Eye signs in a child with *ROBO3* gene mutation

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Key words: HGPPS, horizontal gaze palsy, progressive scoliosis, *ROBO3* mutation

A 10-year-old boy born to a second-degree consanguineous couple presented with generalized tonic-clonic seizures at 7 years of age. Mild developmental delay and progressive scoliosis were noticed from 6 months of age. Neonatal risk factors were low birth weight and birth asphyxia. He underwent multiple spine surgeries from 7 years of age. His younger sibling also had a similar phenotype. Informed consent was obtained from the mother for video recording and clinical photographs. Bilateral horizontal gaze palsy with normal vertical and convergence eye movements were identified [Video 1 and Fig.1]. There was no ptosis, and fundus examination was normal. Bipyramidal signs were observed. Thoracic scoliosis and surgical scar over thoracic spine were identified [Fig. 2]. MRI of the spine showed convexity of the thoracic spine to the right. Brain imaging of sibling revealed butterfly configuration of medulla and midline pontine cleft. Clinical exome revealed a pathogenic homozygous missense variant c.1313T>C in the exon 8 of the *ROBO3* gene (ENST00000397801.1) that results in the amino acid substitution of Proline for Leucine at codon 438 (p.Leu438Pro), confirming the diagnosis of horizontal gaze palsy with progressive scoliosis (HGPPS). His sibling harbored the same variant in homozygous state, while parents were heterozygous for the same variant.

Discussion

HGPPS is an autosomal recessive disorder caused by a mutation in the roundabout guidance receptor 3 (*ROBO3)* gene with hallmark clinical features, including the absence of horizontal eye movements, preserved vertical gaze and convergence movements, and progressive scoliosis.[1,2] Other oculomotor abnormalities are convergence and vertical smooth pursuit defects, strabismus, and congenital nystagmus.[3] *ROBO3* gene mutation might hinder the development of axonal projections of internuclear neurons that coordinates the activity of the third and sixth cranial nerves.[1] Progressive scoliosis can be explained by abnormal control of axial tone due to involvement of central tegmental or reticulospinal tracts and agenesis of fibers within inferior cerebellar peduncles and pontocerebellar tracts.[2,4] Our report emphasizes the need to identify eye signs in children with progressive scoliosis to diagnose HGPPS.

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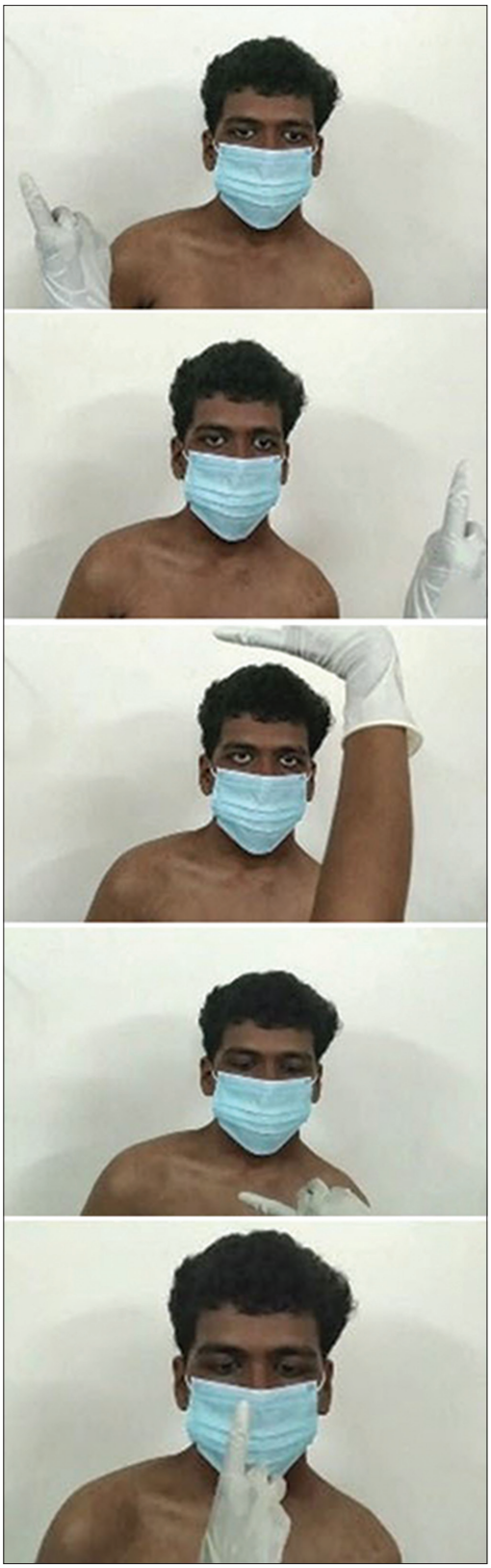

Figure 1: Photograph depicts the absence of horizontal eye movements but preserved vertical and convergence eye movements

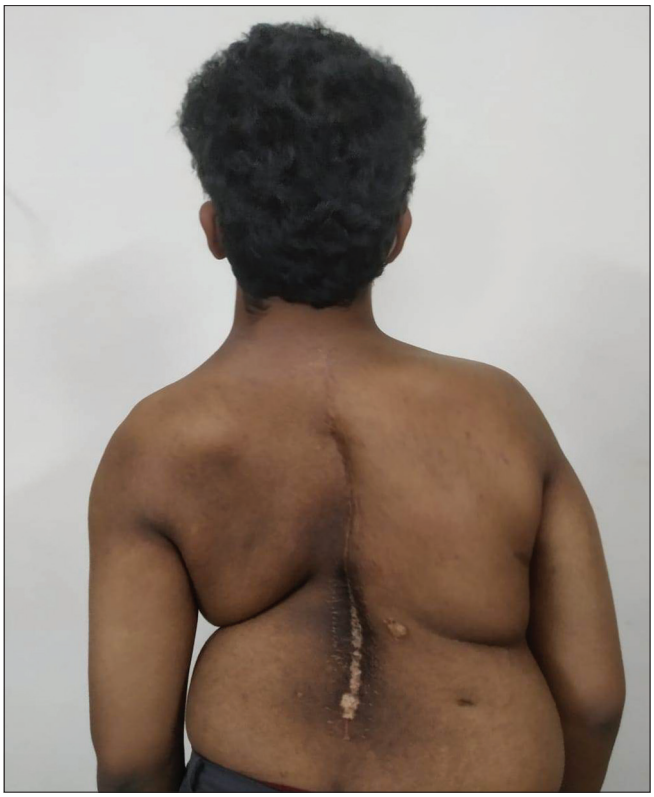

Figure 2: Thoracic scoliosis and surgical scar over the thoracic spine were observed in our proband

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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