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Case Report

An Adolescent Patient with Horizontal Gaze Palsy and Progressive Scoliosis

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Abstract

Horizontal gaze palsy with progressive scoliosis (HGPPS) is an uncommon congenital cranial dysinnervation disorder that affects both eye movement and spinal curvature, marked by limited ability to move eyes in horizontal gaze, worsening curvature of spine and brainstem malformations [1]. Only a few cases have been reported from India [2,3]. It is mainly described in consanguineous families. It is linked to a specific gene mutation in the ROBO3 gene located on the 11q23-q25 region of chromosome 11 [4]. It has characteristic clinical and radiological features. Here we present a case of an adolescent male patient with characteristic features of HGPPS.

Keywords: ROBO 3; Split pons sign; Butterfly Medulla

Case Report

A 14-year-old boy born of 2nd degree consanguineous parentage, presented with complaints of difficulty on looking towards either side since childhood and difficulty in walking since 3 years. There was history of progressive bending of back and along with eye movement restriction causing his difficulty in walking. Apart from this there was no other significant history involving other domains nor similar history among other family members. On examination, he had scoliosis with convexity to left side which persisted on forward bending (Figure 1). CNS examination revealed bilateral horizontal gaze restriction (Figure 2) with mildly impaired tandem walking with no other deficits. MRI Brain plain of the patient revealed brainstem hypoplasia with no facial colliculi, a distinct separation of pons area (referred to as the split pons sign), and medulla that resembled a butterfly in shape (Figure 3). The scoliosis was confirmed by X RAY of the spine. (Figure 4). Whole exome sequencing of the patient was done which showed a mutation in ROBO 3 gene/chromosome 11q23-q25, known to be pathogenic and significant for his condition.

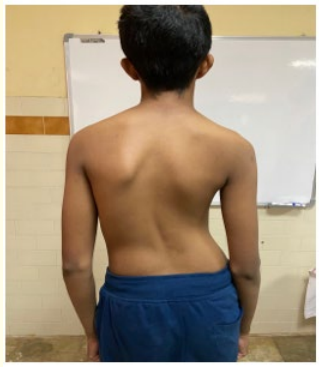

Figure 1

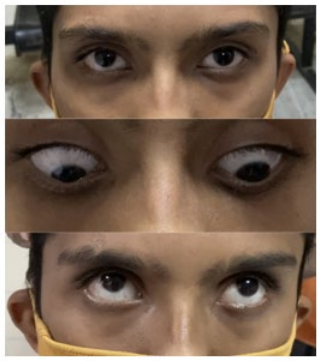

Figure 2

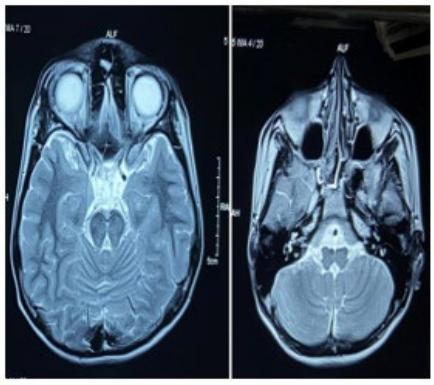

Figure 3

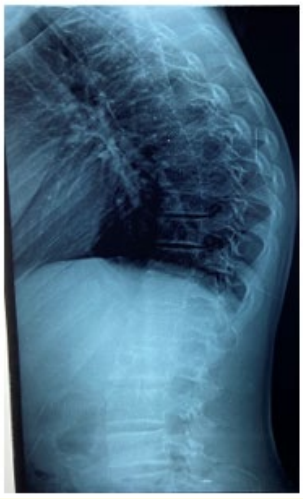

Figure 4

Discussion

Crisfield [1] originally reported the connection between scoliosis and horizontal gaze palsy in 1974 after observing it in four Chinese siblings. It is clinically one of the cranial dysinnervation syndrome (Mobius syndrome, Duane's syndrome etc). Mapping the illness locus on chromosome 11q23-25, Jen., *et al*. reported six patients from two non-consanguineous families [5]. HGPPS occurs due to homozygous mutation throughout the human round about homologous of Drosophilia (ROBO3) gene present on chromosome 11q23–25. ROBO3 gene and it's protein products are responsible for lateral positioning of longitudinal pathways [6]. It is also believed to have a role in direct cell migration [7]. During normal embryonic development in the central nervous system, axonal pathways cross the midline but when there are mutations in ROBO gene, some axonal paths remain uncrossed [5]. Congenital horizontal gaze paresis may also appear clinically in patients with other disorders such as Möbius syndrome and Duane retraction syndrome. In addition, they often have additional neurological symptoms associated with agenesis of other cranial nuclei (such as the facial nuclei), but they do not have a split pons sign that is pathognomonic for HGPPS. Shalini., *et al*. [2] reported a similar case in a 60 year old female from Tamilnadu, India. The brainstem tegmentum's aberrant development is the primary cause of HGPPS. The compromised MLF is the cause of the horizontal gaze palsy, while the cranial nerves supplying the extraocular muscles are normal. The dorsal spine scoliosis that progresses in patients with HGPPS is usually identified in childhood or adolescence, although it can be noticed in the first few months of life. The absence of pontocerebellar tract development and afferent fiber development in the inferior cerebellar peduncles is thought to be the cause of scoliosis in HGPPS patients [8]. Using DTI, Lin., *et al*. [9] showed that the primary structural anomalies causing the clinical symptoms of HGPPS include the posterior displacement of pyramidal tracts along with maldeveloped afferents within the pontocerebellar tracts and inferior cerebellar peduncles. The disease's distinctive radiological and clinical characteristics were also present in our patient. In our case, we did not perform tractography or DTI.

Conclusion

HGPPS is a rare autosomal recessive disorder associated with eye movement abnormalities and scoliosis with characteristic radiological abnormalities mainly in the brainstem like absence

of facial colliculi, split sign of the pons, butterfly appearance of the medulla, pathologically, by tegmental abnormalities, failure to decussate the pyramidal tract and genetically by mutations involving ROBO 3 gene in chromosome 11 q 23-25. Therefore, HGPPS should be taken into consideration in the differential diagnosis of any young patient presenting with increasing external ophthalmoplegia and scoliosis.

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