Case Series

Prenatal diagnosis in Thalassemia – Prevention is better than cure

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Abstract

Thalassemia is one of the common hereditary blood disorders. Various clinical, psychological and financial problems make huge impact in the affected family. In India, there are nearly 42 million carriers of β-thalassemia genes. Identification of carriers and preventing births of thalassemia major patients is essential to decrease the disease burden in the country. All parents who visit our hospital for treatment of their children with thalassemia major were provided genetic counseling regarding the risk of recurrence in future pregnancies. During the study period, two high risk couples who had previously affected children with thalassemia major (three affected children in case 1 and one affected child in case 2) had a subsequent pregnancy. In both the families, mutation testing and prenatal genetic testing (chorionic villus sampling in case 1 and amniocentesis in case 2) were performed. The fetus was confirmed to be unaffected in both the cases. This led to the birth of healthy babies in the families with previous children being affected. Thalassemia major is a preventable disease. Prenatal genetic testing should be performed for all high risk couples.

***Keywords*:** β-thalassemia, Prevention, Prenatal diagnosis

Citation: Vinod Gunasekaran, Malathi G Prasad. Prenatal diagnosis in Thalassemia – Prevention is better than cure. Kauverian Med J., 2024;2(3):28-30.

Academic Editor: Dr. Venkita S. Suresh

ISSN: 2584-1572 (Online)

1. Background

Thalassemia is one of the common hereditary blood disorders manifesting with anemia and hepatosplenomegaly requiring life long blood transfusions, that usually appear in the first two years of life [1]. In India, every year approximately 10,000 children are being born with thalassemia major [1]. It is an autosomal recessive disease. A child is affected if the defective genes are inherited from both the parents who are silent carriers. Given the medical, psychological and financial implications involved in treating thalassemia, preventing the occurrence of disease gains huge importance.

2. Case Presentation

2.1. Case 1

Baby M, 3rd born male child of non-consanguineous parents from Pachai malai hills, Thuraiyur, presented at four months of age with abdominal distension. On examination, the child had hepatosplenomegaly. The parents had previous two children affected with β-thalassemia major, diagnosed elsewhere and were advised regular blood transfusions. Due to logistic reasons, the parents couldn't continue treatment and both the children died at the age of 2–3 years. Investigations in index child confirmed β-thalassemia major. Hemoglobin level started to drop on serial monitoring. After counseling, the index child

was started on regular leucodepleted packed cell transfusions and subsequently on iron chelation as per standard treatment protocol. Genetic studies showed that the father is heterozygous for c.730T>C mutation and the mother is heterozygous for IVS1+5G>C mutation in HBB gene. The baby is compound heterozygous for both the mutations and hence is affected. Genetic counseling was given to parents. Currently, the child is three years old and is thriving well with good compliance to treatment. On August 2020, the mother presented with 12 weeks of gestation. Chorionic villus sampling was performed and was sent for targeted mutation analysis of HBB gene. Fortunately, the fetus was found to be heterozygous for the mutation IVS1+5G>C but does not have the mutation c.730T>C (maternal DNA contamination was ruled out). Hence, the fetus is NOT likely to be affected for HBB gene related thalassemia major. The couple was counseled about the reports and was advised to continue with pregnancy. Subsequent pregnancy was uneventful and baby was delivered in a nearby hospital. Currently, the baby is six months old and is thriving well with no clinical pallor or hepatosplenomegaly. Plan is to do complete blood count and hemoglobin electrophoresis at one year of age to confirm the carrier status.

2.2. Case 2

Baby B, a first born girl child to non-consanguineos parents from Pachai malai hills, Thuraiyur was evaluated at the age of six months by a paediatrician for anemia and hepatosplenomegaly and was diagnosed to have β-thalassemia major. The child was referred to us for further management. Since then, the child is on regular leucodepleted packed cell transfusions and subsequently on iron chelation; and is thriving well. Genetic counseling was given to parents, but they were not willing for genetic studies at that time. On October 2020, the mother presented with 16 weeks of gestation. After counseling, the blood sample of the affected baby and the amniocentesis sample from the mother were simultaneously sent for gene studies. The affected baby was found to be compound heterozygous for the mutations IVS1+5G>C and c.*110T>C of HBB gene. Fortunately, the fetus was found to be heterozygous for the mutation c.*110T>C but does not have the mutation IVS1+5G>C (maternal DNA contamination was ruled out). Hence, the fetus is NOT likely to be affected for HBB gene related thalassemia major. The couple was counseled about the reports and were advised to continue with pregnancy. Subsequent pregnancy was uneventful and baby was delivered in a nearby hospital. Currently, the baby is five months old and is thriving well with no clinical pallor or hepatosplenomegaly. Plan is to do complete blood count and hemoglobin electrophoresis at one year of age to confirm the carrier status.

3. Discussion

The need for prevention in thalassemia is obvious due to the great expense and diffculties in providing optimal treatment for patients, and the fatalities from untreated β-thalassaemia [2]. Apart from primary prevention, prevention of another thalassemia child in a family with affected child would ensure the best possible care for the affected [2]. Preventive programmes based on carrier detection, counselling and foetal diagnosis have been very effective in reducing birth of thal major infants in Sardinia, Cyprus, Greece and Italy [2].

Premarital screening and discouraging marriages between thalassemia carriers have not been successful in our country because of the stigma associated with disclosure of their carrier status. Screening in school and college students have also been unsuccessful as they tend to forget the results by the time they get married. Carrier screening of all pregnant women and cascade screening in relatives of affected child are practically feasible options. If a high risk couple is identified (both are thalassemia carriers confirmed by

genetic diagnosis or if they have an affected child), antenatal testing by chorionic villus sampling or amniocentesis is essential in all future pregnancies as every pregnancy has a 25% chance of giving birth to a child with thalassemia major.

3. Conclusion

Thalassemia major is a preventable disease. Prenatal genetic testing should be performed for all high risk couples.

Acknowledgements

We would like to thank Dr. Vasundhara P Tamhankar and Dr. Parag M Tamhankar, Geneticists, Centre for Medical Genetics, Mumbai for performing the genetic studies in these cases.

Author contributions

Both the authors were involved in the management of the cases. Vinod Gunasekaran drafted the manuscript.

Competing interests

The authors have no competing interest to declare.

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