

Horizontal gaze palsy with progressive scoliosis - A case report

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Abstract

Horizontal gaze palsy with progressive scoliosis (HGPPS) is a rare congenital disorder characterized by absence of conjugate horizontal eye movements and accompanied by progressive scoliosis developing in childhood and adolescence. It occurs due to mutation in *ROBO 3* gene/chromosome 11q23-q25. We report a case of a 60-year-old lady who presented with complaints of defective vision in both eyes. On examination, she had scoliosis with restricted abduction and adduction in both eyes with intact elevation and depression. Magnetic resonance imaging of the brain and orbit showed brainstem hypoplasia with absence of facial colliculi, presence of a deep midline pontine cleft (split pons sign), and a butterfly configuration of the medulla, which are the radiological findings seen in this disorder.

Key words: HGPPS; horizontal gaze palsy; scoliosis

Introduction

Horizontal gaze palsy with progressive scoliosis (HGPPS) is a rare autosomal recessive disorder characterized by congenital absence of conjugate horizontal eye movements, preservation of vertical gaze and convergence and progressive scoliosis developing in childhood and adolescence.^[1] It occurs due to mutation in *ROBO 3* gene/chromosome 11q23-q25. Magnetic resonance imaging (MRI) depicted brainstem hypoplasia with absence of facial colliculi, presence of a deep midline pontine cleft (split pons sign), and a butterfly configuration of the medulla.

Case Report

A 60-year-old patient presented with complaints of defective vision in both eyes for the past 6 months. She did not present earlier as she was asymptomatic before. There was history

of progressive scoliosis since childhood. Her father had similar complaints. On general examination, scoliosis was noted. On ocular examination, visual acuity in both eyes was hand movements. Anterior segment examination showed normal findings with mature cataract in both eyes. Extraocular movements showed restriction of abduction and adduction with intact elevation and depression in both eyes. Neurological examination was normal. MRI of the brain and orbit (Siemens, MAGNETOM Skyra 3T, Muenchen, Germany) showed brainstem hypoplasia with absence of the facial colliculi [Figure 1], presence of a deep midline pontine cleft (split pons sign), and a butterfly configuration of the medulla [Figure 2], which are the radiological findings seen in this disorder. The MRI sequences done were fluid-attenuated inversion recovery (FLAIR) axial, T1 coronal, three-dimensional T2 SPACE, diffusion-weighted images and fat-suppressed T2 coronal. There were no signal changes within the medulla or pons in any of the sequences. Tractography was not done. B scan of both eyes was normal,

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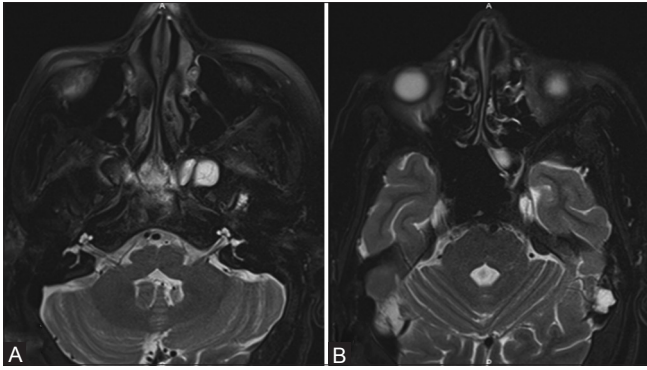


Figure 1 (A and B): (A, B) MRI brain axial T2W image showing absent facial colliculi and tenting of fourth ventricle

and cataract surgery with posterior chamber intraocular lens implantation was advised.

Discussion

HGPPS is a rare recessive congenital cranial dysinnervation disorder that has been reported in several dozen consanguineous families. The first descriptions of associated horizontal gaze palsy and scoliosis date back to 30 years. In 1974, Crisfield^[1] observed four Chinese siblings with severe scoliosis and progressive external ophthalmoplegia, and Dretakis and Kondoyannis^[2] reported five other cases from two non-consanguineous families. In 1975, Sharpe *et al.*^[3] considered the association of paralysis of horizontal gaze, pendular nystagmus, and progressive scoliosis to constitute a distinctive heredofamilial syndrome. In reviewing the literature more than 20 years later, Thomsen *et al.*^[4] found 11 articles reporting 39 patients with a combination of progressive scoliosis and familial congenital gaze palsy. In 2002, Jen *et al.*^[5] described six patients from two non-consanguineous families and mapped the disease locus to a 30-cM interval on chromosome 11q23–25; two additional patients were reported by Pieh *et al.*^[6]

HGPPS occurs due to the mutation in round-about homolog of *Drosophila* (*ROBO3*) chromosome 11q23-q5.^[7] Mutations in *ROBO* gene are associated with non-crossing of selected axonal paths in the central nervous system that are normally subjected to midline crossing during embryonic development.^[8]

Horizontal gaze palsy is rarely reported in isolation and may be diagnosed as Duane syndrome type III. Horizontal gaze palsy together with facial weakness is classified as Mobius syndrome. The only consistently inherited form of congenital horizontal gaze palsy is when it is co-inherited with progressive scoliosis. An individual with HGPPS has absent horizontal eye movement on attempted gaze to right or left but normal vertical gaze upward and develops scoliosis during childhood. Scoliosis can be demonstrated by a coronal

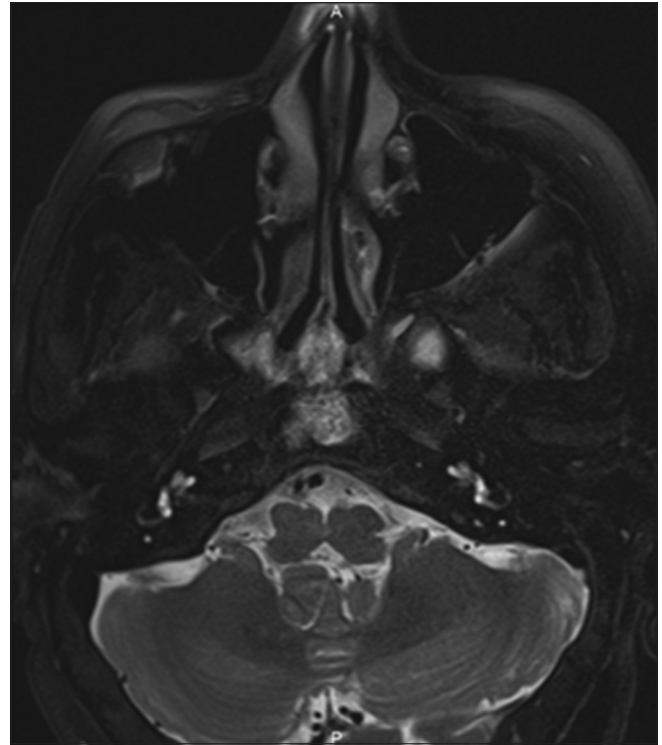


Figure 2: MRI brain axial T2W image showing butterfly-shaped medulla

scout MRI of the thoracic and lumbar spine.

The progressive thoracic scoliosis found in individuals with HGPPS can be detected as early as the first months of life and is typically diagnosed by mid-childhood. No underlying pathology of muscle, spinal cord, or spine has been detected, and the defect seems to most closely mimic idiopathic scoliosis. The pathogenesis of idiopathic scoliosis remains a subject of debate. It has been suggested that a primary neurologic dysfunction at some level of the central nervous system can be one of the underlying causes.^[5]

MRI typically reveals a characteristic brainstem configuration with anterior and posterior midline clefts. The unusual anterior cleft at medullary level is accompanied by anteriorly flattened medulla which gives a butterfly-like configuration in axial sections, as seen in our case. The pons is flattened and the facial colliculi does not protrude into the fourth ventricle. Our patient did not present earlier as she was asymptomatic visually and presented only after she developed severe loss of vision secondary to senile mature cataract in both the eyes. The extraocular muscles and third, fourth and sixth cranial nerves are usually normal. It is possible that the greater degree of brainstem hypoplasia seen in patients with HGPPS, which is characterized by involvement of both the pons and medulla reflects abnormality of additional cell groups that are required for maintenance of axial posture, thus, explaining the association of scoliosis.^[9]

Conclusion

HGPPS is an autosomal recessive condition clinically characterized by the lack of voluntary horizontal eye movements and progressive scoliosis. 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.

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Conflicts of interest

There are no conflicts of interest.

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