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Case Report

Case report of fetal liver cirrhosis due to gestational alloimmune liver disease in a primigravida female, in north east region of India

Priya Gupta^{1*}, Sandip Maheshwari²

¹Department of Obstetrics and Gynecology, Baptist Christian Hospital, Tezpur, Assam, India

²Department of Radiodiagnosis, 155 Base Hospital, Tezpur, Assam, India

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*Correspondence:

Dr. Priya Gupta,

E-mail: sandip_7001@yahoo.co.in

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ABSTRACT

Fetal liver failure is a major cause of neonatal morbidity and mortality, presenting as acute liver failure and/or congenital cirrhosis. There are several causes of fetal liver failure and early diagnosis is mandatory to elucidate the etiology and determine a specific treatment or the best management strategy. Gestational alloimmune liver disease associated with neonatal hemochromatosis (GALD-NH) is a rare cause of fetal liver failure. It should be considered in any neonate with fetal signs of liver failure with no other identifiable causes. GALD-NH is often diagnosed late and patients are therefore referred late to specialized centers, delaying treatment. This case highlighted the consequences of late diagnosis and treatment of GALD-NH and emphasizes the importance of a high grade of suspicion of this disease in order to refer the patient to a specialized center soon enough to perform the appropriate treatment.

Keywords: Neonatal hemochromatosis, Fetal liver failure, Gestational alloimmune liver disease

INTRODUCTION

Congenital liver disease in the fetus encompasses a wide spectrum of conditions, including infectious, metabolic, and hematologic disorders, congenital vascular and heart diseases, drug related toxicity, hypoxia, and Gestational alloimmune liver disease associated with neonatal hemochromatosis (GALDNH).¹ GALD-NH, previously known as neonatal hemochromatosis, typically presents as subacute fetal liver injury and/or congenital cirrhosis.^{2,3}

Liver injury begins during intrauterine life and most patients with GALD-NH show signs of fetal disease. GALD-NH is considered a lethal disease. However, neonatal treatment with exchange transfusion and Intravenous immunoglobulin (IVIG) has now reduced the need for Liver transplantation (LTx) and improved the prognosis. Despite this strategy, GALD-NH is still associated with high perinatal morbidity and mortality rates. The diagnosis of GALD-NH remains challenging and requires a high grade of suspicion. We report a case of

fetal liver cirrhosis leading to failure who underwent extensive investigation and was diagnosed postmortem as having congenital cirrhosis due to GALD-NH.

CASE REPORT

A 24 years old primigravida was referred to the gynecology department of Baptist Christian Hospital, Tezpur for routine evaluation. She was asymptomatic and came for regular check up with amenorrhea of 18 weeks. She was married for 1 year and the family history was uneventful. Her Urine pregnancy test was positive and she was evaluated with ultrasound. PT was hemodynamically stable with pulse 86/min, afebrile to touch and blood pressure 128/78 mmHg in right brachial artery. No pallor was present. On per abdomen examination abdomen was soft and non-tender region. Per speculum examination was insignificant. On per vaginum examination uterus was anteverted and bulky, OS was closed. Her routine investigations were done and were within normal limits. Diagnostic work-up including karyotype, PROM test and

maternal serologic tests (HSV, CMV, parvoB19, EBV) were normal.

A level II ultrasound scan was done to look for any anomalies. The ultrasound showed intrauterine fetus, corresponding to gestation of 17 weeks 2 days. Fetal cardiac activity was present. The fetal liver showed nodular architecture with coarse echotexture (Figure 1). Moderate ascites was present (Figure 2). Scalp edema was present (Figure 3) with minimal bilateral pleural effusion. Suspicious of fetal liver cirrhosis was raised, and the patient was counseled for the poor prognosis of pregnancy. Medical termination of pregnancy was performed at 19 weeks through the caesarean section, after the counseling of the patient (Figure 4). Placenta was excessively thickened (Figure 5). The post-operative period was uneventful. The patient was subsequently discharged in stable condition on 5th day with follow-up on regular basis. Autopsy was performed with formal permission from parents. Histopathological examination revealed fetal liver cirrhosis. Immunostaining with C5b-9 antibody was positive in case (Figure 6). Hence, diagnosis of hemochromatosis was confirmed at autopsy for the case and GALD was confirmed.



Figure 3: Scalp edema was present.



Figure 4: Aborted fetus.



Figure 1: The fetal liver showed nodular architecture with coarse echotexture.



Figure 5: Thickened placenta.

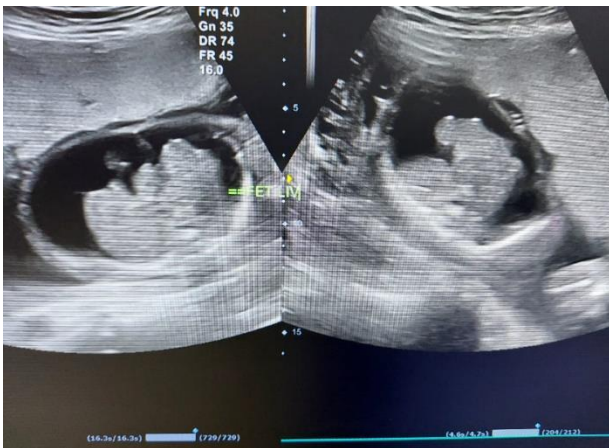


Figure 2: Moderate ascites was present.

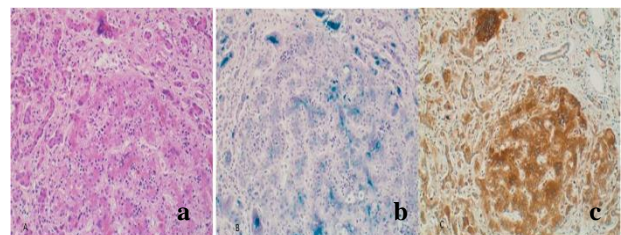


Figure 6: (a) HES (hematoxilin Eosin Saffron) staining (at 100X); (b) Perls staining (at 100X); and (c) C5b9 immunostaining (at 100X). Immunostaining with C5b-9 antibody was positive in case.

DISCUSSION

We reported a case of liver failure in a fetus of a primigravida mother in the north east region of India. The presence of nodular echotexture of liver, with ascites, pleural effusion and scalp edema suggested chronic liver injury. The diagnosis may be difficult to make and the mortality rate is invariably high.^{1,4} Identifying the etiology of fetal liver failure is important in order to define management strategies, prognosis, and the risk of recurrence in subsequent pregnancies.^{6,7}

Among the various causes of fetal liver failure, some are worthy of consideration and further discussion. Antenatal infections with herpes viruses, adenovirus, parvovirus B19, and hepatitis B virus are potential causes of fetal liver failure. Herpes simplex virus is the most common viral etiology of liver failure, carries a high mortality rate, and is rarely accompanied by skin lesions. Transplacental infection usually results in generalized fetal infection, but it is also often associated with multisystem involvement, including the central nervous system.⁸

Tyrosinemia, hereditary fructose intolerance, and galactosemia are the most common metabolic diseases to be considered. Tyrosinemia is caused by a defect in the final enzyme of the tyrosine degradation pathway. Liver failure, ascites and edema with onset in the first weeks or months of life are common. Classic galactosemia is an autosomal recessive disorder of carbohydrate metabolism caused by a severe deficiency of the enzyme Galactose-1-phosphate uridylyltransferase (GALT).

Upon consumption of lactose, the affected infants develop a severe condition with multiorgan involvement, including liver failure. GALD-NH usually manifests as antenatal liver disease. In the present case, although antenatal presentation and absence of significant extrahepatic involvement were considered, several etiologies of fetal liver failure were ruled out by comprehensive laboratory investigations, imaging studies, and histopathological analysis. GALD-NH, although rare, is the main cause of fetal liver failure and/or congenital cirrhosis in neonates.⁸ The exact incidence of the disease remains unknown. Liver injury begins during intrauterine life and is caused by the active transport of anti-fetal liver IgG antibodies from mother to fetus starting around 12 weeks of gestation, which activates the terminal complement cascade and results in hepatocyte injury and death.^{7,8,11} The alloimmune hypothesis has been confirmed by studies showing the involvement of complement in the pathogenesis of hepatocyte injury, which could result only from maternal alloimmunity.⁸

Antenatal manifestations include growth restriction, prematurity, hydrops fetalis, oligohydramnios, fetal hepatomegaly, and ascites.^{3,8} There is often a maternal sibling history of loss of stillbirth or neonatal disease.³ As observed in the present case, the initial presentation may mimic that of any of the many causes of NLF, making the

diagnosis challenging to the medical team. Postnatal clinical manifestation is typically subacute liver injury and/or congenital cirrhosis, characterized by marked coagulopathy and recurrent hypoglycemia within a few hours or days after birth, followed by progressive edema, hypoalbuminemia, ascites, jaundice, and renal impairment.^{7,8} Liver biopsy was performed to exclude other diagnoses and assess liver fibrosis.¹² Postmortem examination is an integral part of the diagnostic evaluation and should be performed in any infant with conditions suggestive of GALD-NH.

Although our patient showed many of the antenatal and neonatal manifestations of GALD-NH, unfortunately, the diagnosis was made only after autopsy. The standard treatment for GALD-NH is directed toward the alloimmune etiology, including IVIG and exchange transfusion.^{3,7} Exchange transfusion is used to remove existing reactive antibody and IVIG (1 g/kg) is administered to block antibody action and interfere with complement activation. The fact that our patient received no specific treatment deserves some comment for learning. We cannot state whether IVIG and exchange transfusion would have changed the prognosis. According to Whittington, the plasticity of the fetal liver affected with GALD-NH allows recovery even from severe injury, but the efficacy of medical treatment in reversing liver disease remains uncertain.¹³

The rate of lethal recurrence in subsequent pregnancies of a woman who has had an infant affected with GALD-NH is 90% without intervention. This rate can be changed by antenatal treatment with IVIG, given at 14 weeks, at 16 weeks, and weekly from 18 weeks of gestation until delivery.^{7,8} In view of the generally poor prognosis, GALD-NH is a frequent indication for liver transplant in neonates.⁷ However, evidence shows that the current standard treatment for GALD-NH is resulting in a significant reduction in the need for LTx, which can be demonstrated by the survival rate of 75% without LTx when the combination of exchange transfusion and IVIG is used as treatment.¹²

CONCLUSION

GALD-NH is a rare but important cause of severe NLF and should be suspected if there is evidence of fetal injury with no other definable cause. A high grade of suspicion is the key for the diagnosis of GALD-NH, and early use of IVIG should not be postponed in order to allow longer survival of the native liver.

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REFERENCES

1. Bitar R, Thwaites R, Davison S, Rajwal S, McClean P. Liver Failure in Early Infancy: Aetiology,

- Presentation, and Outcome. *J Pediatr Gastroenterol Nutr.* 2017;64(1):70-5.
2. Feldman AG, Whittington PF. Neonatal hemochromatosis. *J Clin Exp Hepatol.* 2013;3(4):313-20.
 3. Feldman AG, Whittington PF. Neonatal hemochromatosis. *J Clin Exp Hepatol.* 2013;3(4):313-20.
 4. Shanmugam NP, Bansal S, Greenough A, Verma A, Dhawan A. Neonatal liver failure: aetiologies and management--state of the art. *Eur J Pediatr.* 2011;170(5):573-81.
 5. Chevret L, Durand P, Lambert J, Essouri S, Balu L, Devictor D, et al. High-volume hemofiltration in children with acute liver failure*. *Pediatr Crit Care Med.* 2014;15(7):300-5.
 6. Nicastro E, Iorio R. Neonatal hemochromatosis and exchange transfusion: treating the disorder as an alloimmune disease. *J Pediatr Gastroenterol Nutr.* 2010;50(5):471-2.
 7. Lopriore E, Mearin ML, Oepkes D, Devlieger R, Whittington PF. Neonatal hemochromatosis: management, outcome, and prevention. *Prenat Diagn.* 2013;33(13):1221-5.
 8. Rand EB, Karpen SJ, Kelly S, Mack CL, Malatack JJ, Sokol RJ, et al. Treatment of neonatal hemochromatosis with exchange transfusion and intravenous immunoglobulin. *J Pediatr.* 2009;155(4):566-71.
 9. Laet, C, Leonard VJV. Recommendations for the management of tyrosinaemia type 1. *Orphanet J Rare Dis.* 2013;8(8).
 10. Berry GT. Galactosemia: when is it a newborn screening emergency?. *Mol Genet Metab.* 2012;106(1):7-11.
 11. Debray FG, Halleux V, Guidi O, Detrembleur N, Gaillez S, Rausin L, et al. Neonatal liver cirrhosis without iron overload caused by gestational alloimmune liver disease. *Pediatrics.* 2012;129(4):1076-9.
 12. Whittington PF. Gestational alloimmune liver disease and neonatal hemochromatosis. *Semin Liver Dis.* 2012;32(4):325-32.
 13. Taylor SA, Whittington PF. Neonatal acute liver failure. *Liver Transpl.* 2016;22(5):677-85.

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