Genetic diagnosis of rare mutation in a child with Thalassemia, most common single gene disorder in India

Case description

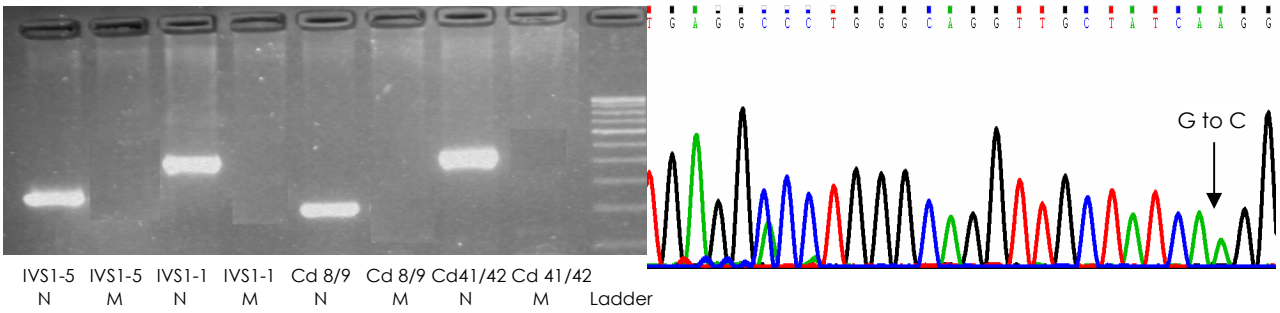
A pediatric doctor from *Nanded, Maharashtra*, referred a couple with a 2yr old male child, diagnosed with thalassemia, who was undergoing regular blood transfusions. The first cousin couple did not have any significant family history. The family was anxious about future pregnancies.

Genetic Counseling

Thalassemia, was explained as an autosomal recessive disorder with recurrence risk of 25%. Prenatal diagnosis can be offered for future pregnancies only if the disease causing mutation is identified in the affected child (Proband). The *beta globin* gene and >250 mutations on it are known to cause Thalassemia. However, 75% of Thalassemia in India is caused by just 5 common mutations. Therefore, testing for the common mutations was first recommended.

Genetic testing for Thalassemia in proband

3ml Blood was collected in EDTA from the affected child, DNA extracted and PCR was done to detect 5 common mutations. The report did not detect any common mutations. To detect rare mutations, full gene sequencing of beta globin was recommended. Sequencing report showed homozygous mutation (**G to C**) in Exon 3.



Prenatal diagnosis

In the pregnancy that followed, amniocentesis was done at 16 weeks. Thalassemia was ruled out in the fetus by DNA testing. They have delivered a normal child.

Points to remember

- It is important to identify disease causing mutation in the family by DNA testing.
- DNA testing should be offered to affected child after 2wks of blood transfusion or before blood transfusion.
- Thalassemia *cannot* be detected by Karyotyping or other biochemical tests.
- 2.7% of Indian population is reported to have unaffected carrier status of Thalassemia. Therefore, screening every pregnant woman by Hb electrophoresis will help in prevention.
- Carrier couple should be offered genetic testing.
- Prenatal diagnosis is the most important application of genetic testing.

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