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Case Report

Acute Liver Failure in a Neonate; A Case Report

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ABSTRACT

Neonatal hemochromatosis is a rare disorder that poses significant mortality and morbidity risks. It is one of the causes of acute liver failure in neonates. We report a case of a 15-day-old girl with complaints of jaundice and progressive liver failure; a family history of 3 early neonatal deaths with similar complaints led to the strong suspicion of Gestational Alloimmune Liver Disease. Clinicians should consider Gestational Alloimmune Liver Disease in cases of fetal demise, stillbirth, and neonatal acute liver failure, as treatment is available and effective for subsequent pregnancies.

Keywords: Gestational Alloimmune Liver Disease (GALD), Liver Failure, Neonatal Hemochromatosis.

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INTRODUCTION

Neonatal hemochromatosis (NH) is a rapidly progressive disease presenting within a few days after birth with fulminant hepatic failure and ensuing multiorgan failure with hepatic and extrahepatic siderosis (EHS) sparing the reticuloendothelial system. NH carries a recurrence rate of 90% in the offspring of affected women.[1] Gestational alloimmune liver disease (GALD) has been established as the cause of foetal liver injury resulting in nearly all cases of NH. In GALD, mothers are exposed to a foetal antigen that they do not recognize as "self" and consequently begin producing IgG antibodies directed against foetal hepatocytes. These antibodies bind to foetal liver antigen and activate the terminal complement cascade resulting in hepatocyte injury and death.[2] The understanding of the pathophysiology of the disease has also led to antenatal treatment with IVIG from 16 weeks gestation. It has been shown to prevent the development of NH in subsequent pregnancies.[3] We report a case of a 15-day-old girl with complaints of jaundice and progressive liver failure; a family history of 3 early neonatal deaths with similar complaints led to the strong suspicion of GALD.

CASE REPORT

A female neonate, born at 39 weeks of gestation via a Caesarean section following an uneventful pregnancy to a G4 p1 mother, was referred on the 15th postnatal day from a periphery hospital with complaints of progressive jaundice for 10 days, blood vomiting for 3 days along with feeding difficulties.

Physical Examination: Revealed a deeply jaundiced infant, dehydrated, lethargic with poor neonatal reflexes.

Vital Signs Revealed: Heart rate; 170 beats per minute; respiratory rate; 52 breaths per minute; temperature: 99-degree Fahrenheit, pre-ductal oxygen saturation; 93% in room air, capillary refill time; >3 seconds and blood sugar; 39 mg/dl.

Systemic Findings: Included a liver enlarged 4cm below the right costal margin with a total span of 9cm. The stools were yellow colored. The rest of the examination was unremarkable. Initially, she was resuscitated with a bolus of normal saline and 10% glucose. Broad-spectrum antibiotics were started as per unit policies.

There was a family history significant of 3 early neonatal deaths with similar complaints that remained undiagnosed, and no interventions were done antenatally. Her laboratory values and other investigations are shown in Figure. Toxoplasmosis, HSV, and CMV serology were also negative.

During the next few days, the baby's condition deteriorated, and her liver function worsened gradually; coagulation tests showed disseminated intravascular coagulation (DIC) not resolved even on treatment with platelets, fresh frozen plasma, and vitamin K. She had progressive metabolic acidosis and persistent severe anemia despite RCC transfusion. TORCH titers, thyroid function tests, and panel for inborn error of metabolism were within normal range.

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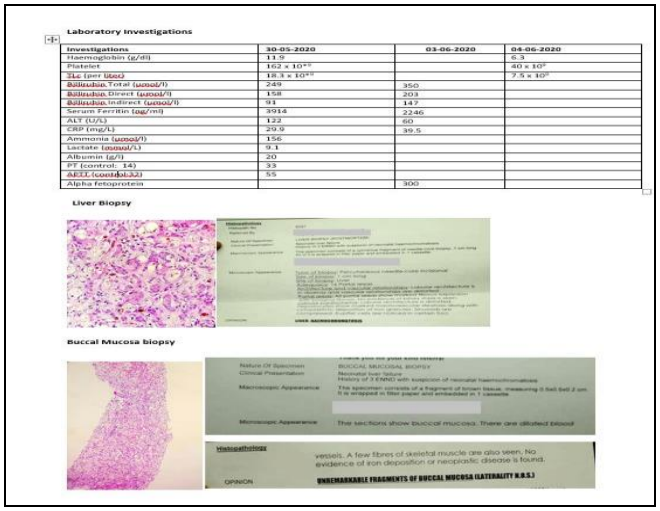
On the third day of admission, she was mechanically ventilated and started on ionotropic support, but in spite of all measures, the infant died due to liver failure. After obtaining consent from parents, posthumous liver biopsy and buccal biopsy were performed, revealing lobular architecture being distorted and hepatocytes showing marked macrovesicular steatosis along with cytoplasmic deposition of iron granules and PERL staining being positive for iron. These findings are suggestive of neonatal hemochromatosis.


Laboratory Investigations

Investigations	30-05-2020	03-06-2020	04-06-2020
Haemoglobin (g/dl)	11.9		6.3
Platelet	162 x 10^{+3}		40 x 10^{3}
TLC (per liter)	18.3 x 10^{+9}		7.5 x 10^{3}
Bilirubin Total (umol/l)	249	350	
Bilirubin Direct (umol/l)	158	203	
Bilirubin Indirect (umol/l)	91	147	
Serum Ferritin (ng/ml)	3914	2246	
ALT (U/L)	122	60	
CRP (mg/L)	29.9	39.5	
Ammonia (umol/l)	156		
Lactate (mmol/L)	9.1		
Albumin (g/l)	20		
PT (control: 14)	33		
APTT (control:32)	55		
Alpha fetoprotein		300	

Liver Biopsy

Buccal Mucosa biopsy

Figure: Investigation Reports of the Patient

DISCUSSION

GALD is the cause of foetal liver injury leading to nearly all cases of NH.[4] Infants with NH were found to be cirrhotic, raising the suspicion of intrauterine liver injury. A woman can have multiple unaffected infants prior to having an affected infant; however, after the index case, there was a 90% probability that each subsequent baby born to that mother would be affected,[1] as suspected in this particular case with the history of three early neonatal deaths at around the same age as our index case with similar complaints of gastrointestinal bleeding and jaundice leading to multiorgan failure.

Illness usually manifests within hours of birth, though some have been identified at a few weeks of age.[5] Patients have features of liver failure with hypoalbuminemia, hypoglycemia, coagulopathy, low fibrinogen, and, frequently, thrombocytopenia and anemia. Ascites develop shortly after that, as does hyperbilirubinemia.[6] All these features were evident in our index case. Very high serum ferritin levels are a constant finding, and liver biopsy demonstrates nodular cirrhosis, pronounced fibrosis, and typically significant siderosis with lobular architecture in disarray; vascular relationships are distorted with cytoplasmic deposition of Iron granules.[7]

Whittington and Hibbard described in 2004 a preventive antenatal management for pregnant women whose previous pregnancy resulted in an infant with NH (based on the alloimmune theory), which consisted of IVIG 1 g/kg weekly starting at 18 weeks of gestation (at which point maternal IgG antibodies are actively transported across the placenta).[3] They reported 16 pregnancies that progressed uneventfully and resulted in all infants surviving. This case report aims to increase awareness of GALD being a cause of neonatal failure and to be better prepared for future pregnancies.

The prognosis for untreated NH is guarded. Previous trials of therapeutic interventions, including antioxidants and iron chelation therapies, revealed survival rates of 10% to 20%.[8] Treatment with double volume exchange transfusion in combination with IVIG has been successful. This therapeutic procedure aims to eliminate existing antibodies, followed by the blockade of antibody-induced complement activation. Survival with this regimen has been stated to be approximately 80% without liver transplantation.[9,10] Although we were able to give IVIG, the hemodynamic instability with severe liver failure did not allow us to go ahead with exchange transfusion, which further emphasizes the need for early diagnosis and prenatal management.

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Authors' Contributions:

Following authors have made substantial contributions to the manuscript as under:

MF & ST & MS: Conception, study design, data acquisition, drafting the manuscript, critical review, approval of the final version to be published.

FI & HA: Critical review, concept, drafting the manuscript, approval of the final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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