Indian Journal of Pediatrics (July 2021) 88(7):722
https://doi.org/10.1007/s12098-021-03780-y

SCIENTIFIC LETTER

Syndromic Diabetes Mellitus Due to Coinheritance of *ABCC8* and *TRRAP*

Sadhana Narala[1] · Rajendra Prasad Anne[1] · Rahul Reddy Chintala[2] · Sai Kiran Deshabhotla[1]

Received: 12 February 2021 / Accepted: 15 April 2021 / Published online: 27 April 2021

To the Editor: A 33-wk female child was born to 38-y-old 3rd gravida mother with 2 previous first trimester abortions. Emergency C-section was done for reversed end diastolic flow. The baby weighed 900 g (−2.95 z score on Fenton-2013 chart), length was 39 cm (−1.62 z score), and head circumference was 28 cm (−1.48 z score). Features of dysmorphism were noted in the form of broad nasal bridge, smooth philtrum, cleft palate, inverted nipples, dysplastic nails with distal phalanx hypoplasia of 5th finger.

Baby had hyperglycemic records from day 3 of life requiring insulin infusion on multiple occasions, diuresis, glycosuria, ketonuria, and poor weight gain. Because of persistent hyperglycemia and dysmorphism, syndromic permanent neonatal diabetes mellitus (NDM) was considered. A trial of oral glibenclamide was given on day 25 of life in an attempt to wean from insulin infusions. Transient response was noted and later, intravenous insulin was reinitiated. Exome sequencing revealed presence of heterozygous *ABCC8* mutation (c.379A>C), a cause of nonsyndromic NDM [1]. There was also heterozygous *TRRAP* mutation (c.3124G>A), an autosomal dominant disorder with various dysmorphic features [2].

The index case represents an uncommon genotype of syndromic NDM, wherein *ABCC8* mutation resulted in the sulfonylurea responsiveness and *TRRAP* mutation resulted in dysmorphism. The *ABCC8* mutation, which results in dysfunction of SUR1 regulatory subunit of K-ATP channel, can result from autosomal dominant, recessive or compound heterozygous mutations. Sulfonylurea treatment usually results in good glycemic control in heterozygous *ABCC8* mutations [3]. However, transient response, as noted in the index case, was seen in about 15% cases. TRRAP is a scaffolding protein, which recruits histone acetyltransferases to chromatin. Although *TRRAP* mutations cause multisystem malformations and dysmorphism, the phenotype seen in the index case has not been previously reported [2]. It is an evolving syndrome with variable phenotypic characteristics, and these abnormalities could have resulted from *TRRAP* mutations.

Declarations

Conflict of Interest None.

References

1. Ellard S, Flanagan SE, Girard CA, et al. Permanent neonatal diabetes caused by dominant, recessive, or compound heterozygous SUR1 mutations with opposite functional effects. Am J Hum Genet. 2007;81:375–82.
2. Cogné B, Ehresmann S, Beauregard-Lacroix E, et al. Missense variants in the histone acetyltransferase complex component gene TRRAP cause autism and syndromic intellectual disability. Am J Hum Genet. 2019;104:530–41.
3. Rafiq M, Flanagan SE, Patch A-M, et al. Effective treatment with oral sulfonylureas in patients with diabetes due to sulfonylurea receptor 1 (SUR1) mutations. Diabetes Care. 2008;31:204–9.

✉ Rajendra Prasad Anne
Rajendra.omc@gmail.com

[1] Department of Neonatology, Fernandez Hospitals, Unit 2, Opposite Old MLA Quarters, Hyderguda, Hyderabad, Telangana 500029, India

[2] Department of Pediatric Endocrinology, Fernandez Hospitals, Hyderabad, Telangana, India