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A RARE CASE OF TRANSIENT APLASTIC ANEMIA IN A PATIENT WITH ACUTE HEPATITIS E

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ABSTRACT

Hepatitis E is a self limiting disease transmitted by faeco-oral route. Clinical features include fever, malaise, nausea, vomiting and diarrhoea. Hepatitis induced aplastic anaemia is a rare extra hepatic manifestation with a prevalence of 2-5% in the west and has a fatality of 85%.The treatment comprises of administration of immunosuppressive drugs and bone marrow transplantation in resistant cases. Here we report an atypical case of transient aplastic anaemia in a patient with acute hepatitis E infection who showed clinical improvement without the use of steroids.

INTRODUCTION:

Hepatitis E is transmitted via enteric route and causes disease that is usually self-limiting. Case fatality is common in pregnancy and underlying chronic liver disease [1]

Clinical features develop after an incubation period of two to six weeks and consist of fever, malaise, anorexia, nausea, vomiting, diarrhoea, hepatomegaly. Extrahepatic manifestations include neurological disorders, kidney injury and haematological disorders like aplastic anemia [2].

Hepatitis- associated aplastic anaemia (HAAA) is a type of acquired aplastic anemia following an acute Hepatitis E infection characterised by marrow failure and pancytopenia. HAAA has a prevalence of 2-5% in the west and 4-10% in Hepatitis E infection in cases of HIV in far east [3]. Case reports from India and incidence rate is unknown. The fatality due to HAAA is as high as 85% [4]. Several factors have been implicated in the etiology of hepatitis induced aplastic anaemia such as viral infection, autoimmune response, post bone marrow and liver transplantation, drugs. Hepatitis A,B,C,E and G viruses have been associated with this. The pathogenesis is immune mediated, resulting in marrow hypocellularity usually two to three months following the infection [2]. Here we present an interesting case of aplastic anaemia following an acute hepatitis E infection.

CASE:

35 year old obese male with a BMI of 38.6 with no known comorbidities presented to the Emergency department with yellowish discolouration of eyes, loose stools and loss of appetite since two months. He also gave history of decreased urine output over the past fortnight.He denied any history of fever, vomiting, abdominal pain, malena, hematochezia or hemetemesis. Past medical and family history was insignificant. History of alcohol consumption was present. His blood pressure was dropping (80/50 mm hg) and hence he was admitted to the intensive care unit where he was started on inotropes. On examination, there was pallor, jaundice and pitting pedal edema .Right ear discharge was present and a swab was taken.An infected wound measuring 4 cms due to multiple lacerations on left forearm inflicted by quacks as a remedy for jaundice was found. There was foul smelling discharge from the wound. Discharge from the wound was sent for culture and sensitivity. Abdominal examination revealed uniform distension with full flanks, massive hepatosplenomegaly and shifting dullness. Other systems were unremarkable. Initial laboratory evaluation on admission, day 7 and on the day 14,i.e on discharge from hospital are tabulated in the figure/table 1

Tests	**ADMISSION**	DAY 7	**DAY 14**
Hamoglobin (gm/dl)	6.6	8.6	8.7
Total leucocyte count (cells/ mm^3)	2200	4200	9200
Differential count	Neutrophil:64 , Lymphocyte:35 ,Eosinophil:01	Neutrophil:73, Lymphoytes-25,Eosinophil:2	Neutrophil:80, Lymphocytes:19
Platelet count (cells/ mm^3)	110000	73000	146000
Total bilirubin (mg/dl)	8.0	15.1	17.21
Direct bilirubin (mg/dl)	6.68	13.29	15.03
Aspartate transaminase (IU/ml)	168	79	106
Alanine transaminase (IU/ml)	55	33	36
Alkaline phosphatase (IU/ml)	50	39	67
Prothrombin time (seconds)	19.0	16	15.3
International normalised ratio(INR)	1.33	1.07	1.5
aPtt (secs)	43.4	40.5	35.0
Blood urea (mg/dl)	111.5	26.3	30
Serum creatinine (mg/dl)	2.10	0.73	0.80
Uric acid (mg/dl)	16.9	3.8	2.2
Calcium (mg/dl)	7.9	8.5	8.8
Phosphorous (mg/dl)	2.6	1.5	1.3

Serum Potassium (mEq/dl)	4.01	3.93	3.70
Albumin (gm/L)	3.3	2.7	2.9

Figure/Table 1: Laboratory evaluation on admission, day 7 and on the day 14,i.e on discharge from hospital.

Figure/Table 2: Image of the patient lying supine with chest and abdomen exposed

Ultrasound of the abdomen showed fatty hepatomegaly (20.5cms) and massive splenomegaly (17.8cms) with portal vein diameter of 10mm. Patient was transfused 4 units of packed red blood cells and started on empirical antibiotics in view of sepsis after blood for aerobic and anerobic cultures were drawn. Deranged renal function hinted towards a pre renal Acute Kidney Injury and was treated with intravenous fluids. Anemia was evaluated with serum ferritin, total iron binding capacity and serum Iron which were 5170 nanogram/millilitre , 212.10 microgram/decilitre and 207 microgram/decilitre respectively indicating towards anemia of chronic inflammation. Peripheral smear showed pancytopenia. Reticulocyte count was 1.1%. Direct and indirect coomb's test was done in view of suspected autoimmune process in the presence of raised LDH of 2335 units/litre ,both of which showed negative results. Vitamin B12 assay was 507 pg/ml which was normal. Meanwhile he was started on topical antibiotics for ear discharge while awaiting culture reports. An upper GI endoscopy was done which showed mosaic like pattern in the fundus. Infective markers for viral hepatitis were sent which showed IgM HEV to be positive, while markers for other hepatitis virus came negative. Follow up on the culture showed growth of coagulase negative Staphylococcus aureus in the blood, wound and ear swab. The antibiotics were changed accordingly to Linezolid. Patient improved subsequently with his blood counts reaching normal levels. At that point he was shifted to wards and subsequently discharged.

DISCUSSION:

Hepatitis E viral infection has been regarded as the most common form of hepatitis in endemic developing countries. While the disease is generally self limiting, extra hepatic manifestations such as aplastic anaemia has a fatality rate as high as 85%.The onset of pancytopenia takes a period of two to three months following an attack of acute hepatitis.

Aplastic anaemia presents with pallor, multiple bleeding manifestations, hypogammaglobulinemia, neutropenia, fever and secondary bacterial infections [4].Our patient, in a setting of preexisting gastroenteritis since the past two months, presented with recent onset of pallor and features of multiple secondary bacterial infections such as fever, acute otitis media and forearm wound infection with coagulase negative staphylococcus aureus.

Following thorough evaluation, our differentials were tumor lysis on a pre-existing myeloproliferative disease, hemophagocytic lymphangiohistiocytosis (HLH) and chronic liver disease (CLD) with hypersplenism due to intake of alcohol, megaloblastic anemia in an alcoholic due to vitamin B12 deficiency. In the setting of hyperuricemia and deranged renal function test in the form of elevated serum creatinine and blood urea, diagnosis of tumour lysis syndrome in the background of a myeloproliferative disorder was considered. Absence of hyperkalemia and normal corrected serum calcium virtually ruled it out. Since B12 level was normal and no megaloblasts were detected in the bone marrow, diagnosis of megaloblastic anemia was unlikely.

A possibility of a hemophagocytic lymphangiohistocytosis was considered.The criteria for hemophagocytic lymphangio histocytosis are presence of fever, splenomegaly, decreased cell counts in two out of the three lineages, elevated levels of blood triglycerides or decreased amount of fibrinogen, Ferritin more than 500 nanogram per millilitre, haemophagocytosis in bone marrow, lymph nodes or spleen, reduced activity of natural killer cells, levels of soluble CD 25 greater than 2400 units per millilitre [5]. Bone marrow aspirate with biopsy was done which showed evidence of bone hypocellularity and no evidence of haemophagocytosis Our patient met four of the eight criteria while diagnostic requirement is five out of the above eight, hence ruled out.

Presence of ascites, hepatosplenomegaly, jaundice with deranged liver function test, also the mosaic pattern in fundus seen in endoscopy made the possibility of Chronic liver disease with portal hypertension, hypersplenism likely. But untimely remission of symptoms in a span of a week would not explain hypersplenism.
When the above possibilities were excluded, a diagnosis of hepatitis induced aplastic anaemia (HAAA) was made which was supported by IgM anti-HEV antibody positivity.

CONCLUSION:

According to literature, majority cases of HAAA are fulminant unless timely treatment with immunosuprresive drugs is administered, and in resistant cases bone marrow transplantation is needed [4].The atypical feature of this case is that the aplastic syndrome was transient and the patient improved without steroids.

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