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Case Report

The battle against neonatal alloimmune thrombocytopenia: a success story at institute of obstetrics and gynecology, Egmore

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ABSTRACT

Neonatal alloimmune thrombocytopenia (NAIT) is a rare hematological disorder that causes early onset isolated thrombocytopenia in neonates without any other underlying condition. NAIT occurs when maternal immunoglobin G is formed against the fetal platelets as it contains a paternal antigen, this results in thrombocytopenia in the fetus by two mechanisms, namely clearance of the antibody bound platelets and direct suppression of megakarypoiesis. Mrs X, a 28-year-old G2P1L0, hailing from a suburban town in Tamil Nadu at 18 weeks of gestation was referred by the Department of Paediatric Hematology of Institute of Child Health and Hospital for Child with history of NAIT in the previous baby. The full term boy baby had succumbed to intracranial hemorrhage involving ventricle and basal ganglia on Day 21 of life. Blood sample from both parents as well as the baby were sent to National Institute of Immunohaematology for human platelet antigen genotyping to confirm the diagnosis of NAIT. With accordance to the Severity based approach for prenatal management of NAIT by American College of Obstetricians and Gynecologists, the mother was started on intravenous immunoglobin at 20 weeks of gestation at the rate of 0.5 g/kg/week. Relentless effort put in by a team of obstetricians, neonatologists, hematologists, geneticist and many more paved ways to the successful outcome of this case report.

Keywords: NAIT, IV Immunoglobulin, Thrombocytopenia

INTRODUCTION

Neonatal alloimmune thrombocytopenia (NAIT) is a rare hematological disorder that causes early onset isolated thrombocytopenia in neonates without any other underlying condition.[1] The pathology behind this rare condition is best understood when in comparison with the well-known devil of Rh incompatibility. Similar to it, NAIT occurs when maternal immunoglobin G is formed against the fetal platelets as it contains a paternal antigen, most commonly HPA-1a, i.e. 80% of the cases. Second most common antigen being HPA-5b i.e. 15%, followed by other antigens resulting for the rest 5% of cases such as HPA-1b, HPA-15, HPA-3 and HPA-9b.[2]

This results in thrombocytopenia in the fetus by two mechanisms, namely clearance of the antibody bound platelets and direct suppression of megakarypoiesis.[3]

When Mrs X, 28-year-old, G2P1L0 presented to IOG Egmore with the history NAIT in the first child, it took few of the best obstetricians at our esteemed institution by surprise to encounter something they have only seen in literature embodied. This emphasizes the rarity of this particular disease, as it is the first recorded case of NAIT of the 180-year-old renowned Institution. The occurrence of NAIT is estimated to be as one in 1000-2000 live births.[4]

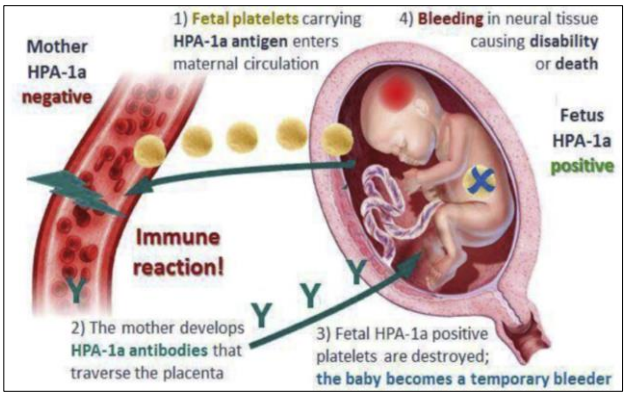

Figure 1: Pathogenesis of FNAIT.

CASE REPORT

Mrs X, a 28-year-old G2P1L0, hailing from a suburban town in Tamil Nadu who is a home maker by was referred to Institute of Obstetrics of Gynecology, Egmore, Chennai at 18 weeks of Gestation by the Department of Paediatric Hematology of Institute of child Health and Hospital for Children, Chennai with the history of her first born child being a victim to the little known illness, NAIT. Mrs X was in a non-consanguineous marriage, with history irregular menstrual cycle, and conceived with aid of ovulation induction.

On admission, Mrs X's physical examination, routine investigation, sonographical imaging were nothing out of ordinary to suggest about the impending doom of her pregnancy. It was only when history about her past pregnancy was probed upon, it threw light upon the dire care she needed in this pregnancy.

Two years prior to the current pregnancy, Mrs X had delivered a full-term boy baby of birth weight 2.69 kg by eemergency lower segment caesarean section (LSCS) in view of fetal distress and meconium-stained liquor at Chengalpattu Medical College Hospital. The antenatal period was unremarkable with no alarm signals. The child cried immediately after birth with an acceptable APGAR score 7/10 and 8/10 but was taken into NICU care owing to respiratory distress and was started on CPAP support. The child was weaned off of CPAP after 1 day. The child seemed to be recovering well till the first 5 days of life, when the baby had a convulsion, calcium and sepsis screen following which were normal, NSG was done to show diffuse parenchymal and intraventricular bleed, following which the baby was intubated in view of poor sensorium. Platelet counts found to be low, there by 12 units of platelets and 4 units of FFP were transfused in vain. Hence, intravenous immunoglobin was started on day 6 of life at the rate of 1g/kg/day and this was given for 3 days. Despite all these measure and untiring efforts put in by the Department of Neonatology of the hospital, the baby succumbed to the diffuse intracranial hemorrhage involving ventricle and basal ganglia on day 21 of life. However, the remarkable doctors at the institution were able to recognize the condition and rightly referred the parents for genetic counselling.

Blood sample from both parents as well as the baby were sent to National Institute of Immunohaematology for human platelet antigen genotyping to confirm the diagnosis of neonatal alloimmmune thrombocytopenia, further to know that it was one of the rarer variant of the rare condition with incompatibility of HPA-3b and HPA-15b antigen between the mother and baby.

Our team of obstetricians understood the need of utmost efforts in the antenatal period to ensure a successful outcome of the pregnancy. Our effort was relentlessly supported my Department of Pediatric Hematology who not just helped us understand the condition better but also provided us with a well framed protocol to tackle the scenario.

As per the protocol the mother was started on tablet prednisone 30 mg per kg of body weight at 18 weeks of gestation and continued till delivery. With accordance to the severity based approach for prenatal management of NAIT by American College of Obstetricians and Gynecologists, the mother was recommended to be started on intravenous immunoglobin at 20 weeks of gestation at the rate of 1 g/kg/week.[5] Due to the constraints in the availability and the affordability of drug, she received intravenous immunoglobulin at the rate of 0.5/kg/week. The mother received a total of 11 doses of intravenous immunoglobin infusion during course of her pregnancy.

At 22 weeks of gestation, the mother developed gestational diabetes mellitus and was started on Insulin. Sugars values were periodically monitored and Insulin dose was meticulously adjusted.

Fourth weekly periodic ultrasonography (USG) brain of fetus of done to ensure the efficiency of treatment by ruling out intracranial haemorrhages.

At 34 weeks and 4 days of gestation Mrs X presented to IOG casualty with complaints of draining per vagina and pain abdomen. She was taken up for emergency LSCS to deliver an alive preterm girl baby of birth weight 2.470 kg who cried immediately after birth with APGAR of 7/10 and 8/10. The baby was shifted to NICU for preterm care. The baby had normal perinatal transition. USG cranium was done and found to be normal study. Baby did not have any thrombocytopenia. Baby on discharge from NICU on day 8 of life was euglycemic, hemodynamically stable with a platelet count 2.1 lakhs.

On post-operative day 10, the mother was discharged with post-partum advice to taper the steroid dose and to maintain appropriate glycemic control. Mrs X left the IOG premises carrying not just her family's bundle of joy but the fruit of the relentless effort put in by a team of obstetricians, neonatologists, hematologists, geneticist and many more.

DISCUSSION

NAIT is a rare disorder to occur but the commonest cause of early onset isolated thrombocytopenia in an otherwise healthy neonate. The current modality of treatment is proven to be promising but doesn't come without paying a huge price, both literally and figuratively. The biggest challenge faced by the obstetricians at IOG Egmore, was acquiring the drug of choice in this case scenario, intravenous immunoglobulin.

The cost of a single dose of IV immunoglobulin required as per the recommendations of ACOG (1 g/kg/week) would have been Rs 59,640. Owing to cost factor, ICH had recommended a dosage of 0.5/kg/week, which brought the estimate of the fund requirement of the entire treatment course to Rs 4,47,300, which was still a huge sum for a government institution in India to spend on a single patient. After exploring a lot of resources, the administrators of IOG Egmore, sought the aid of National Health Mission, without whose timely help this story wouldn't have been one of success. It is noteworthy to state the successful outcome of pregnancy was achieved with half of the recommended dose of intravenous immunoglobulin, which could possibly open scope of research in this current modality of treatment.

As mentioned above, the present treatment modality is rather extensive and expensive has paved way for various recent advances in the management of NAIT in developed countries.

These include screening of antenatal mothers for HPA-1a and DRB3*0101 HLA antigen which helps identify the immune response gene via which HPA-1a negative women produce anti-HPA-1a antibodies. Alternatively, another screening modality that is being explored is fetal cell free DNA typing, this is preferred when the paternal genotype is unavailable.[6]

Another modality that is being explored is prevention of NAIT by prophylaxis by giving hyper immune gamma globulin, "NAITgam" to susceptible mothers as done by the counterpart anti-D immunoglobulin in hemolytic disease of fetus and newborn.[6]

Another promising advancement that can entirely replace the current modality of prednisone and IVIG transfusion is the inhibition of FC receptor, which will bring down all the IgG, there by working against all IgG mediated diseases.

Patient's point of view

Mrs X who initially stepped into IOG filled with hope, was taken on a roller coaster of emotions owing to her lack of understanding of the condition itself and also the uncertainty of the outcome of the treatment.

However, the mother certainly did reap the fruit for all her troubles when she had a successful outcome of pregnancy.

CONCLUSION

NAIT, a rare condition with quite a handful of reported success stories throughout the globe and dare we say not any in India has now become well known to about 150 budding obstetricians pursuing post-graduation at IOG Egmore. This is certainly a promise of the better management and outcome of the condition in the many years to come.

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