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Original Research Paper

General Medicine

A PATIENT WITH UNKNOWN CAUSE OF SEVERE LIVER PROFILE DERANGEMENT – A CASE REPORT

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ABSTRACT A case was reported where patient reported grossly deranged LFT after few days of illness but no obvious cause found. Clinically patient was stable , no obvious radiological abnormality was found. All systemic examination was normal. Patient do not have any related or unrelated past history. During hospital stay there was gradual improvement. A case is presented where patient was clinically stable despite grossly deranged Liver profile.

KEYWORDS :

INTRODUCTION

Most tests measure hepatocellular damage rather than function, so they are rather misnamed. True liver function tests (LFTs) are those that measure synthesis of proteins made by the liver (albumin, clotting factors) or the liver's capacity to metabolise drugs[1]

Elevated liver function tests are found in approximately 8% of the general population. These elevations may be transient in patients without symptoms, with up to 30% of elevations resolving after three weeks. Thus, care should be taken when interpreting these results to avoid unnecessary testing.[2] A borderline AST and/or ALT elevation is defined as less than 2 times the upper limit of normal (ULN), a mild AST and/or ALT elevation as 2 to 5 times ULN, moderate AST and/or ALT elevation 5 to 15 times ULN, severe AST and/or ALT elevation greater than 15 times ULN, and massive AST and/or ALT greater than 10,000 IU/l.The magnitude of AST and ALT elevation varies depending on the cause of hepatocellular injury.[3]

Aminotransferase includes AST and ALT. They are markers of hepatocellular injury. They participate in gluconeogenesis by catalyzing the transfer of amino groups from aspartic acid or alanine to ketoglutaric acid to produce oxaloacetic acid and pyruvic acid, respectively. AST is present as cytosolic and mitochondrial isoenzymes and is found in the liver, cardiac muscle, skeletal muscle, kidneys, brain, pancreas, lungs, leucocytes, and red cells. It is not as sensitive or specific for the liver as ALT and elevation in AST may be seen as secondary to nonhepatic causes as well. AST activity in neonates and infants is approximately twice that in adults, but these decline to adult levels by approximately six months.[4]

Acute hepatocellular injury can be seen secondary to several drugs, including but not limited to acetaminophen, allopurinol, NSAIDs, alcohol, anti-tuberculosis medications such as isoniazid, pyrazinamide, rifampin, statins, antifungals such as ketoconazole, antibiotics such as tetracyclines, anti-seizure drugs such as valproic acid and phenytoin, antidepressants such as fluoxetine, antipsychotics such as risperidone and antivirals such as valacyclovir and ritonavir.[5]. Acute cholestasis can be seen secondary to drugs, including anabolic steroids, NSAIDs, tricyclic antidepressants, alcohol, antibiotics such as azithromycin, amoxicillin, nafcillin, rifampin, and trimethoprim-sulfamethoxazole. Long-term use of these agents can also lead to chronic hepatocellular and/or cholestatic liver damage.[6]

Autoimmune hepatitis is a chronic disease characterized by continuing hepatocellular inflammation, necrosis, and a tendency to progress to cirrhosis. It is more common in young women than men, with a 4:1 ratio. The patient usually presents with high LFTs without apparent cause.[7] These patients can have positive autoantibodies, including antinuclear antibodies, anti-smooth muscle antibodies, anti-liver/kidney microsomal antibodies, and antibodies to the liver antigen.[8]

Case Report

A young, 34 year old, male patient came to the emergency with complain of Fever of 101 degree for 4 days. There was associated mild nausea and vomiting. There was loss of appetite and bloating from the same duration.

On examination BP was 120/82 mmHg, pulse rate 100 /min, regular in rhythm, normal character, Spo2 99%,RBS was 89 mg/dl, RR 14/min. Patient was concious, oriented, responding to commands. There was no bleeding manifestations, no rashes or bodyache.

There was H/O road traffic accident 20 days back. He had trauma over face and left side of jaw but no fracture reported. He was admitted outside but there was no trauma to liver or any other major organ. Patient remained stable and vitals were normal. No vasopressor support needed during previous or present admission.

There is no h/o Diabetes, Hypertension, cardiac disease, Respiratory disease, Jaundice or any liver dysfunction. No obvious drug history though he is occasional alcoholic .

Following investigations done.

Abdominal USG showing enlarged liver (15.9 cm) with diffusely raised echotexture of liver parenchyma with pericholecystic and peribiliary cuffing, Gall bladder was collapsed , CBD normal, portal vein caliber is normal (11mm), pancreas normal, spleen in size 10 cm, Ectopic right kidney

USG hepatoportal doppler showing early changes of hepatic parenchymal disease without any portal hypertension.
Chest X-Ray was normal.

Other investigatons – Hb 13 gm/dl, TLC 5560/cmm, platelet count 2.2 lacs /cmm , MCV 95fl , PT/INR 16.70 /1.25, S. Albumin 3.73 g/dl , S. Potassium 4.3 mmol/ l S. sodium 130 mmol/l KFT normal.

S.IGE 1748 IU/ml D-dimer 3.15 ug/ml
HbsAg -ve , Anti HCV -ve , Anti HAV IgM-ve , Anti HEV -ve , HIV -ve.
Dengue NS1 IgG/IgM , PBS for Malaria , Leptospirosis , Scrub typhus IgM all negative.
Liver autoimmune profile (ANA , AMA, ASMA, Anti-LKM-1) negative.
S.Ferritin 1347 ng/ml (slightly raised)
S. LDH 460 u/l (slightly raised)
FT3 FT4 normal, TSH 0.53 uIU/ml

Typhidot IgG/IgM normal
Chikungunya IgG/Igm -ve
KFT remains normal
Gamma glutamyl transferase – 309.93 U/L
Below is the trend of LFT changes during the stay in hospital.

		day 1	day 2	day 3	day 4	Day 5	Day 6	Day7	Day8
S.BIL(mg/dl)									
DIRECT		3.36	5.18	6.05	6.85	7.01	6.92	8.98	7.91
INDIRECT	1.87	3.4	3.73	5.41	4.41	4.16	5.12	4.06	
SGPT (U/L)		5647	4845	1344	2158	1789	1016	836	662
SGOT (U/L		6749	2923	2966	1007	662	366	325	275
S. ALP(U/L)		120	141	138	148	126	135	175	172

Rest routine reports remained normal.
Liver biopsy was not done.
Subsequently patient was discharged in view of stable condition and falling trend of liver enzymes. Patient was asked to follow up in hospital with further reports of LFT.

S. Alk phosphatase remained normal but GGT was elevated. Serum bilirubin started decreasing in further reports.

There was no clear cause found except that LDH and S.Ferritin was elevated suggesting more in favour of ischemic hepatitis than any viral cause.

DISCUSSIONS

The case was reported 20 days after Road traffic accident , but the usual presentation should had history of hypotension, shock and bleeding which will cause ischemic hepatitis. There was lack of any intake of hepatotoxic drugs. Patient was admitted outside following the accident only for 5-6 hours, where the main complain was pain in one side of face and jaw. This history was important as to look for any cause of ischemic hepatitis leading to SGPT/SGOT to 5647/6749 U/L. S. Alk phosphatase level never increased throughout the course of admission.There was no H/o blood transfusion. Though transaminases decreased but s.bilirubin keeps on increasing. All possible causes for acute hepatitis ruled out by testing

There are many causes of LFT derengements
The clinical presentation of acute hepatitis depends on the underlying etiology. It can clinically manifest with various clinical signs and symptoms, ranging from asymptomatic elevated liver function tests to acute liver failure requiring liver transplantation.

The possible etiology and severity of the hepatocellular injury can be determined based on the abnormality of one or more of these biochemical tests that are involved in the performance of a specific liver function[9][10][11]. Also, it is very important to maintain suspicion for an extrahepatic process that could be contributing to abnormal liver function tests such as pregnancy, lactic acidosis, sepsis, and cardiac dysfunction. This patient is male and all the reports in this patient is normal. Even 2d echo reports is normal.

Due to result of decreased total hepatic blood flow secondary to low cardiac output, shock, or cardiac arrest, Ischemic hepatitis or "shock liver" may occur. Serum transaminase levels rise rapidly, generally peaking in 48 to 72 hours (often in the thousands), and are usually accompanied by twofold to fourfold elevations in total serum bilirubin, which may take longer to peak. A dramatic rise in lactate dehydrogenase is often seen and can help distinguish ischemic hepatitis from viral or drug-induced hepatitis. Lactate may also be elevated.This was seen in our case.

The histopathology features of acute hepatitis secondary to viral infections usually show intranuclear viral inclusions and surrounding neutrophils. Classical historical features of autoimmune hepatitis demonstrate portal inflammation and interface hepatitis formally known as piecemeal necrosis which is essentially the presence of portal inflammatory cells between the portal and liver parenchyma[12]. Diffuse microvesicular steatosis, Mallory bodies, fibrosis, or cirrhosis of the typical findings seen in alcohol-related liver injury[13]. Iron accumulation with hepatocellular hemosiderin pigment and increase hepatic copper concentrations and liver biopsy samples are the classical histopathological findings in patients with hereditary hemochromatosis and Wilson's disease respectively[14].

As liver biopsy is invasive procedure and patients remained stable throughout the stay in hospital, liver biopsy was not attemped and also denied by the patient.

Above case might be needed more aggressive investigations for the search of cause of severe liver dysfunction.

There was elevated S.Ferritin and LDH which is more in favour of ischemic hepatitis though clinical history is absent.

Measurement of serum ferritin can be useful in identifying hemochromatosis, but ferritin is a positive acute phase reactant, so it is raised in many illnesses as well as being released from damaged hepatocytes in acute hepatic failure.[15].

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