

MITCHELL-RILEY SYNDROME, A REPORT OF NOVEL MUTATION IN A PALESTINIAN FAMILY RESULTING IN NEONATAL DIABETES

Abdulsalam Abu-Libdeh, Mohammad Adawi & Bassam Abu-Libdeh

Division of Pediatric Endocrinology, Department of Pediatrics, Makassed Islamic Charitable Hospital, Mount of Olives, Jerusalem

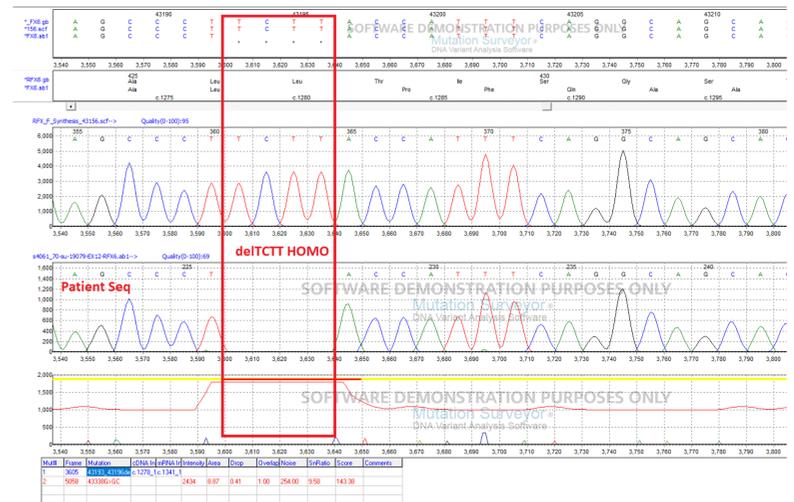
Objectives: Mitchell Riley syndrome is a rare autosomal disorder, characterized by severe neonatal diabetes associated with hypoplastic or annular pancreas, duodenal or jejunal atresia, intestinal malrotation, gallbladder hypoplasia or agenesis, and cholestatic disease, less common features were reported such as severe neonatal anemia, hemochromatosis and biliary atresia.

Mitchell-Riley syndrome is caused by a mutation in regulatory factor X (RFX), mutations in RFX6 are assumed to be the cause of neonatal diabetes in this syndrome.

Here we report a novel mutation of RFX6 gene in a Palestinian infant with Mitchell Riley syndrome.

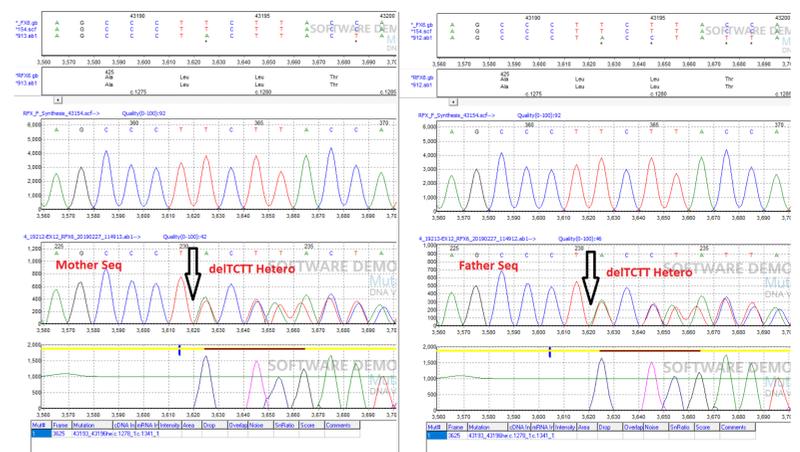
Clinical presentation and Methods: We report a female newborn, for a consanguineous Palestinian parents, fetal ultrasound revealed intrauterine growth restriction, mild polyhydramnios and findings suggestive of duodenal atresia. She was born at 38 weeks of gestation, birthweight 1705 gm. Initial abdomen x-ray showed classic double bubble sign, and was operated at 4th day of life; during which developed hyperglycemia 330 mg/dl and clinical picture suggestive of neonatal diabetes. Also developed clay colored stool, several measures were taken to improve feeding tolerance including hydrolyzed, elemental formula, MCT oil as well as chicken soup; however non proven to be beneficial to improve her FTT and she remained dependent on total parenteral nutrition.

Results: Sequencing of the RFX6 gene of the patient revealed a novel homozygous mutation C.1278 1281delTCTT in exon 12 of RFX6 gene. Father and mother were heterozygous for the same mutation.



The patient is homozygous for the mutation c.1278-1281delTCTT (p.L426LdelTCTTfsx26) in exon 12 of RFX6 gene.

c.1278-1281delTCTT mutation is a deletion mutation of TCTT at codon 426 that leads to frame shift and premature termination of protein translation.



Segregation study showed that both parents were heterozygous for the mutation c.1278-1281delTCTT (p.L426LdelTCTTfsx26) in exon 12 of RFX6 gene.

Conclusions

- To the best of our knowledge this is the seventeenth proband with Mitchell-Riley syndrome worldwide, and the first description of this disease in a Palestinian family with molecular confirmation allowing accurate genetic counseling, early diagnosis of affected kindreds, early therapeutic interventions and avoiding complications.