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CASE REPORT

Successful Outcome of Pregnancy in Niemann–Pick Disease Type B: A Case Report and Review of Literature

Manisha Madhai Beck[5] · Susanna Thomas[1] · S. Sowmya[2] · Ashish Goel[3] · Sumita Danda[4]

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Abstract

Niemann–Pick (NPD) is a rare autosomal recessive disease, caused by deficiency of acid sphingomyelinase enzyme leading to accumulation of lipids mainly in the reticuloendothelial system and lungs. We describe the case of a 29-year-old primigravida, recently diagnosed with NPD type B. At initial evaluation, her platelets were normal, liver enzymes slightly elevated and splenomegaly on scan. Pregnancy care was by a multidisciplinary team which routinely monitored her liver and pulmonary functions along with platelets. Labor was induced at 37 + 1 weeks of gestation because of fetal growth restriction. She underwent an cesarean section for failed induction and delivered a healthy male baby. *Conclusion:* Successful outcomes in such pregnancies depend upon close monitoring by a multidisciplinary team.

Keywords Niemann–Pick disease · Lysosomal storage disorder · Pregnancy · Chronic liver disease · Metabolic storage disorder; multidisciplinary care

Introduction

Niemann–Pick disease (NPD) is a rare autosomal recessive disorder, caused by the deficiency of acid sphingomyelinase (ASMD) enzyme. This leads to accumulation of sphingomyelin and cholesterol in vital organs [1]. It has a prevalence of 0.4–0.6/100,000 births [2].

NPD- A is the infantile form and leads to severe neurodegeneration and death by 3 years of age [3]. In type B, patients survive into adulthood, and however, they have hepatosplenomegaly, thrombocytopenia and dyslipidemia.1 Neurological involvement is rare [3].

Pregnancy has rarely been described in affected women. The management of such pregnancies is quite challenging and often fraught with complications such as postpartum hemorrhage, liver failure and even maternal mortality [3]. We describe a case of successful pregnancy outcome with NPD-B. A written informed consent was obtained from the couple for this case report.

Case Report

A 29-year-old primigravida, presented to us at 11 + 2 weeks for antenatal check-up, having been recently diagnosed with NPD -B.

Dr Manisha Madhai Beck, Professor and Head, Department of ObGyn, Unit 4, Christian Medical College, Vellore; Dr Susanna Thomas, Postgraduate Registrar, Department of ObGyn, Christian Medical College, Vellore; Dr Sowmya Sathyendra, Professor and Head, Department of Obstetric Medicine, Christian Medical College, Vellore; Dr Ashish Goel, Professor, Department of Hepatology and Gastroenterology, Christian Medical College, Vellore; Dr Sumita Danda, Professor and Head, Department of Medical Genetics, Christian Medical College Vellore.

✉ Manisha Madhai Beck
beckmanisha@yahoo.com; og4@cmcvellore.ac.in

1 Department of Obstetrics and Gynaecology, Christian Medical College, Vellore, Tamil Nadu 632004, India

2 Department of Obstetric Medicine, Christian Medical College, Vellore, Tamil Nadu 632004, India

3 Department of Hepatology and Gastroenterology, Christian Medical College, Vellore, Tamil Nadu 632004, India

4 Department of Medical Genetics, Christian Medical College, Vellore, Tamil Nadu 632004, India

5 Department of Obstetrics and Gynaecology, Unit IV, Christian Medical College, Vellore, Tamil Nadu 632004, India

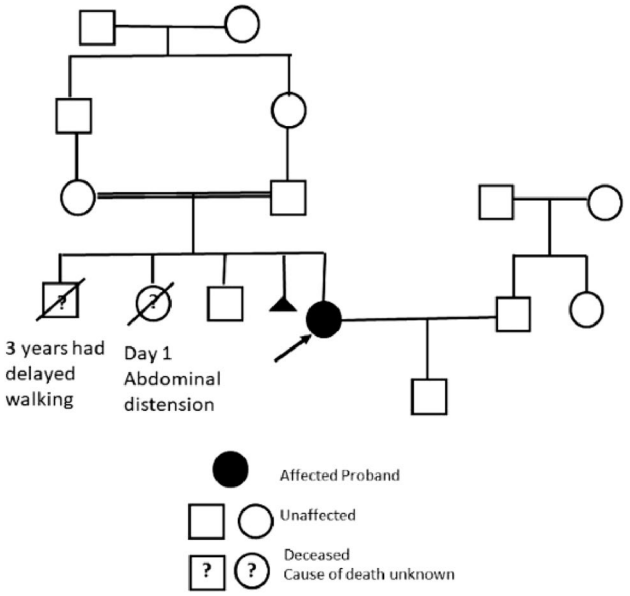

Fig. 1 Pedigree chart of the patient

She was the youngest child, born to parents of a third-degree consanguineous marriage. Her oldest sibling had died at 3 years of age due to suspected liver condition and had had a history of delayed motor milestones. She had another sibling who died immediately after a spontaneous preterm delivery at home. She has a brother who is unaffected by the disease (Fig. 1).

She had history of stunted growth and failure to thrive since her childhood which was not evaluated. There was no history of delayed milestones. At 28 years, she was evaluated for a painful abdominal distension, with repeated episodes of cough and breathlessness.

She was found to have hepatosplenomegaly with features suggestive of early chronic liver disease (CLD) with portal hypertension. Contrast-enhanced CT (CECT) of the chest was suggestive of cystic bronchiectasis. Liver biopsy done was suggestive of metabolic storage disorder. There were no varices on upper GI (gastrointestinal) endoscopy.

Fluorometry assay revealed sphingomyelinase levels of 2.4 nmol/17 h/mg (18.7% of normal). Clinical exome sequencing of patient's DNA detected a homozygous missense variation in exon 3 of the SMPD1 gene. This was classified as a likely pathogenic variant as per the American College of Medical Genetics (ACMG) classification. This confirmed the diagnosis of NPD-B the chronic visceral ASMD (Acid sphingomyelinase deficiency) type.

Husband underwent a genetic test, using Niemann–Pick disease (NPD) Next-generation sequencing (NGS) panel on a commercial basis (Medgenome Pvt Ltd) and no variants of the SMPD1 gene were detected. The couple had been counseled that if any variants were detected in the husband's SMPD1 gene prenatal testing by amniocentesis would be offered.

As husband was not a carrier for the above genetic condition, fetus was unlikely to be affected by NPD. Hence, invasive testing for prenatal diagnosis was not carried out. However, couple were explained that all children will be carriers as this is an autosomal recessive condition, and that testing for carrier status of this baby would be done postnatally.

Patient was counseled regarding need for close pregnancy surveillance under a multidisciplinary team. She was told about potential complications in this pregnancy, such as liver failure or decompensation, fetal growth restriction and postpartum hemorrhage.

Pregnancy was taken care of by a multidisciplinary team involving an obstetrician, obstetric physician, hepatologist, geneticist and neonatologist.

At her booking visit, she was found to have elevated liver enzymes with a normal coagulation profile. Her liver enzymes were slightly elevated (AST:53U/L;ALT:43U/L), but coagulation profile was normal. Her baseline platelet count was normal. Lipid profile showed hypo-HDL cholesterolemia and increased levels of total and LDL cholesterol. Hence, she was started on low fat, low cholesterol diet. Statins were not commenced as they are contraindicated in pregnancy.

Ultrasound done showed normal liver size (14.3 cm) with multiple calcified granulomas in both lobes (Fig. 2). Spleen measured 15.2 cm (craniocaudal) with enlarged portal vein (13.6 mm) and splenic vein. Her pulmonary functions were assessed using a 6-min walk test, and arterial blood gas was normal. Hence, no active intervention was advised.

She had regular antenatal visits every 3 weeks initially followed by fortnightly visits. Liver function tests and platelet counts were checked at each visit, and signs of liver decompensation were looked for.

Fetal surveillance with serial growth scans was started at 28 weeks. Fetal growth restriction (FGR) was detected at 32 weeks, following which she was monitored on weekly basis with fetal biophysical score and non-stress test. Two weekly scans were done to look for interval growth.

Labor was induced at 37 + 2 weeks due to FGR. LFTs, coagulation profile and complete blood count done prior to induction were normal. Epidural analgesia was initiated in early labor to prevent maternal distress.

Labor was tolerated well; however, she underwent LSCS for failed induction and delivered a baby boy weighing 2.5kgs with Apgar score 9/10. She did not have post-partum hemorrhage and did not require blood transfusion. She had received prophylactic antibiotics at the time of surgery.

On third postnatal day, she was evaluated for puerperal fever and diagnosed to have urosepsis caused by *Escherichia*

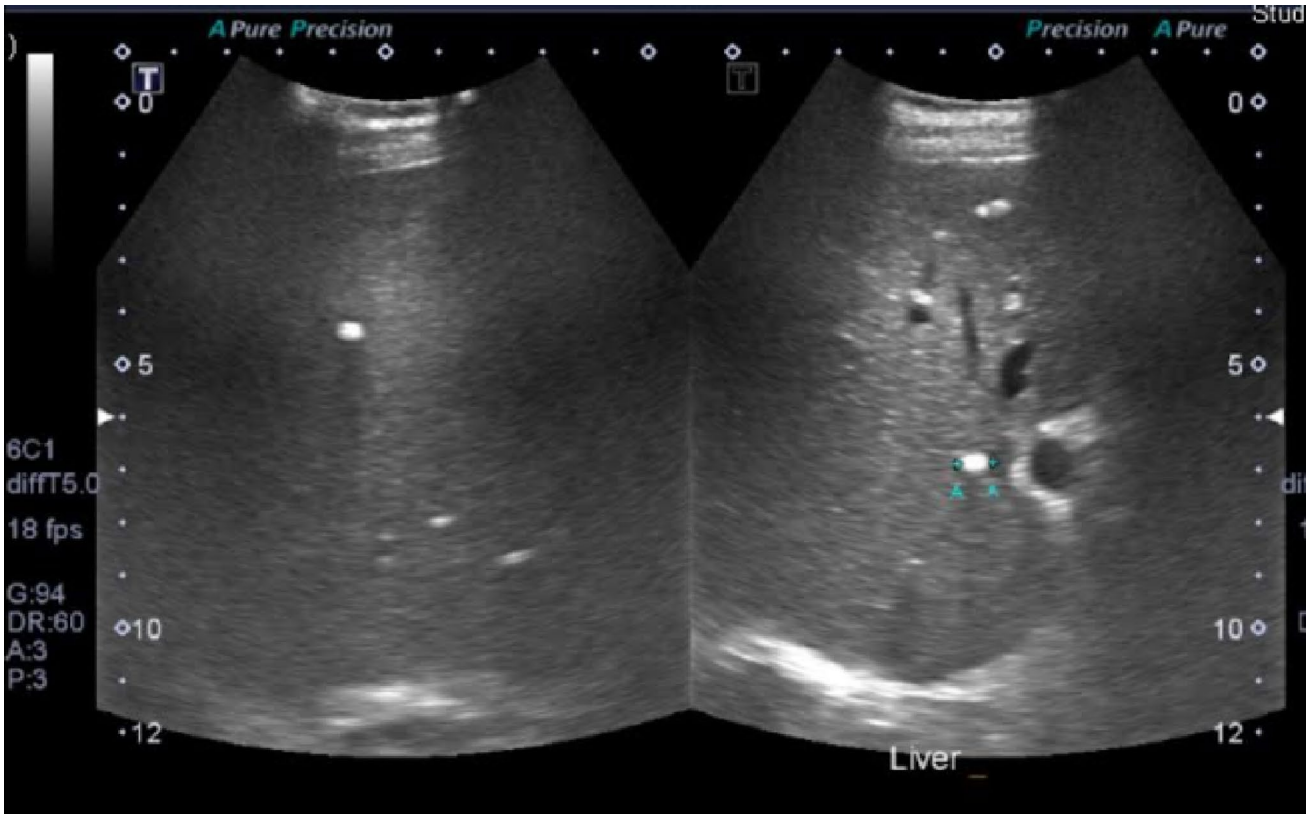

Fig. 2 Ultrasonographic image of the liver showing multiple calcified nodules in both the lobes

coli. She was commenced on broad spectrum intra-venous antibiotics for 14 days. There was good response to antibiotics within the first 24 h.

The mother and baby were discharged in good condition.

Review of Literature

Classically, the diagnosis of NPD ASMD type is made when the enzyme activity is less than 10% of normal. In our case, although the enzyme was present in subnormal range, genetic confirmation clinched the diagnosis.

The clinical features vary significantly. While some may have slightly elevated liver enzymes and mild organomegaly (like our patient), others may have the full-blown disease with liver cirrhosis, pulmonary insufficiency, coronary artery disease and fatal bleeding [4].

Close monitoring of the pregnancy by a multidisciplinary team is the key to success. Frequent evaluation of LFTs, platelet count and signs of maternal decompensation is important.

Fetal growth restriction is a common association, and hence, fetal surveillance should commence by no later than 32 weeks. LSCS should be reserved for obstetric indications. Vaginal delivery is preferred, in the absence of maternal thrombocytopenia or varices and fetal distress. Strict intrapartum monitoring of fetal condition using either CTG(Cardiotocography) or 1:1 intermittent auscultation is mandatory.

Close monitoring for postpartum infections is also important. Vigorous treatment of any infection with broad-spectrum antibiotics is important to prevent maternal morbidity due to decompensation caused by sepsis. Postnatally, these women may be started on statins.

Long-term follow-up is also needed. Coronary artery disease, progression to liver failure, worsening pulmonary functions and osteoporosis are some of long-term complications of NPD.

Author contribution MMB, ST, SS were involved in concept and design. ST, AG, MMB, SD contributed to collection of data and drafting the manuscript. SS, SD, AG, MMB were involved in critical evaluation and revision.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Informed Consent Obtained.

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