CASE REPORT

Horizontal gaze palsy and scoliosis: a case report and review of the literature

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Abstract

Background: The syndrome of horizontal gaze palsy with progressive scoliosis (HGPPS) is a rare human disease and while its association with scoliosis was first reported in 1974, thirty years later the responsible genetic mutations are being elucidated. This progress was due to the reporting of single interesting cases.

Case description: We present the case of a 27 year-old male patient who was admitted for elective scoliosis correction surgery and who represented after an uncomplicated discharge with headache and vomiting; because of a gaze palsy he underwent brain imaging that confirmed a brainstem abnormality, consistent with the syndrome of horizontal gaze palsy with progressive scoliosis (HGPPS), a rare autosomal recessive human disease.

Conclusion: This rare syndrome is a good example of how single case reports can lead to advances in laboratory research and genetic characterisation of diseases, together with implications for neurodevelopment. Vigilance in the neurological examination in an otherwise 'non-neurological' scoliosis will help identify potential such cases, whilst further genetic/molecular analysis may shed further light into neuro-embryological development and patterning. Hippokratia 2013; 17 (4): 370-372.

Keywords: Horizontal gaze palsy, scoliosis, neurodevelopment, developmental biology, patterning

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Introduction

The syndrome of horizontal gaze palsy with progressive scoliosis (HGPPS) is a rare human disease. The association with scoliosis was first reported in 1974, whilst thirty years later the responsible gene ROBO3 and mutations were being elucidated[1,2]. This progress was due to the reporting of single interesting cases. Studies of human genetic disorders affecting eye movement have helped define neuronal codes that underlie axonal pathfinding[3,4]. Horizontal gaze palsy may be due to defects to the abducens nuclei (cranial nerve VI), which contain both ipsilaterally projecting motor neurons and contralaterally projecting interneurons. It may also be due to supranuclear control regions, such as the pontine paramedian reticular formation, that project to the abducens and occculomotor nuclei[5,6]. HGPPS is an autosomal recessive disease. MRI images show a midline cleft at the medulla and an enlarged fourth ventricle. The hindbrain abnormalities in HGPPS have not been completely characterised. Yet the patients are remarkably neurologically intact. These findings suggest normal sensorimotor integration and that the axonal pathways have responded appropriately to short and long range cues to find their targets, although contralateral to the targets to the normal population[1-5,7].

Case Report

We present the case of a 27 years old asylum seeker who was admitted for an elective correction of his progressive scoliotic deformity. He had a right thoracic scoliosis extending from T5 to L1 with a quite prominent rib hump to the right (Figures 1 and 2). He was in a lot of emotional distress regarding his appearance.

His past medical history was only remarkable in that he had been tortured in his homeland and jailed for 2 years. Family history was significant and included a scoliosis operation for his sister, who had unfortunately died 2 days following her operation. Additionally, his nephew from his other sister had also been diagnosed with scoliosis.

On examination he was a young fit man with a stiff curve. Neurological examination of the upper limbs showed normal tone bilaterally, with normal power in all myotomes and normal sensation to light touch and pin prick. His reflexes were symmetrically normal. Lower limb neurology was again normal. Cranial nerve examination revealed a horizontal gaze palsy with 20° downgaze and 10° upgaze. Pupils were normal and visual acuity was 6/18 on the left and 6/12 on the right due to myopic astigmatism. Up-beat nystagmus was observed.

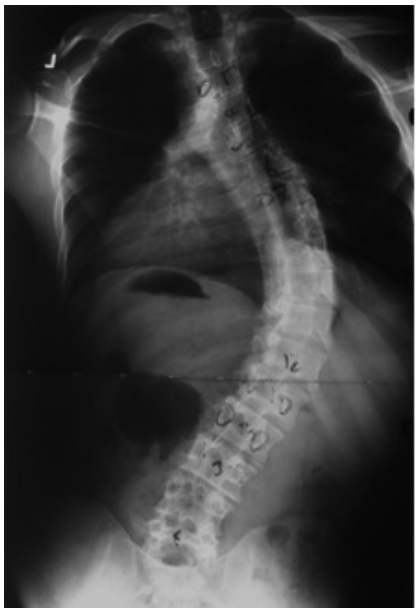

Figure 1: Antero-posterior radiograph of the spine demonstrating a right thoracic scoliosis extending from T5 to L1 with a prominent rib hump to the right.

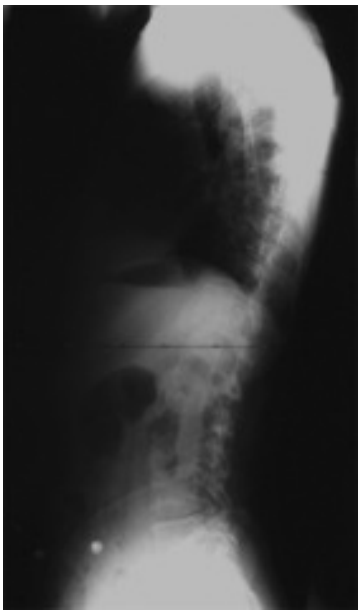

Figure 2: Lateral radiograph of the whole spine demonstrating adequate sagittal balance despite the scoliotic deformity visible on the antero-posterior radiograph.

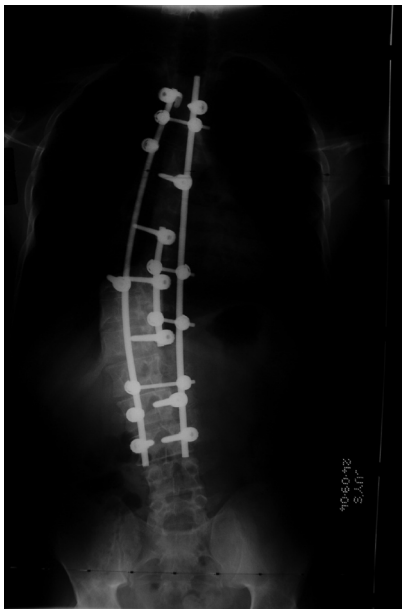

Figure 3: Postoperative antero-posterior radiograph showing the instrumented fusion of the scoliotic deformity.

He had a positive jaw reflex, but no Hoffman's sign or upgoing plantars. There was no cognitive abnormality.

A posterior surgical approach was used with instrumented fusion from T3 to L3 (Figures 3 and 4). The curve was stiff and the ligamentum flavum exhibited ossification. Intraoperative somatosensory evoked potentials were recorded within normal values. He had a normal postoperative period and was discharged on the 9th day, able to mobilise independently. However, he represented 2 weeks later complaining of episodes of frontal headache and vomiting.

On examination the wound had healed well. In order to further investigate his horizontal gaze palsy he underwent an MRI scan of his brain. This showed evidence of old trauma to the posterior parietal region on the left with a small amount of scarring of the brain cortex in the vicinity. The pons and the medulla were partially split in the midline. The vermis was small and had a midline groove (Figure 5). A few days later his headache responded well to intravenous fluids and simple analgesia and he was discharged home.

Discussion

The patient presented with severe right thoracic scoliosis, extending from T5 to L1 vertebrae and ophthalmic examination showed complete horizontal gaze palsy with 20° downgaze and 10° upgaze. An upbeat nystagmus was also observed. Brainstem developmental abnormalities were detected by MRI studies, featuring a partial midline split in the medulla oblongata and pons with posterior focus. Both physical and radiological examinations strongly suggest a diagnosis of HGPPS, a finding corroborated by previous descriptions of this genetic syndrome[5,8]. Apart from the common signs of this disease, the patient also presented with ossification of the ligamentum flavum. Thus far, no correlation between ligamentum flavum ossification and HGPPS has been discovered, and this is usually associated with myelopathy. The originating factors of this condition have not yet been identified and further investigations are required to allow an informed discussion of the finding.

A clinical misdiagnosis is highly unlikely in this situation since the combination of progressive scoliosis with full horizontal gaze palsy is, so far, exclusive to HGPPS. Nevertheless we recognise that genetic testing aimed at detecting a ROBO3 mutation would further validate this result. Interestingly, a recently published study has described a case of an 8-year-old Serbian child presenting with all the clinical features of HGPPS where a mutation in the ROBO3 gene was absent or not successfully identified[9]. Therefore the authors hypothesise that this recessively inherited condition may not only be caused by detrimental alterations in the genetic sequence of the ROBO3 gene. Epidemiologically HGPPS mostly concentrates in families of Saudi[2,6], Turkish[6], Irish[10] and Tunisian[11] ethnicities. To our knowledge a case of HGPPS in an Iraqi individual has yet to be published, therefore we suggest that this patient is likely to carry a novel mutation in the ROBO3 gene, which adds further value in commencing genetic investigations in this patient.

The study of conditions affecting horizontal eye movement has helped elucidate the causes of horizontal gaze palsy seen in HGPPS. It is thought that the altered medullary and pontine morphologies observed in HGPPS patients may be a result of failed decussation of corticospinal and dorsal column/medial lemniscus pathways[2,12].

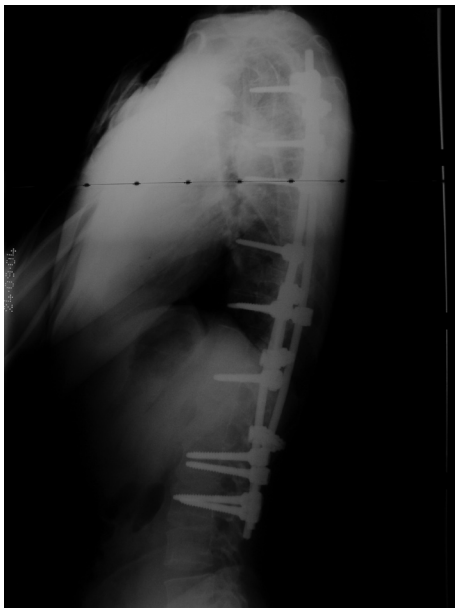

Figure 4: Postoperative lateral radiograph showing the instrumented fusion of the scoliotic deformity.

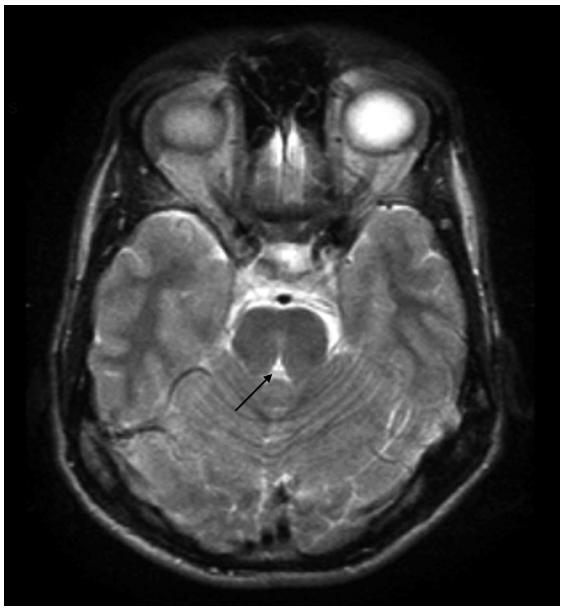

Figure 5: MRI axial view showing the brainstem (pointed by the arrow) with a midline split in the medulla and pons; and a midline groove in a small vermis.

Thus the failure in crossing of these neuronal pathways is believed to be responsible for the lack of horizontal eye movement in such patients. Consequently it is hypothesised that the products of the ROBO3 gene may be involved in promoting the crossing of these neuronal pathways during development. Progressive scoliosis is also a pathognomonic feature of HGPPS and research has proposed a functional and anatomical abnormality in the pontine reticular formation as the potential causative factor[2]. In spite of this, ROBO3 mutations may also induce detrimental musculoskeletal changes capable of promoting scoliosis.

Even though some studies have attempted to clarify the mechanisms that lead to the clinical observations characteristic of HGPPS, there is still a great requirement for research aimed at determining the molecular mechanisms involved in the stimulation of pathway decussation by ROBO3 products. Furthermore, it is also unclear how a mutation in ROBO3 during development causes progressive scoliosis after birth. Thus we propose that the study of HGPPS can significantly improve our understanding of the relationship between neuronal pathway decussation and horizontal gaze and the mechanisms behind the initiation of scoliosis.

Conflict of Interest

None.

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