Case Reports

Neonatal Haemochromatosis - A Case Report

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Bangabandhu Sheikh Mujib Medical University (BSMMU) and also to highlight the clinical and diagnostic features. As far our knowledge goes, it might be the first reported case in the local journal.

Case Report

Noha, 1 month and 27 days old female child, only issue of her consanguineous parents hailing from Laxmipur was admitted with the complaints of jaundice since 8th day of age and passage of dark urine for same duration. She had no history of passage of pale stool, delayed passage of meconium, constipation, excessive sleepiness, feeding difficulties, vomiting, fever, convulsion or bleeding from any site. Noha's mother is 22 years old. She was on regular antenatal check up and there was no history of fever, rash, jaundice or taking any medication during her pregnancy. Mother did not have any history of abortion or stillbirth. Noha was delivered at term with average birth weight. Her postnatal period was uneventful. She was on exclusive breastfeeding. On examination, Noha was well and alert, but deeply icteric. She was mildly pale and mildly stunted (LAZ score -1.2) but not wasted (WHZ Score -0.75). Her OFC was 36 cm (-2SD) and upper segment lower segment ratio was 1.57:1. The size of anterior fontanelle was normal (2x2cm) and posterior fontanelle was almost closed. Her vital signs were within normal limit. She had no facial dysmorphism and no associated apparent congenital anomalies. Bedside urine for reducing substance and albumin was also found nil. She had hepatomegaly which was firm and nontender but no other organomegaly or ascites. Opthalmoscopic examination was done to see any evidence of cataract, chorioretinitis, cherry red spot and posterior embryotoxon, but was not found.

Laboratory investigations showed normal total and differential count with mild anaemia (Hb 10.3gm/dl) and normal ESR (05 mm in 1st hour). Liver function test showed serum total bilirubin was 14mg/dl of which direct bilirubin was 13mg/dl. Serum ALT was normal (32 U/L), prothrombin time was prolonged (control 11.8s, patient 21s, INR 1.8), serum albumin was

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reduced (26 g/L) and random blood glucose level was within lower limit of normal (3.1 mmol/L). Serum ferritin level was markedly elevated (3717 \( \mu g/L \)), serum total iron binding capacity was reduced (100 \( \mu g/dl \)) and serum total iron level was within normal limit (98 \( \mu g/dl \)). Free T4 and TSH was normal, TORCH screening was nonreactive, urinanalysis and chests X-ray were also normal. Ultrasonogram of hepatobiliary system showed contracted gall bladder with minimal ascites.

Considering the history, clinical findings and investigations, Noha was diagnosed as a case of neonatal haemochromatosis. Noha was managed with supportive treatment by oral ursodecholic acid (20mg/kg/day), phenobarbitone (5mg/kg/day), injection vitamin K (0.2mg/kg/day for 3 days) and fresh frozen plasma (10ml/kg). She received chelation therapy with desferioxamine (30mg/kg/day iv). She was also treated with antioxidant therapy with vitamin E (25 IU/kg/day orally) and injection N-acetylcystine (200mg/kg/day in initial 24 hours and then 100mg/kg/day in IV infusion). One week after receiving chelation / antioxidant therapy some investigations were re-evaluated. After treatment serum ferritin level reduced remarkably (869 \( \mu g/L \)). But serum bilirubin level and prothrombin time were not improved. Treatment continued further one week. But her clinical and biochemical parameters did not improve further.

**Discussion**

Neonatal haemochromatosis (NH) is a rare disorder of iron storage in newborns resulting in rapid liver failure\(^{11}\). Hepatic failure is usually determined by the onset of hepatic encephalopathy. However, as encephalopathy is difficult to assess in the newborn, liver failure in these patients can be defined a synthetic liver dysfunction, causing coagulopathy\(^{12}\). Newborns with NH frequently are premature or small for gestational age. The pregnancy may be complicated by intrauterine growth retardation, oligihydramnios, placental oedema or sometimes polyhydramnios\(^{2,5}\). Illness usually is evident within hours of birth, although some have been diagnosed at a few weeks of age\(^{2,6}\). Hepatocellular synthetic insufficiency can explain the coagulopathy, low fibrinogen and hypoalbuminemia. The hypoalbuminemia in turn contributes to a low intravascular oncotic pressure, edema, contracted blood volume, oliguria, and resultant oligohydramnios\(^{6}\). The oedema and ascites may be attributable to anaemia, heart failure or portal hypertension. The characteristically low transaminases and hypoglycemia that is secondary to poor glycogen store are evidence of overall hepatocellular loss. The frequently seen anaemia probably is multifactorial, caused by severely limited hepatic erythropoisis, acquired defect in erythocyte membrane as a result of liver disease\(^{6}\). Most patients with NH do not have significant congenital anomalies. However patients with 2 separate syndromes have been described with some frequency. Four children have been reported with trichomalacia, diarrhoea, facial dysmorphology and some degree of congenital heart disease\(^{13}\). Verloes and colleagues\(^{13}\) coined the name “Tricho-Hepato-Enteric syndrome.” In addition, 4 patients have been reported with NH and renal tubular dysgenesis. This supports to belief that NH is the result of an in utero insult to the fetus\(^{14,15}\). Our studied case Noha presented at one week of age with hepatic failure as evident by coagulopathy. Moreover, she had hypoalbuminemia; serum ALT level was low in comparison to high bilirubin level and blood glucose level was within lower limit of normal. Noha had no facial dysmorphism and no apparent associated congenital anomalies.

Serum concentrations of ferritin are elevated in patients with NH. Body iron stores normally are high in infancy; Furthermore, elevated ferritin is nonspecific and simply may represent total body overload, nonspecific liver disease or inflammation\(^{5,16}\). When measured, the iron binding capacity is low, reflecting the impaired synthetic ability of the liver\(^{2,5}\). Although the iron deposition in NH is most notable in the liver, iron deposition in the extra hepatic sites including the salivary gland (buccal mucosal biopsy) makes it possible to verify the diagnosis histologically without the need for a liver biopsy\(^{17}\). Salivary gland siderosis also was seen in patients with tyrosinemia, parvo virus B19, rubella, alpha thalasaemia, but these generally could be distinguished on other clinical and laboratory grounds\(^{17}\). MRI can be useful in the diagnostic evaluation of an of newborn with possible NH. Because of paramagnetic influence of ferric ions (Fe+++), the signal intensity of liver and pancreas will be lower than that of normal intensity spleen. In situations where foetus is at risk of having NH, MRI can also be used to evaluate the infant during the third trimester of gestation. In this case, foetal liver intensity can be compared with other foetal tissues and with mother’s liver.

In our case biochemical evidence showed high serum ferritin level with low iron binding capacity. Biopsy could
not done in our case due to the presence of coagulopathy which was not corrected even after supportive therapy. MRI could not be done due to financial constrains\textsuperscript{18}.

Untreated, the disorder is almost uniformly fatal with a mortality rate of >60\%\textsuperscript{2,19}. From 1993 the use of an antioxidant cocktail and/or iron chelation has been suggested with initial reports of improved outcome\textsuperscript{7}. The hypothesis that iron induced oxidant injury causes liver damage has lead to introduction of chelation and antioxidant injury\textsuperscript{2,12,19}. M. Flynn et al suggested that early treatment with antioxidant cocktail is beneficial and may be curative in those who presented with milder phenotype\textsuperscript{7}. They used N-acetylcystine, selenium, prostaglandin E in parenteral route and vitamin E in oral route as antioxidant cocktail\textsuperscript{7}. They got favourable response to whom antioxidants were started earlier (by day 5), had lower peak ferritin level (<4200 µg/L) and milder phenotype\textsuperscript{7}. In our case, we were unable to use a complete regime of anti oxidant cocktail due to nonavailability of drugs (Injection prostaglandin and selenium) in our country. Besides, though the case was phenotypically milder, the treatment was started later (exceeding 2 months of age). Our case responded partially as evident by lowering of serum ferritin level, but no improvement of other biochemical parameters (serum bilirubin, ALT, prothrombin time, albumin) after one week of treatment. However, in some series, medical treatment did not appear to modify the overall prognosis and it has been suggested that in the absence of initial improvement of liver function with antioxidants and chelation therapy listing for liver transplantation should be timely considered\textsuperscript{20}. Accumulating experience indicates that recurrences of severe NH can be prevented by treatment during gestation\textsuperscript{21}. The treatment consists of intravenous immunoglobulin (IVIG) at a dose of 1 g/kg body weight from the 18\textsuperscript{th} week till the end of gestation\textsuperscript{21}. Treatment with high dose IVIG during gestation appears to have modified recurrent neonatal haemochromatosis, so that it was not lethal to the fetus or newborn\textsuperscript{21}. There have also been isolated reports of spontaneous recovery from NH in the literature and in a case report\textsuperscript{22}.

**Conclusion**

Rapidly progressive liver failure secondary to neonatal haemochromatosis remains a challenge. Early recognition, referral and initiation of antioxidant treatment with the option of liver transplantation provide these newborns with the best chance of survival for the otherwise lethal disease.

**References**


