Indian J Pediatr
DOI 10.1007/s12098-015-1953-6

SCIENTIFIC LETTER

Mutation Analysis of *TBX1* in Children with Conotruncal Heart Anomalies

Teena Koshy[1] · Vettriselvi Venkatesan[1] · Kalpana Gowrishankar[2] · Venkatachalam Perumal[1] · Shruthi Mohan[1] · Solomon Franklin Durairaj Paul[1]

Received: 6 September 2015 / Accepted: 4 November 2015

To the Editor: Conotruncal heart anomalies (CTA) are structural malformations involving the outflow tract. While the exact incidence of CTA in India is not known, it remains the most common type of structural birth defect with a major impact on pediatric morbidity and mortality. While most CTA are sporadic, a few are associated with genetic syndromes; the 22q11 deletion syndrome (22q11.2DS) being the predominate one. The CTA related to the 22q11.2DS are usually associated with a common 3 Mb or 1.5 Mb proximally deleted region, both of which include the *TBX1* gene. However, mutations of the *TBX1* gene have also been reported in patients who do not have the 22q11.2 deletion but present with CTA. The *TBX1* gene encodes a transcription factor of the T-box family and mouse models have demonstrated that *TBX1* haploinsufficiency cause cardiac outflow tract lesions.

In a case- control study involving 96 cases of CTA and 100 control subjects, ranging in age from newborns to 18 y, fluorescence *in situ* hybridization (FISH) was performed on the cases to rule out the 22q11.2 μ-deletion. Further, screening for mutations or sequence variants in four exons of the T- box region, which showed 98 % homology to mouse *TBX1*, was performed using Sanger sequencing.

One out of the 96 cases with CTA (1 %) was found to have the 22q11.2 μ-deletion. However, no pathogenic mutations or sequence variants of *TBX1* were detected in the patients and healthy controls. While this is in agreement with the report by Conti et al. [1], it is also in contrast with a few studies that have documented either mutations or polymorphisms in *TBX1* associated with isolated CTA [2–5]. Our results, though negative, provide corroborative evidence that *TBX1* mutations may not be associated with CTA in the selected pediatric population.

Conflict of Interest None.

Source of Funding None.

References

1. Conti E, Grifone N, Sarkozy A, et al. DiGeorge subtypes of nonsyndromic conotruncal defects: evidence against a major role of *TBX1* gene. Eur J Hum Genet. 2003;11:349–51.
2. Xu Y, Chen S, Zhang J, et al. Novel *TBX1* loss-of-function mutation causes isolated conotruncal heart defects in Chinese patients without 22q11.2 deletion. BMC Med Genet. 2014;15:78.
3. Çabuk F, Karabulut H, Tuncali T, et al. *TBX1* gene mutation screening in patients with non-syndromic fallot tetralogy. Turk J Pediatr. 2007;49:61–8.
4. Gong W, Gottlieb S, Collins J, et al. Mutation analysis of *TBX1* in non-deleted patients with features of DGS/VCFS or isolated cardiovascular defects. J Med Genet. 2001;38:e45.
5. Griffin HR, Topf A, Glen E, et al. Systematic survey of variants in *TBX1* in non-syndromic tetralogy of fallot identifies a novel 57 base pair deletion that reduces transcriptional activity but finds no evidence for association with common variants. Heart. 2010;96:1651–5.

✉ Solomon Franklin Durairaj Paul
wise_soly@yahoo.com

[1] Department of Human Genetics, Sri Ramachandra University, Porur, Chennai 600 116, India

[2] Department of Medical Genetics, Childs Trust Medical Research Foundation, Nungambakkam, Chennai, India

Published online: 04 December 2015