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CASE REPORT

Four Siblings With Congenital Scoliosis and Dysmorphism: A Rare Case of Familial Spondylocostal Dysostosis

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ABSTRAK

Skoliosis kongenital adalah perkembangan tulang belakang yang tidak normal yang merangkumi pembentukan sebahagian tulang sahaja, kurangnya pemisahan di antara tulang belakang atau kehilangan bahagian tertentu tulang belakang. Etiologi sebenar skoliosis kongenital masih tidak jelas. Walau bagaimanapun, ia dipengaruhi oleh kecenderungan genetik dan faktor persekitaran. Kami melaporkan siri kes skoliosis kongenital dengan ciri-ciri dismorfik dalam empat orang adik-beradik dan membincangkan mengenai sindrom spondylocostal dysostosis yang mempunyai kaitan dengan skoliosis kongenital. Ciri-ciri dismorfik termasuk hipertelorisme, 'ptosis' kedua-dua mata, 'high arch palate', langit-langit yang tinggi dan leher 'webbed'. Pembedahan instrumentasi tulang belakang dilakukan dalam tiga adik beradik. Semua pesakit pulih dengan baik selepas pembedahan tanpa komplikasi kecederaan saraf. Rawatan susulan pada tahun pertama dan kedua selepas pembedahan menunjukkan tiada perubahan pada kadar lengkung dan tulang belakang telah bercantum.

Kata kunci: dysostoses, hipertelorisme, kongenital, skoliosis

ABSTRACT

Congenital scoliosis is an abnormal development of the vertebrae resulting in combination of partial formation, lack of separation or missing portion of the vertebra. The exact aetiology of congenital scoliosis remains unclear. It is influenced by genetic predisposition and environmental factors. We report a case series of congenital scoliosis with dysmorphic features in four siblings and discuss

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the description of spondylocostal dysostosis syndrome associated with congenital scoliosis. The dysmorphic features include hypertelorism, bilateral ptosis, high arch palate and webbed neck. Posterior spinal instrumentation and fusion surgery was performed in three siblings. All patients did well post-operatively with no neurological complications. Subsequent follow-up at one and two years after the operation showed that the curves remained unchanged and the fusions were solid.

Keywords: congenital, dysostoses, hypertelorism, scoliosis

INTRODUCTION

Congenital scoliosis occurs approximately 0.5 or 1 in 1000 births (Ghebranious et al. 2007). Congenital scoliosis is rarely seen in more than one member of a family. It is often associated with abnormalities of multiple organ systems and other dysplastic anomalies (Kaspiris et al. 2008). Clinical manifestation of congenital scoliosis may be linked to about seventy different syndromes (Heddequist & Emans 2007). Familial incidence of congenital deformity on record involves other congenital anomalies, spondylocostal dysplasia, and spondylothoracic dysplasia (Akbarnia & Moe 1978). A chromosomal study identified a large number of chromosomal deletions, specifically at regions 2p13-15, 15q12 and 6q13, which lead to the conclusion that the region is involved in its development genetically (Giampieto et al. 2003).

Klippel-Feil syndrome, Sprengel Deformity, Goldenhar's syndrome (craniofacial disorders, epibulbar dermoids and microtia), Jarcho-Levin syndrome, Allagile syndrome, and VACTREL (vertebral malformation, cardiac malformations, tracheoesophageal fistula, renal radial anomalies and limb defects) are among the syndromes which are associated with congenital scoliosis (Kaspiris et al. 2008).

Spondylocostal dysostosis is rare, and it causes abnormal bone development in the spine and the ribs. Spondylocostal dysostosis type I can be inherited in an autosomal recessive pattern, while other types can be inherited in an autosomal dominant pattern. This case series highlights the cases of congenital scoliosis with dysmorphism in four siblings, to add to the limited cases published, to date.

CASE REPORT

Four siblings were seen at our centre for progressive spinal curvature. There was no history of consanguinity of the parents. There were four children born in this family and all of them were affected with congenital scoliosis. Both parents were of average stature with no known history of spinal deformity in the family. The mother had no exposure to smoke, drugs or toxins during pregnancy. All four children were born full-term, with uneventful antenatal, prenatal and postnatal

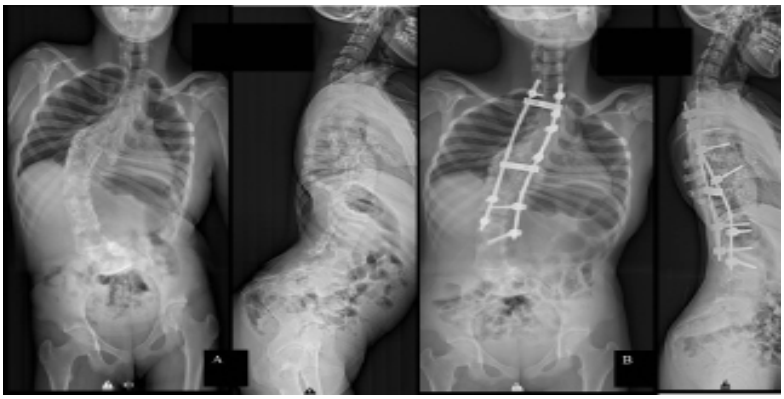

Figure 1: (A) Whole spine radiograph showing thoracolumbar curve with Cobb's angle of 80°, apex at T11 and failure of vertebral segmentation at multiple levels. (B) Improvement in Cobb's angle of 56° with improvement in lung volume post-surgery.

history. All of the siblings attained normal developmental milestone with normal intelligence. They all had short stature with dysmorphic features. Only the eldest child complained of respiratory symptoms, the rest of the siblings were asymptomatic.

Case 1

The eldest sibling was an 18 year-old girl, who was referred to us at the age of 12 years for scoliosis. She complained of poor effort tolerance and easily fatigued on exertion. Her mother noticed her spinal deformity since the age of five years but did not seek any medical treatment. On examination, she had dysmorphic features which included hypertelorism, bilateral ptosis, high arch palate, pectus excavatum and neck webbing. Spine examination revealed right thoracic hump, hyperlordotic lumbar spine with left pelvic and right shoulder tilt.

Spine radiograph showed failure of segmentation at multiple levels, mid-thoracic and thoraco-lumbar scoliosis with Cobb's angle of 80° (Figure 1). The curve was not corrected on side bending. Computed tomography scan showed failure of segmentation of T3 and T4, T6-T11 and L1-L3 and L4 to S1. Magnetic resonance imaging (MRI) revealed narrowed neural foramina at the level of T10-T11 and T11-T12 on the left. No evidence of canal stenosis, no syringomyelia or tethered cord was observed. Lung function test showed moderate restrictive lung disease secondary to scoliosis. In view of her progressive spinal curve and respiratory problem, posterior spinal instrumentation and fusion surgery was done from level T2-L1, when she 16 years old. Post-surgery, she was asymptomatic and well.

Case 2

The second sibling was a 15-year-old girl and her mother first noticed deformity when she was eight years old. Physical examination showed similar features of dysmorphism (hypertelorism, bilateral ptosis, high

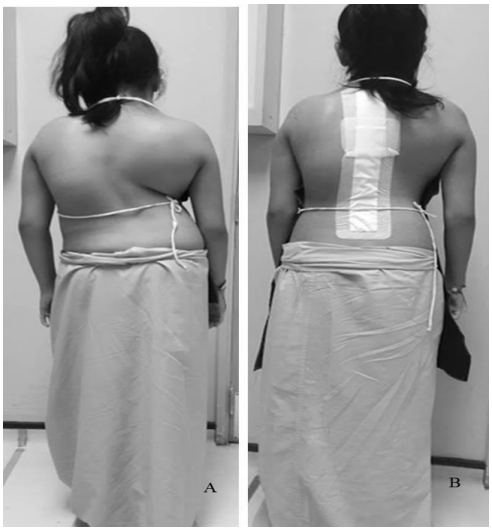

Figure 2: Comparison of thoracic hump improvement with balanced shoulder and pelvis before (A) and after surgery (B).

arch palate and webbed neck. She had no pectus excavatum. She had left thoracic hump with left shoulder and right pelvic tilt (Figure 2).

Whole spine radiograph showed thoracolumbar scoliosis with Cobb's angle of 76° (Figure 3). Computerised tomography (CT) spine revealed failure of segmentation at level T8-T11 and L4 to L5. MRI findings showed no cord abnormalities. Posterior spinal instrumentation and fusion surgery from T4 to L2 was done at the age of 14 years. Post-surgery, she recovered well with balanced shoulder and pelvis (Figure 2).

Case 3

The third sibling was a 13 year-old girl, noted to have spinal deformity since she was seven years old. Physical examination showed similar features of dysmorphism (hypertelorism, bilateral ptosis, high arch palate and webbed neck). She had no pectus excavatum. She had right thoracic hump with right shoulder and left pelvic tilt (Figure 4). Whole spine radiograph showed lower thoracic scoliosis with Cobb's angle of 84° (Figure 5). CT spine revealed failure of segmentation at level T1 and T2, T6 and T7, and T8 to T11. MRI findings showed no cord abnormalities. Posterior spinal instrumentation and fusion from level T4 to L2 was done when she was 14 years old. Post-

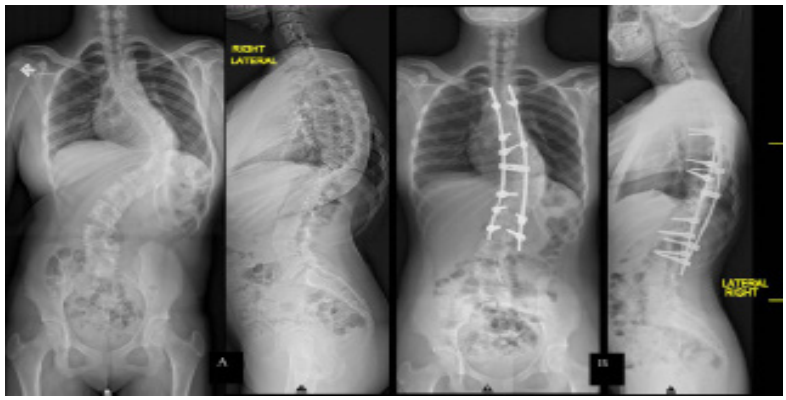

Figure 3: (A) Whole spine radiograph showing thoracolumbar curve with Cobb's angle of 76°, and failure of vertebral segmentation at multiple levels. (B) Post spinal instrumentation surgery showed improvement of Cobb's angle to 50°.

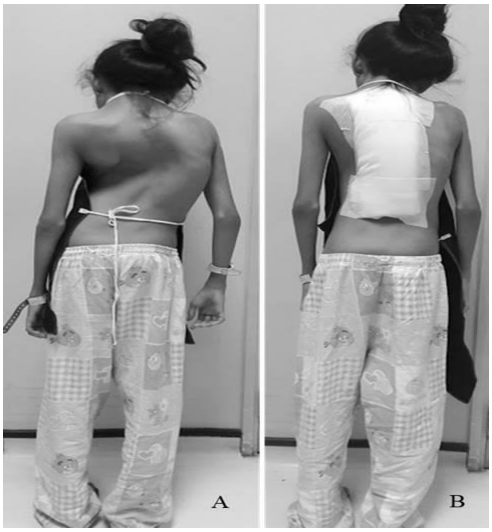

Figure 4: Comparison of thoracic hump improvement with balanced shoulder and pelvis before (A) and after surgery (B).

surgery, she recovered well with balanced shoulder and pelvis (Figure 4).

Case 4

The youngest sibling was a 9-year-old boy who was screened at 5 years due to three siblings having congenital scoliosis. Patient was also asymptomatic. Clinically, he had no obvious scoliosis with balanced shoulder and pelvis. He also presented with dysmorphic features (hypertelorism, bilateral ptosis, high arch palate, low set ears and webbed neck). He had pectus excavatum (similar to his eldest sister). Whole spine radiograph was done at the age of 5 years and it revealed mild thoracic scoliosis (Cobb' angle of 10°) with failure of segmentation at multiple levels. CT scan showed failure of segmentation of T3-T5, and T7-T11. MRI findings revealed no syringomyelia or tethered cord. Clinical examination at 9 years, showed no thoracic or lumbar hump with balanced shoulder and pelvis. However, the Cobb's angle increased to 26° (Figure 6) and he was put on thoracolumbarsacral orthosis (TLSO).

DISCUSSION

Congenital scoliosis is frequently associated with developmental abnormalities of other organs.

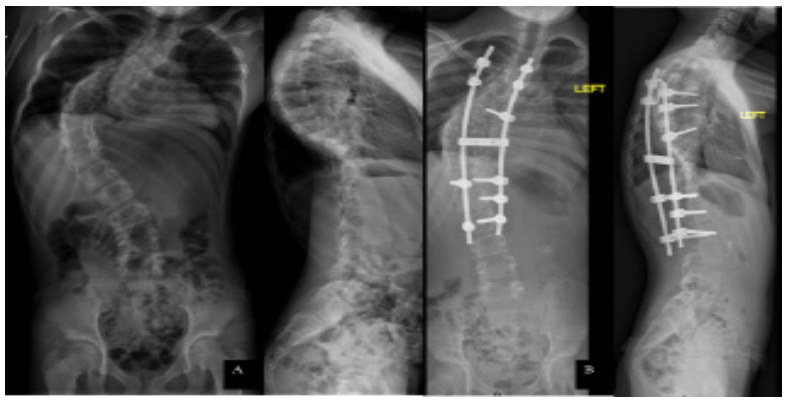

Figure 5: (A) Whole spine radiograph showing thoracic curve with Cobb's angle of 95°, and failure of vertebral segmentation at multiple levels. (B) Post spinal instrumentation surgery showed improvement of Cobb's angle to 53°.

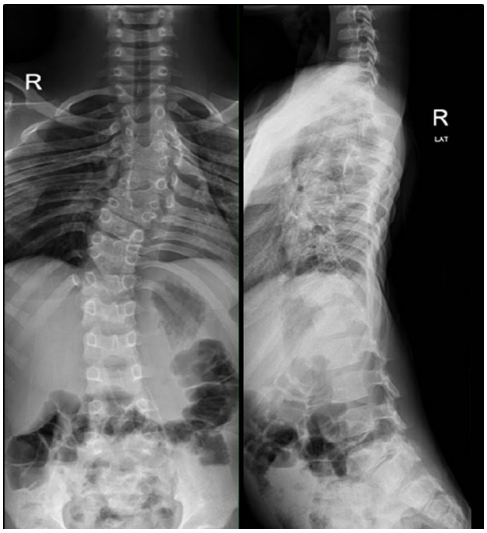

Figure 6: Whole spine radiograph revealing Cobb's angle of 26° and failure of segmentation of multiple thoracic vertebrae.

Cardiovascular system anomalies may be involved in over 25%, such as the ventricular or atrial septal defects, tetralogy of Fallot, and transposition of the great vessels. Both spinal canal and genitourinary system originate in the foetal mesoderm and develop at the fifth week of pregnancy. This common origin during development, may result in genitourinary abnormalities in 20-43% of cases (Kaspiris et al. 2008). Gastrointestinal system abnormalities may include tracheo-oesophageal fistulas and esophageal atresia (Kaspiris et al. 2008).

Nervous system anomalies which include diastematomyelia, Chiari malformation and intradural lipoma may be present in 35% of cases (Kaspiris et al. 2008). Café-au-lait spots, skin tags and hairy patches may be present in the subcutaneous tissue of the scoliotic spinal cord area (Kaspiris et al. 2008). Congenital scoliosis results in increasing asymmetry of lung size and can influence the respiratory function (Kaspiris et al. 2008). Previous study showed that there is no correlation between the Cobb angle and pulmonary function (Redding et al. 2008). The most reliable method for quantifying pulmonary asymmetry is by ventilation lung scan, and not by the measurement of Cobb angle.

There are two types of congenital spinal deformity characterised by multiple vertebral and rib malformations. Spondylothoracic dysostosis (also known as Jarcho-Levin syndrome) is an autosomal-recessive deformity and is associated with early infancy death from respiratory failure (Roberts et al. 1988). Other features include wide nasal bridge, broad forehead, upwardly slanted eyelids, nostrils that are tipped forward (anteverted nares), and an enlarged posterior skull. The second variety is known as spondylocostal dysostosis, and it may be inherited as a recessive or a dominant trait with normal life expectancy (Roberts et al. 1988). Our patients showed dominant inheritance as all the siblings were affected.

In spondylothoracic dysostosis, there are severe rib deformities with multiple posterior fusions producing a small thorax and a crab-like radiographic appearance. However, in spondylocostal dysostosis, the ribs are only slightly affected. In our patient, the entire sibling presented with short stature, which is common in spondylocostal dysostosis. The affected child had low birth-weight and was of short stature (short-trunk dwarfism). At puberty, the standing

height remains just below the third centile because vertebral growth is diminished and there is virtually no adolescent growth-spurt (Roberts et al. 1988). The height at maturity is much reduced, usually below 155 cm.

Approximately, one-third of children with spondylothoracic dysostosis and a quarter of those with spondylocostal dysostosis have other malformations (Casamassima et al. 1981). In both conditions, the most common anomalies are congenital heart disease and renal. Urogenital abnormalities, polydactyly, trachea-oesophageal fistula and renal atresia have also been reported. These malformations occur in the same non-random fashion as in congenital scoliosis and follow the VACTERL pattern. This is not surprising because they all arise from abnormal development of paraxial mesoderm.

A recent genetic study has identified new compound heterozygous *LFNG* mutation the causal gene for spondylocostal dysostosis (Otomo et al. 2019). Another genetic study suggests that congenital scoliosis and spondylocostal dysostosis can result from different severity of bi-allelic loss of *TBX6* function (Otomo et al. 2019). Chromosomal mapping needs to be done in the patients' family, in order to study the chromosomes involved in this genetic condition. However, as the siblings' father had passed away, the sample for chromosomal study could only be taken from the siblings. The father was noted to have neck webbing when he was alive. Lastly, genetic counselling may be of benefit for families with this disorder. Autosomal dominant inheritance means that one copy of an altered gene in each cell is sufficient to cause the disorder. Therefore, their future partners need to understand that their offsprings will have similar spinal and ribs deformity, which may or may not require surgical correction with normal life expectancy.

CONCLUSION

Spondylocostal dysostosis with dysmorphic features is rare. The management of congenital scoliosis depends on symptoms and severity of the spinal deformity.

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