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A ROBO GEN(I)E THAT SPLITS THE BRIDGE OF VAROLI!!

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INTRODUCTION

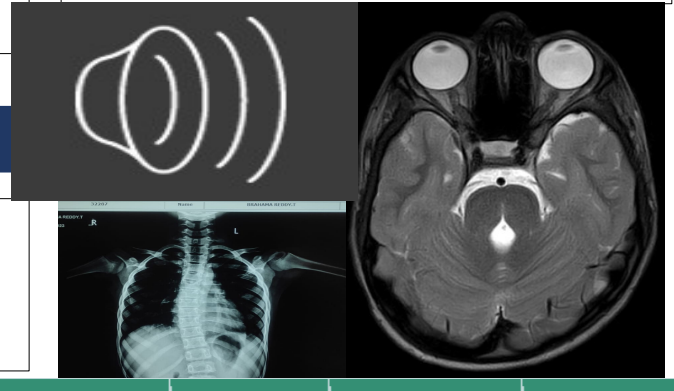
Horizontal gaze palsy with progressive scoliosis (HGPPS) is a rare congenital disorder with autosomal recessive inheritance caused by the loss-of-function mutations in both the alleles of **ROBO3** gene on chromosome **11q23-q25**, characterized by impaired conjugate horizontal eye movements and progressive scoliosis developing in childhood and adolescence. The first description of the syndrome was published in 1974 by Crisfield.Till date around 15 cases have been reported worldwide.No exact percentage of prevalence has been described so far

AIMS / OBJECTIVES

We described an rare case of HGPPS patient and performed whole-exome sequencing (WES) to identify the causative gene.

MATERIALS / METHODS

A 9 yrs old male child born out of second degree consanguineous marriage presented with complaints of Difficulty to look sideways, both on right and left side requiring him to turn his head to see laterally since early childhood. Vertical gaze was preserved, and no abnormalities suggesting facial paralysis were noted.on examination Scoliosis – Present .Other symptoms were denied. No medications or related drugs had been administered thus far. VOR - Impaired
The patient underwent brain MRI and WES for further evaluation



Gene# (Transcript)	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification$
***ROBO3* (+)** (ENST00000397801.6)	Exon 14	c.2132del **(p.Pro711LeufsTer21)**	Homozygous	Familial horizontal gaze palsy with progressive scoliosis-1 (HGPPS1) (OMIM#607313)	Autosomal recessive	Pathogenic **(PVS1,PM2,PP3)**

RESULTS & DISCUSSION

MRI brain suggestive of split pons representing brainstem dysplasia with relatively intact vermis .
Whole exome sequence: **ROBO 3 gene** defect positive and it is pathogenic variant. .The ROBO3 gene is critical for hindbrain axon midline crossing. The ROBO3 protein determines axon path finding, crossing, and resultant hindbrain morphogenesis in human. Horizontal gaze palsy is due to failure of decussation of aberrant supranuclear inputs from pontine reticular formation and median longitudinal fasciculus. The mechanism of scoliosis is still unclear, not linked to ROBO3 mutations, and probably due to abnormality of cell groups that control axial posture. In addition these children may have nystagmus, ametropia, and amblyopia. Radiologically, it is diagnosed by the absence of facial colliculi, split sign of the pons, butterfly appearance of the medulla, and pathologically, by lack of pyramidal tract decussation. Spinal surgery is usually required due to the abnormal spine curvature once it becomes moderate to severe, worsening over time and leading to severe pain. Regular ophthalmological checkup to prevent vision loss. Genetic counselling.

CONCLUSION

This case is an eye opener to show the of clinic-radiological correlation.
The early diagnosis of HGPPS is important for the prevention of the ocular and orthopedic problems that are associated with this pathology. A multidisciplinary approach to this pathology is necessary for a correct diagnosis. Radiological studies, ophthalmological and optometric examinations, and genetic analyses must be carried out.