromosome 20 which cause HIGM type 2 (HIGM2).[10]

In X-linked HIGM syndrome, boys present with very small tonsils, no palpable lymph nodes, and often profound neutropenia. Mutation in CD154 (gene product) results in inability to signal B cells to undergo isotype switching and thus the B cells produce only IgM. Patient becomes symptomatic during the 1st or 2nd year of life with recurrent pyogenic infections including otitis media, sinusitis, and pneumonia. There is increased incidence of extensive verruca vulgaris, cryptosporidium enteritis, and malignancies. In a study of patients with the CD40 ligand defect, 23.3% had died at mean age of 11.7 year.[9]

Autosomal recessive HIGM patients usually have normal number of circulating B lymphocytes. However, in contrast to patients with CD40 ligand defect, B cells from these patients are not able to switch from IgM secreting to IgG, IgA, and IgE secreting cells; even when co-cultured with monoclonal antibodies to CD40 and variety of cytokines. Thus, in these patients, there is truly an intrinsic B cell abnormality. Patient with autosomal recessive HIGM2 syndrome usually have lymphoid hyperplasia, are generally older at age of onset, do not have susceptibility to *Pneumocystis carinii* pneumonia (PCP),[6,7] often do have isohemagglutinins and are much less likely to have neutropenia unless it occurs on an autoimmune basis. They have tendency to develop autoimmune and inflammatory disorders including diabetes mellitus (DM), polyarthritis, autoimmune hepatitis, hemolytic anemia, immune thrombocytopenias, Crohn's disease, and uveitis. With early diagnosis and monthly infusion of immunoglobulins, patients with AICDA mutation syndrome generally have more benign course than do boys with CD40 ligand defects.

Liver disease, a serious complication of HIGM1 was observed in more than 80%[6,11] of affected males by age of 20 years. Among these, hepatitis and sclerosing cholangitis are frequent and may or may not result from an identifiable infectious agent. Malignancies of liver like hepatocellular carcinoma, bile duct carcinoma, and adenocarcinoma of liver are common complications in adolescent and young adults and account for approximately 25% of mortality associated with HIGM1.[6,11] There are no case reports showing association of HIGM with liver abscesses.

Since our patients presented with multiple liver abscesses which required prolonged antibiotics, so immunodeficiency workup was done and they were found to have elevated IgM levels with low IgG. We were unable to do genetic as well as CD40 ligand studies on them.

In conclusion, high index of suspicion of a probable immune deficiency status in patients with liver abscesses will improve the detection rate of immunodeficiency and help in appropriate management of these children.

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