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Case Report

Internal Medicine Section

Cirrhosis: An Unusual Presentation of Sickle Cell Disease

RUPAL DOSI[1], RUSHAD PATELL[2], POOJA JARIWALA[3], PURAV SHAH[4], SARFARAZ JASDANWALA[5]

ABSTRACT

Hepatobiliary complications of sickle cell disease are relatively rare but well recognised in literature. Clinical syndromes range from mild intrahepatic cholestasis and gallstones to life threatening sequestration crisis. Most patients, homozygous for sickle cell anaemia, present before adolescence. We report a case of an adult man with no prior symptoms who presented for the first time with decompensated cirrhosis, which was found to be due to underlying previously unrecognised sickle cell anaemia.

Keywords: Cirrhosis, Sickle cell hepatopathy, Sickle cell disease

CASE REPORT

A 35-year-old male presented to us with oedema discoloration of eyes and urine, gradually progressive lower limb oedema and abdominal distension since a month. On examination, vital signs were within normal limits but pallor, icterus, clubbing and bilateral pitting pedal oedema were noted. Systemic examination revealed an enlarged liver, up to 4cm below the lower costal margin and signs of ascites. There was no personal or family history of previous blood transfusions, joint pains or recurrent jaundice. There was no history of alcohol intake.

Laboratory investigations [Table/Fig-1] were suggestive of severe anaemia (hemoglobin 4.3 gm/dl; normal range 14-17 gm/dL). Increased reticulocyte count (16.5 %), lactate dehydrogenase (1562 U/L; normal range 225-450 U/L) and hyper bilirubinemia pointing to a hemolytic aetiology. Multiple drepnocytes (sickle cells) were noted on peripheral smear. A hemoglobin electrophoresis study showed a broad abnormal band (89.2%) corresponding to Hemoglobin S, suggestive of sickle cell anaemia. Other investigations suggestive of chronic liver disease included thrombocytopenia (85,000 normal range 150000-450000) elevated Aspartate Transaminase (92 U/L; normal range <49 U/L), alkaline phosphatase (211 U/L: normal range 28-111 U/L), hypoalbuminemia (2.2gm/dl; normal range 3.6-4.4 gm/dl) and an elevated prothrombin time (test 25 seconds, control 15 seconds INR 1.75; normal range <1.2). Ultrasound of the abdomen showed hepatomegaly (166mm) with an altered echo-pattern suggestive of cirrhosis. The gall bladder showed thickened oedematous walls with hypo echoic sludge within. Portal vein dilation (15.6 mm) was reported however, splenomegaly was not seen. Free fluid in the peritoneal cavity was also noted which on analysis revealed a SAAG of 1.8 supporting portal hypertension. Upper endoscopy revealed grade 2 non bleeding varices. Other investigations including renal function test, an electrocardiogram and an echocardiogram revealed no abnormalities. Viral markers for chronic hepatitis B and C were negative and serum ferritin was normal. Considering the risk of bleeding a liver biopsy was decided against.

The patient was treated with folic supplementation and transfused. A regimen of salt restriction, spironolactone and beta-blockers was begun for his ascites and liver disease and a considerable clinical improvement with reduction in bodyweight and oedema was noted on follow up six months after presentation. Pneumococcal vaccination and hydroxyurea were also administered following hematological consult.

DISCUSSION

SCD is commonly seen in patients arising from malaria endemic tropical and subtropical regions of the globe. Owing to the singular property of polymerisation of sickle hemoglobin (HBS), vaso-occlusion of both small and large blood vessels in various organs occurs leading to several different complications. A number of clinical syndromes and pathologies have been recognised in patients with sickle cell hepatopathy [1,2]. Amongst these hepatic complications, cholelithiasis, cholangitis and acute and chronic sequestration are well documented.

Green et al., first described the aetiology of liver disease in sickle cell patients. His autopsy records on several patients showed hyperplasia of Kupffer cells, sinusoidal dilatation and erythrophagocytosis, which resulted in hypoxia, necrosis and cirrhosis at a later stage [3]. Various aetiologies for cirrhosis in SCD include (1) hypoxic injury due to sickling (2) viral hepatitis due to repeated transfusions (3) gallstones due to hemolysis (4) iron overload due to repeated transfusions and absence of chelating factors (5) chronic alcohol intake [4]. After ruling out iron overload and viral hepatitis it was concluded that our patient's liver disease is due to SCD per se.

The spectrum of sickle cell hepatopathy ranges from mild asymptomatic liver function test abnormalities to severe hyperbilirubinemia and decompensated liver failure. In a study by Maher et al., the mean values for ALT, AST and ALP were 41 IU, 57.5 IU and 268.5 IU respectively and the mean value for total bilirubin was 4.6 mg/dL and for conjugated bilirubin it was 3.6 mg/dL [5] these features correlate with our patient's profile. Another study that compared the presentations of 38 patients with SCD referred for hepatic evaluation found that only 18 % had cirrhosis but most patients were already diagnosed with SCD previously [6].

Although the autopsy findings first described by Green et al., [3] have been replicated on biopsy specimens of patients with sickle hepatopathy, biopsies are usually withheld unless essential due to the higher risk of bleeding that has been observed in these patients [2,7]. In our patient evidence of hepatic disease with portal hypertension was seen on laboratory, radiologic and endoscopic studies a biopsy was avoided due to the serious risk of hemoperitoneum.

The most notable factor in our patient is the decompensated cirrhosis as the first presentation of his hereditary hematological disease at the age of 35, which is well above the median age at diagnosis of two years (with a range of 2.5 months to 14 years) [8]. Our patient reported no prior symptoms and never had a blood transfusion.

TEST	LAB VALUES	REFERENCE RANGE
Hemoglobin	4.3 gm/dL	Males : 14-17 gm/dL Females : 12-16 gm/dL
Total RBC count	2.25 million/cmm	Males : 4.5-5.5 million/cmm Females : 3.8-4.8 million/cmm
Hct	13.25%	Males : 40-50% Females : 36-46%
Total count	17700/cmm	4000-11000/cmm
Neutrophils	73%	40-80%
Lymphocytes	25%	20-40%
Eosinophils	1%	1-6%
Monocytes	1%	2-10%
Basophils	0	0-1%
MCV	59 fL	82-92 fL
MCH	19 pg	27-32 pg
MCHC	32 gm/dL	32-35 gm/dL
Platelet count	85000/cmm	150000-410000/cmm
Reticulocytes	16.8%	0.5-2.5%
TEST	**LAB VALUES**	**REFERENCE RANGE**
Urea	51 mg/dL	15-45 mg/dL
Creatinine	1.4 mg/dL	0.8-1.3 mg/dL
Total Bilirubin	8.8 mg/dL	0-1 mg/dL
Direct Bilirubin	4 mg/dL	0-0.4 mg/dL
Indirect Bilirubin	4.8 mg/dL	0.2-0.8 mg/dL
SGPT (ALT)	21 U/L	<49 U/L
SGOT (AST)	92 U/L	<49 U/L
Alkaline Phosphatase	211 U/L	28-111 U/L
LDH	1562 U/L	225-450 U/L
Sodium (Na)	140 mmol/L	135-145 mmol/L
Potassium (K)	5.4 mmol/L	3.5-5.5 mmol/L
HIV 1 and 2 -ELISA	Negative	
HBsAg	Negative	
HCV-RNA	Negative	
TEST	**LAB VALUES**	**REFERENCE RANGE**
Hb A2	4.2%	Upto 4%
Hb F	4.7%	Upto 2%
Sickle cell window	89.2%	0%
D-window	-	0%
C-window	-	0-4%
Prothrombin Time: Patient Control	25 seconds 15.1 seconds	
INR	1.75	

ASCITIC FLUID ANALYSIS		
Physical Examination	Amount	5 ml
	Colour	Yellow
	Appearance	Clear
	Blood	Absent
Microscopic Examination	Total count	250/cmm
	Total RBCs	Rare
Differential Count	Polymorphs	5%
	Lymphocytes	25%
	Mesothelial Cells	70%
Biochemical Examination	Sugar	99 mg/dL
	Protein	1.7 gm/dL
	Albumin	0.4 mg/dL
Microbiological Examination	Gram stain	No organism seen
	ZN stain	AFB not detected
TEST	**LAB VALUES**	**REFERENCE RANGE**
Serum Albumin	2.2 gm/dL	3.6-4.5 gm/dL
Ascitic Fluid Albumin	0.4 gm/dL	
SAAG	1.8	>1.1 s/o portal hypertension

[Table/Fig-1]: Laboratory investigations

CONCLUSION

It is important for clinicians to recognise the less well-known hepatic presentations of SCD and institute treatment as early as possible for their optimum care and prognosis.

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PARTICULARS OF CONTRIBUTORS:
1. Professor, Department of Medicine, Medical College Baroda, Gujarat, India.
2. Senior Resident, Department of Medicine, Medical College Baroda, Gujarat, India.
3. Resident, Department of Medicine, Medical College Baroda, Gujarat, India.
4. Intern, Department of Medicine, Medical College Baroda, Gujarat, India.
5. Resident, Department of Internal Medicine, Monmouth Medical Center, New Jersey, USA.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Rushad Patell,
32 Alka Society, Akota, Gujarat-390020, India.
E-mail: rrushadpatell@gmail.com

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