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CASE REPORT

CRIGGLER-NAJAR SYNDROME TYPE II IN PREGNANCY: A RARE CASE REPORT

Richa Suresh Sankhe[1], Ganesh A. Shinde[2], Jeena Pavithran[3]

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ABSTRACT: CNS type II is rare, and only a few pregnancies with this condition have been reported. Maternal treatment with phenobarbital lowers the unconjugated bilirubin and avoids foetal and new born sequelae.

KEYWORDS: Criggler-najar syndrome-CNS.

INTRODUCTION: CNS is a rare autosomal recessive disorder of bilirubin metabolism, caused by mutation of bilirubin uridine glucoronosyl transferase gene (UGT1A 1) resulting in either complete deficiency of UGT enzyme (CNS type-I) or decreased activity of UGT (Type 2). Incidence is less than 1 case per 1 million births. Only a few hundred cases have been described, including 10 cases of pregnancy with CNS. Exact prevalence is not known.

First case of CNS type I was reported by Criggler and Najar in 1952,(1) which results in severe unconjugated hyperbilirubinemia and thus neurologic impairment (Kernicterus) in the new born. Affected individuals do not respond to Phenobarbital therapy, need prolonged hours of intensive phototherapy, exchange transfusions and, without liver transplantation, usually die in infancy from kernicterus. Arias first described CNS Type II in 1962,(2) which causes milder unconjugated hyperbilirubinemia, responds to phenobarbital treatment and present with episodes of jaundice responding to phenobarbitone.

CASE REPORT: A 28 years Gravida 2 Para 1 Living 1, hailing from Uttar Pradesh reported to us at 22 weeks of gestation for antenatal registration with complaints of yellowish discoloration of sclera and malaise. She revealed a past history of multiple episodes of treatable jaundice requiring hospital admissions since childhood, details of which were not available. There was no history of consanguinous marriage.

She gave a history of full term normal vaginal delivery 3 years back at Uttar Pradesh. At birth the baby was icteric and required phototherapy for 5 days, following which the bilirubin level was in normal range. This was thought to be a case of breastfeeding jaundice and treated. The patient was not investigated then and was completely unaware of her condition.

On admission in our set up, patient looked deeply icteric.

Her complete haemogram was normal, anti HAV, anti HbsAg, anti HBC, anti HBE antibodies were negative. She had raised total biliurubin of 12.3mg/dl, conjugate biliurubin of 1.4mg/dl, unconjugated biliurubin 10.9mg/dl, total proteins: 7.6g/dl, albumin: 4.3mg/dl and normal liver enzymes.

USG of upper abdomen was normal, no organomegaly. Obstetrics scan documented a single live intrauterine gestation with cephal presentation, normal liquor, placenta and no gross congenital anomalies.

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Gastroenterology reference was taken and patient was diagnosed a case of CNS Type II. She was started on phenobarbitone tablet 30mg od and kept on a regular follow up 2 weekly. Following treatment with phenobrbitone, her subsequent bilirubin levels started falling and were in the range of 7 to 8mg/dl throughout pregnancy.

She went into spontaneous labour at 38 weeks of gestation and delivered a male child of 2800gms vaginally without any complication. The new-born had no obvious abnormality on physical examination and bilirubin levels were also in the normal range. The new-born was kept under observation for 5 days and was then discharged. Brainstem auditory evoked potential at 1 month of age was normal. Post-partum period was uneventful.

DISCUSSION: CNS type II pregnancy is extremely rare but important clinical entity to recognize, because adverse foetal outcome may result if bilirubin level is not adequately controlled. After reviewing much literature by different authors we realized that pregnancy is not contraindicated in CNS type II and good results are seen with use of phenobarbitone during pregnancy. Follow up of new-born is required for growth, development & hearing functions.

Several reports regarding the study of placental metabolism of bilirubin suggest that conjugated bilirubin does not cross the placental barrier. On the contrary maternal-derived unconjugated bilirubin crosses the placental barrier by passive diffusion, so the fetus is at risk for bilirubin-induced neuronal degeneration leading to permanent neurologic impairment such as ataxia, deafness, spasticity, mental retardation, choreoathetosis, seizures, or death.[3] These complications have been described in a case of untreated hyperbilirubinemia in a pregnant CNS type I patient, leading to quadriplegia of the neonate. In all other reported cases, the neonates had a good outcome without treatment,[4-6] or required only phototherapy,[7] one case required blood transfusion along with phenobarbital and phototherapy.[8] So, the pregnancy in CNS should aim at maintaining bilirubin levels to a low level which can be achieved with phenobarbitone.

The teratogenicity of phenobarbitone, when taken in first trimester is of concern. No study has been conducted so far to study the effects of phenobarbitone referring to CNS. All studies refer to therapy of epileptic women in pregnancy. No statistically significant associations between development of congenital abnormalities and anti-epileptic drugs was found in a recent study.[9]

Our patient was started on phenobarbitone at 24 weeks of gestation and teratogenicity was not a concern. No case of kernicterus has been reported below levels of 9mg/dl and hence bilirubin levels were closely monitored and maintained at that range, with successful outcome of pregnancy.

So we can conclude that, though CNS type II is a rare disorder in pregnancy, pregnancy is not contraindicated. The use of phenobarbitone to maintain the bilirubin levels below 10mg/dl appears to be a safe option.

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AUTHORS:

1. Richa Suresh Sankhe
2. Ganesh A. Shinde
3. Jeena Pavithran

PARTICULARS OF CONTRIBUTORS:

1. Resident, Department of Obstetrics and Gynaecology, Lokmanya Tilak Municipal Medical College, (LTMMC), Sion, Mumbai.
2. Professor & Head of Unit, Lokmanya Tilak Municipal Medical College, (LTMMC), Sion, Mumbai.
4. Resident, Department of Obstetrics and Gynaecology, Lokmanya Tilak Municipal Medical College, (LTMMC), Sion, Mumbai.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Richa Suresh Sankhe,
Type III B/12, TAPS Colony,
Boisar P. O: TAPP,
Dist., Palghar-401501,
Maharashtra.
E-mail: richasankhe22@gmail.com

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