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Case Report

Hepatopathy in sickle cell disease with osteomyelitis: a challenging diagnosis: case report

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ABSTRACT

'Sickle hepatopathy' is a condition which is seen in only 10% cases of sickle cell disease (SCD). Sickle hepatopathy could be due to acute sickle crisis, sequestration, cholangiopathy, severe intrahepatic cholestasis or as a result of chronic blood transfusion related infection and hemosiderosis. Differentiating the cause for hepatopathy in SCD is challenging. Hepatopathy manifestation can range from mild liver function test abnormality to life threatening fulminant hepatic failure. Hence, demanding prompt recognition and management. Here we reported a one such case of 13 year old male with progressing jaundice and bony pain with swelling of lower limbs was diagnosed as SCD with right proximal tibia sickle osteomyelitis and left knee septic arthritis with hepatopathy who was managed with supportive care and surgical intervention.

Keywords: SCD, Sickle hepatopathy, Osteomyelitis, Sequestration

INTRODUCTION

In sickle cell disease (SCD) due to sickle hemoglobin (HbS) results in chronic hemolytic anemia and vaso-occlusive crisis which leads to multi systemic manifestation. Rarely, 10% of adult SCD patient can develop 'sickle hepatopathy' also known as 'hepatic sickle cell crisis' which is under reported in pediatric age group. Sickle hepatopathy is an umbrella term which indicated liver damage caused by various etiologies like acute sickle crisis, hepatic sequestration, cholangiopathy, severe intrahepatic cholestasis or as a result of chronic blood transfusion related infection and hemosiderosis.[2-4] Differentiating the cause for hepatopathy in SCD is challenging. It needs methodical evaluation and assessment of response to treatment.

CASE REPORT

A 13 year old male child first born to second degree consanguineous married couple, hailing from Kodagu District, Karnataka was brought to our pediatric emergency department with complaints of pain in left knee joint and below right knee since 7 days, fever with chills since 6 days, yellowish discoloration of eyes and skin with high colored urine since 4 days. It was associated with progressive swelling of bilateral lower limbs and restriction of range of movements at both knee joints. Past history of incision and drainage of right hand 2nd digit and left hand 4th digit at 3 month of age due to abscess collection which has ultimately resulted in contracture. At 11 years of age child developed easy fatigability, generalized weakness and was found to have low hemoglobin (Hb) and started on iron supplementation. H/o 2 episodes of chest pain in last 2 years which was attributed to gastritis after normal ECG. No h/o of recurrent blood transfusion, major abdominal surgery or any bleeding diathesis or liver disease in the family. On examination child was sick looking, febrile, hemodynamically stable. Developmentally appropriate for age with anthropometry suggestive of chronic malnutrition. Head to toe revealed hemolytic facies (Figure 1), pallor, icterus, no pedal

edema, contracture of right hand 2nd digit and left hand 4th digit (Figure 2) and on local examination of lower limbs, left knee joint and 5 cm distal to right knee joint showed swelling with erythema, tenderness and restriction of range of movement at knee joints. Systemic examination showed distended abdomen with diffuse tenderness, predominantly over upper abdomen, liver span of 14 cm with Hackett's grade 2 spleenomegaly, other systemic examination were unremarkable.

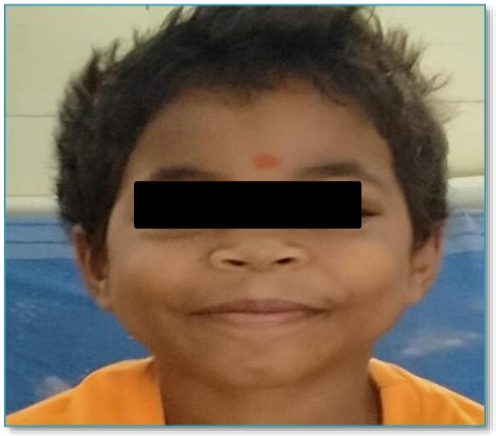

Figure 1: Hemolytic face.

Figure 2: Contracture of right hand 2nd digit and left hand 4th digit.

Investigations showed hemolytic anemia picture with conjugated hyperbilirubinemia with normal liver enzymes and synthetic functions initially. Reticulocyte count of 8.4%, corrected reticulocyte count- 4.2%. Inflammatory markers were elevated.

Ultrasound abdomen revealed spleenomegaly (18 cm) with altered echo-texture of spleen. Liver echo-texture and span, along with biliary system were normal. Sickling test was positive.

Table 1: Serial monitoring of liver function test and complete hemogram.

Date	14/9	16/9	18/9	19/9	21/9	22/9	23/9	25/9	29/9	16/10	18/10	21/10	23/10
HB (g/dl)	8.3	6.5	5.8	5.5	6.5	5.3	6.1	6.9	9.7	3.1	4.6	6.6	8.3
WBC ($\times 10^3$)	14.44	9.15	11.70	21.10	18.80	12.68	12.73	11.39	7.73	2.80	4.32	3.73	4.75
Platelets ($\times 10^3$)	67	33	118	168	33	220	221	221	310	67	170	95	218
TB (mg/dl)	16.10	18.6	16.37	7.89	13.38		6.69	4.663	3.292				1.66
DB (mg/dl)	12.82	15.5	11.68	7.014	7.44		5.999	4.391	2.958				1.1
ALT (U/l)	16.9	11	12.7	10.2	10.7		72.4	49.9	24.8				23.6
AST (U/l)	46.7	29	36.7	23.3	34.1		69.5	68.2	29.4				28.2
ALP (U/l)	225	164	175	159	203		130	121	113				150
Albumin (g/dl)	3.04	3.4	3.6	2.54	2.39		2.5	2.33	2.22				2.65
PT (sec)		13.2			16.3		16.5						
APTT (sec)		16			37.4		33.6						
INR		1.05			1.22		1.23						1.03
CRP (mg/l)		148											
Ferritin (ng/ml)						1408							
ESR (mm/hr)		112				114							112

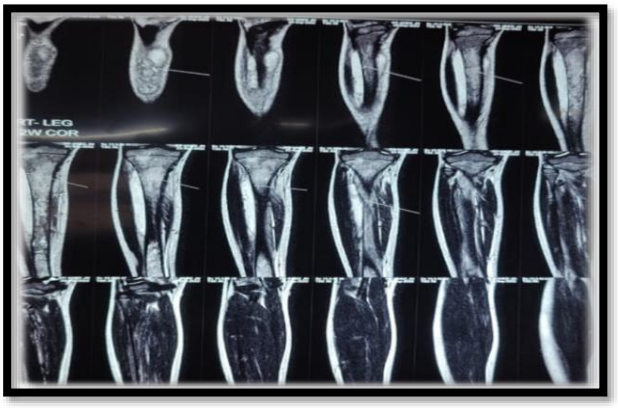

Figure 3: MRI suggesting sub-periosteal abscess in lateral aspect of proximal 2/3rd tibia.

In view of conjugated hyperbilirubinemia chronic liver disease work up were also done while waiting for HB electrophoresis and it was normal (Wilson, autoimmune, viral hepatitis A, B, C, E). Serial monitoring of liver function test and complete hemogram investigations are as per (Table 1).

USG of knee joints showed no abnormality in right knee joint with minimal effusion in left knee joint. X-ray of bilateral knee joints and proximal tibia normal. MRI of right tibia revealed sub-periosteal abscess in lateral aspect of proximal 2/3rd tibia and left knee joint showed moderate collection with synovial thickening suggestive of infectious synovitis with septic arthritis (Figure 3).

HB electrophoresis report confirmed SCD. Final diagnosis of SCD with right proximal tibia sickle osteomyelitis and left knee septic arthritis with hepatopathy was made. With appropriate supportive care and surgical intervention child clinically improved.

DISCUSSION

SCD is an autosomal recessive genetically transmitted hemoglobinopathy. Sickle hemoglobin (HbS) occurs when thymine is substituted for adenine in the 6th codon of the beta globins gene, resulting in the production of valine instead of glutamine. Due to this sickle shaped RBC they can manifest with multisystem complication like splenic sequestration, sickle cell pain (Dactylytis), osteomyelitis, avascular necrosis, priapism, stroke and acute chest syndrome.[5]

Hepatobiliary complications of SCD are not well established in pediatric age group. Allali et al in their cohort retrospective study on 616 SCD pediatric patients reported 37% of the children developed one hepatobiliary complication. The most frequent was cholelithiasis, in 25% of cases. Overall, 6% of the children experienced acute sickle cell hepatic crisis, sickle cell intra-hepatic cholestasis, or acute hepatic sequestration, with severity ranging from mild liver pain and increased jaundice to multiple organ failure and death.[1,6] Systematic evaluation and timely management with exchange transfusion/simple blood transfusion, supportive care and tackling the cause will reduce the progressing liver cell injury and mortality.[7,8] It is also equally important to rule out other causes of chronic liver disease like Wilson, autoimmune hepatitis, systemic sepsis etc.[9]

In our case report, patient born to consanguineous marriage couple, hailing from sickle belt, with features of osteomyelitis with anemia and progressing jaundice with significant past history led to the provisional diagnosis of sickle cell anemia and hepatopathy. With systematic approach SCD was confirmed by sickling test and Hb electrophoresis. Hepatopathy was attributed to severe systemic sepsis caused by osteomyelitis after ruling out other causes and as liver enzymes and synthetic functions (PT, INR) of liver were initially normal.[10] In adults incidence of acute osteomyelitis presenting as cholestasis is around 1-4%. Border line alkaline- phosphatase elevation was attributed to osteomyelitis with sepsis as on USG abdomen biliary system was unremarkable. Meanwhile child had significant fall in hemoglobin with splenic enlargement; splenic sequestration was suspected and managed with analgesics and PRBC transfusion. Good hydration, pain management and hydroxyurea therapy is equally important as it can prevent further sickling of RBC.[8] With appropriate antibiotics and surgical intervention child clinically improved and liver function tests started normalizing. Hepatic sickle cell crisis/ sequestration could also be a possibility in our case, as few patients can have normal liver enzymes and normal coagulation profile and it is self-limiting over 1-3 weeks.[9-11] Hence hepatopathy in SCD is a challenging diagnosis, systematic approach and ruling out other causes of underlying chronic liver disease will decrease the morbidity, mortality and need for liver transplantation.

CONCLUSION

All anaemia in paediatric age group has to be evaluated appropriately. SCD should be suspected in patients presenting with progressing jaundice, anaemia with osteomyelitis. Hepatopathy in SCD needs systematic approach to diagnose the cause as clinical manifestation can overlap. Multidisciplinary management in SCD can decrease the morbidity and mortality.

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