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Clinical Image

Coexistence of Rett & Angelman syndrome: A rare clinical presentation

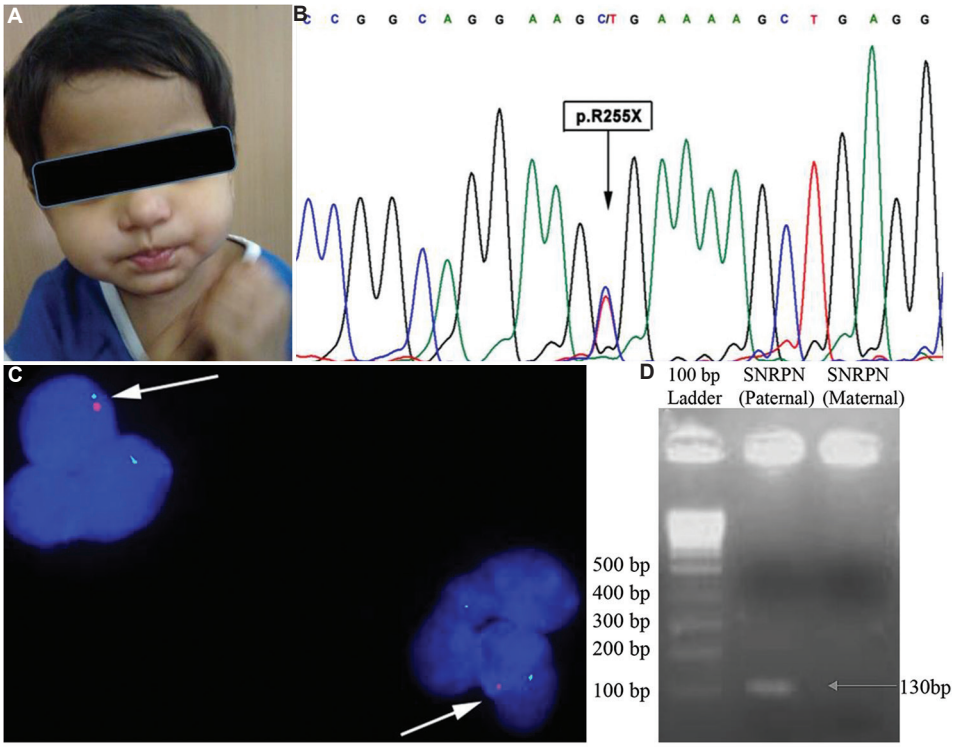

Figure. (**A**) The clinical photograph of the patient; (**B**) DNA chromatogram showing the presence of p.R255X mutation in exon 4 of *MECP2* gene; (**C**) fluorescence *in-situ* hybridization confirming the deletion of 15q11.2-13.1 (arrows); (**D**) methylation-specific PCR indicating the absence of maternal copy confirming the Angelman syndrome.

A two year old female child[†] was referred to the department of Paediatric Neurology, P.D. Hinduja Hospital, Mumbai, India, in January 2015 for delayed development. The patient developed epilepsy at the age of nine months (Figure A). Complete physical and neurological evaluation revealed the presence of microcephaly and generalized hypotonia deep tendon jerks. She did not have any purposeful hand use and later developed midline stereotypies such as hand wringing, jerky movements and mouthing. She also had inappropriate laughter and hypopigmentation. She was treated for controlling of epilepsy. A clinical presentation of global developmental delay in a female child with early-onset autistic features and typical

[†]Consent to publish clinical information and images obtained from patient's parent

electroencephalographic finding is suggestive of Rett syndrome.

Genetic analysis was carried out using microarray and methyl-CpG-binding protein 2 (*MECP2*) gene sequencing. A nonsense mutation p.R255X (Figure B) was identified that caused a premature termination of MeCP2. Microarray analysis of the same patient revealed a deletion of 15q11.2-13.1 region that encompasses the Prader-Willi/Angelman syndrome critical region (chr15: 23,827,659-28,705,281). This deletion was also confirmed using fluorescence *in situ* hybridization (Figure C). The deleted region contained 12 protein-coding genes.

The parental origin of this deletion was found to be maternal using methylation-specific PCR (Figure D), thereby confirming Angelman syndrome. Although the genetic basis of Rett and Angelman syndrome is well characterized, their coexistence has not been reported so far. This rare clinical presentation will throw some light on gene–gene interactions and their phenotypical significance.

***Conflicts of Interest*:** None.

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