Case Report

Concurrent Scoliosis and Dentofacial Anomaly: A Case Report

Samuel Bennett^a Colin Whitewood^b Jiake Xu^a

^aMolecular Laboratory and Division of Regenerative Medicine, M Block QEII Medical Centre, School of Biomedical Sciences, The University of Western Australia, Perth, WA, Australia;

^bDepartment of Orthopaedics, Perth Children's Hospital, Perth, WA, Australia

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Abstract

The relationship between scoliosis, dentofacial anomaly, and malocclusion is poorly understood. We report a novel and complex pediatric case of concurrent juvenile scoliosis, dentofacial anomaly, and malocclusion, successfully treated and managed by an interdisciplinary hospital team over a 15-year period. The degree of severity of the scoliosis and dentofacial anomaly necessitates surgical intervention. Successful orthopedic surgical procedures have improved the patient's quality of life. Future surgical correction of the dentofacial anomaly and malocclusion is necessary to improve the patient's condition from psychosocial, aesthetic, and functional standpoints. The patient's condition is characterized by multiple congenital abnormalities, developmental delay, seizure disorder, juvenile scoliosis, and dentofacial anomaly with malocclusion. Intriguingly, a unifying diagnosis for the patient's condition could not be confirmed despite the indication of a syndromic cause. The collection of characteristics is suggestive of the chromosome 22q11.2 deletion syndromes (including velocardiofacial syndrome [VCFS] or DiGeorge syndrome) as possible genetic causes. Clinical genetics testing was unable to establish a diagnosis of chromosome 22q11.2 deletion, VCFS or DiGeorge syndrome. Further investigation of the genotype-phenotype relationships of scoliosis, dentofacial anomaly, and malocclusion is required to improve medical knowledge, diagnostic capability, and patient care, specifically relating to cases of undiagnosed diseases. Future research utilizing next-generation sequencing techniques is necessary to aim for precise genetic diagnosis, including knowledge of the underlying cellular and molecular mechanisms, for the development of the potential of therapeutic approaches targeting gene repair.

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Introduction

Scoliosis is a disorder characterized by lateral curvature and rotation of the spine [1]. The etiology of scoliosis is largely unknown; however, 3 types of scoliosis have been identified: idiopathic, congenital, and neuromuscular. The most common form of scoliosis is idiopathic. Idiopathic scoliosis may be classified by the age of onset: infantile (age <3 years), juvenile (age 5–8 years), and adolescent (age 10 years until fully grown) [2]. The prevalence of idiopathic scoliosis is 1–3%, and females are more affected than males [3, 4]. Family history is a risk factor and recent genetic advances identify several candidate loci for idiopathic scoliosis, particularly the *LBX1* region as a prime susceptibility locus [5]. Congenital scoliosis is defined as a lateral spinal deformity caused during embryonic vertebral development and affects approximately 1 per 1,000 live births [6, 7]. The etiology of congenital scoliosis is largely unknown and is attributed to genetic and environmental factors [8]. Approximately 38–55% of congenital scoliosis deformities occur as a syndrome [6]. Recent research has identified a subtype of congenital scoliosis demonstrating compound inheritance of a pathogenic mutation and a hypomorphic allele of the *TBX6* gene, responsible for approximately 10% of congenital scoliosis cases [9, 10]. The third type of scoliosis occurs following neuromuscular disease or dysfunction, such as muscular dystrophy or paraplegia.

The relationship between scoliosis, dentofacial deformity, and malocclusion is poorly understood. There is evidence of an association between scoliosis and malocclusion in the scientific literature. Patients with idiopathic scoliosis have asymmetric features of malocclusion and a higher proportion of Class III malocclusion as compared with patients unaffected by scoliosis [11]. Patients with craniofacial anomalies, including characteristic malocclusion and dentofacial deformity, show an increased predisposition to spinal deformity [12, 13]. Further research and investigation of clinical data, in addition to genotype-phenotype relationships and molecular mechanisms of scoliosis, malocclusion, and facial deformity is, therefore, required to improve our knowledge and understanding of the etiology of undiagnosed diseases, such as those documented by this case report.

Case Report

We present a complex pediatric case of juvenile idiopathic scoliosis with concurrent malocclusion and dentofacial anomaly treated and managed by an interdisciplinary hospital team over a 15-year period. Intriguingly, a unifying diagnosis for the patient's rare and unusual condition could not be determined despite the suggestion of a syndrome.

Results

The male South Asian patient was born via cesarean section at 41 weeks due to large birth weight (4.75 kg) and, subsequently, developed moderate neonatal hypoglycemia. Feeding difficulties became apparent from 6 months of age and persisted into childhood. The patient was first seen at Princess Margaret Hospital for Children on 25 September 2003, aged 3 years and 7 months due to feeding and behavioral difficulties. Hyper nasality of speech was detected during the initial assessment; however, there was no suggestion of cleft lip and/or palate upon further examination. The summary of interdisciplinary findings is as follows:

Fig. 1. Foramen magnum and spinal cord narrowing were detected by MRI in 2004. MRI, magnetic resonance imaging.

- Congenital abnormalities
 - Visual impairment (retinal anomaly resulting in myopia)
 - Kidney enlargement and dysplasia
 - Aortic dilatation
 - Phalangeal abnormalities
- Epilepsy
- Global developmental delay
- Family history of developmental delay
- Thoracolumbar scoliosis
- Craniocervical abnormality: atlanto-occipital fusion and foramen magnum narrowing
- Dentofacial anomaly
- Malocclusion
- Left leg shortening
- Ligamentous laxity

The collectiveness of the patient's abnormalities is suggestive of a syndrome. To date, no unifying diagnosis can be reached. A possible connective tissue abnormality may explain much of the patient's condition. Interestingly, a consistent finding during multiple orthopedic surgical assessments and procedures was that there are multiple congenital bone abnormalities and that the bone quality was poor. Although possibly suggestive, no diagnosis of bone dysplasia or pathology could be made.

The seizure disorder appears to be an idiopathic condition. The underlying cause of the seizures is unknown although febrile convulsions were suggested as a possible initiating factor. Research appears to suggest that moderate neonatal hypoglycemia resulting in brain injury may predispose those affected to impaired neurodevelopment during childhood [14, 15]. Further, there is a family history of developmental delay as the patient's paternal uncle is also affected. In addition, magnetic resonance imaging detected narrowing of foramen magnum and the spinal cord, with atlanto-occipital fusion, which might contribute to the neurological symptoms (Fig. 1).

Fig. 2. Long-term full-spine conventional radiograph and measurement of scoliosis.

Due to the constellation of abnormalities, the patient was referred for clinical genetics assessment, evaluation, and testing to investigate the chromosome 22q11.2 deletion syndromes, including velocardiofacial syndrome (VCFS) or DiGeorge syndrome, as a possible cause of the patient's condition. Cytogenetics testing in 2004 found the following karyotype: male, 46 XY, and 22q11.2. No evidence of deletion of genetic material at the VCFS/DiGeorge region of band q11.2 on either chromosome 22 was detected. Fluorescence in situ hybridization testing of chromosome 22 and subtelomeric deletion studies were normal. Therefore, a diagnosis of 22q11.2 deletion, VCFS, or DiGeorge syndrome could not be confirmed.

Orthopedic assessment and management of scoliosis commenced in 2006 when the patient was 6 years of age. At this stage, an upper thoracic Cobb angle of 28° was measured, and brace therapy was commenced (Fig. 2). Long-term full-spine radiographic assessment and progression of scoliosis were recorded. By 2016, the patient's scoliosis was characterized as "inverse-S" with "lumbar lordosis," and the degree of curvature (Cobb angle = 73°) indicated the need for surgical treatment. Presurgical 3D reconstructed volume-rendered computed tomography images from anterior, lateral, and posterior views were taken in 2014 (Fig. 3). Surgical intervention in 2015 was performed to achieve decompression of the craniocervical junction and C1 stability, with posterior fusion from Occipital-C4. In 2016, surgical posterior instrumentation and stabilization of T2-L4 were performed. Postsurgical spinal radiograph taken in 2017 confirmed successful orthopedic correction (Fig. 4). Patient recovery from surgery and at subsequent follow-up appointments indicated a satisfactory outcome. The patient is currently able to perform administrative duties in an office setting and enjoys working in a team environment. Current biochemical results are within accepted normal limits (Table 1).

The patient is affected by severe dentofacial deformity characterized by facial dysmorphism, mid-facial deficiency with reduced cranial base length, and retrognathic maxilla. Facially, the patient has a bulbous nose tip and hooded eyes, which are a feature of 22q11.2 deletion syndrome (Fig. 5) [16]. Moreover, the patient has several cephalometric features of VCFS, including reduced cranial base length, maxillary deficiency, and retroclination of the lower incisors (Fig. 6), with cephalometric summary presented in Table 2 [17]. Salient characteristics of the malocclusion include horizontal maxillo-mandibular dental arch discrepancy and severe dental crowding. The

Fig. 3. Presurgery full-spine 3D CT reconstructions. CT, computed tomography.

Fig. 4. Postsurgery full-spine conventional radiograph.

patient's dentofacial deformity and malocclusion remain a functionally and psychosocially debilitating conditions. Serial cephalometric growth assessment indicates that facial growth has ceased and that surgical-orthodontic correction of the patient's dentofacial anomaly and malocclusion may proceed. Further team evaluation of this stage of care is ongoing.

Table 1. Summary of biochemistry results

Test	Patient	Normal range
<i>Full blood picture</i>		
Hemoglobin	131	135–180 g/L
White cell count	9.45	4.0–11.0 × 10 ⁹ /L
Platelet count – blood	197	150–400 × 10 ⁹ /L
Red cell count	4.58	4.5–5.5 × 10 ¹² /L
Hematocrit	0.39	0.4–0.54 L/L
<i>Liver function</i>		
Protein total – plasma	73	60–80 g/L
Albumin – plasma	36	35–50 g/L
Globulins – plasma	37	25–42 g/L
Bilirubin total – plasma	9	<20 µmol/L
<i>Urea and electrolytes</i>		
Sodium – plasma	138	135–145 mmol/L
Potassium – plasma	4.1	3.5–5.2 mmol/L
Bicarbonate – plasma	30	22–32 mmol/L
Urea – plasma	5.9	3.0–8.0 mmol/L
Creatinine – plasma	56	50–100 µmol/L
<i>Calcium and magnesium</i>		
Calcium – plasma	2.24	2.1–2.6 mmol/L
Magnesium – plasma	0.66	0.7–1.1 mmol/L

Fig. 5. Frontal facial photograph.

Discussion

The complexity and collective characteristics of this case prompted several members of the hospital interdisciplinary team, including medical genetics, to investigate the possibility of a known syndromic cause, most likely the chromosome 22q11.2 deletion syndromes, including VCFS or DiGeorge syndrome. The patient has the following characteristics of chromosome 22q11.2 deletion syndromes: cardiac anomalies, renal anomalies, ophthalmological

Fig. 6. Lateral cephalogram.

Table 2. Cephalometric summary

Parameter	Measurement	Patient	Normal
Cranial base	SN, mm	60	72
Maxilla	SNA, °	71	81
Mandible	SNB, °	75	78
Maxilla-to-mandible	ANB, °	–4	2.5
	Wits, mm	–14	0
Dental	/1 to Md plane, °	83	92
Facial height	LFH/TFH, %	57	55
Soft tissue	UL to E line, mm	–12	–4
	LL to E line, mm	–8	–2

S, sella turcica; N, nasion; A, point A; B, point B; Wits, Wits measurement; /1, lower incisor; Md, mandibular; LFH, lower facial height; TFH, total facial height; UL, upper lip; E line, Rickett's E line; LL, lower lip.

abnormalities, neurological, dentofacial anomalies, vertebral anomalies, cervical spine anomalies, lower limb anomalies, and developmental delay during infancy and childhood [16]. Despite these characteristics, genetics testing could not confirm a diagnosis of chromosome 22q11.2 deletion. There are numerous possible explanations for the lack of a diagnosis including, the underlying genetic cause of the patient's condition may be a point mutation in a causative gene, such as TBX1; a deletion that is too small to be detected by fluorescence in situ hybridization; an atypical deletion; a nonchromosome 22 cause with the same clinical characteristics [16, 18, 19]. Further research and investigation of the genetic etiology and genotype-phenotype relationships of undiagnosed diseases, such as those documented by

this case report, is required utilizing contemporary approaches, including next-generation sequencing methods. Aiming for precise genetic diagnosis, including knowledge of the underlying cellular and molecular mechanisms, will improve the potential of therapeutic approaches targeting gene repair.

Conclusion

A novel and complex case of multiple congenital abnormalities and scoliosis combined with dentofacial anomaly were successfully treated and managed by a hospital interdisciplinary team over a 15-year period. Despite the suggestion and investigation of a syndromic cause of the patient's condition, clinical genetics evaluation and testing could not confirm such a diagnosis. Further research and investigation of undiagnosed diseases are required to improve medical diagnosis and knowledge, patient treatment, and care.

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Statement of Ethics

The authors have no ethical conflicts to disclose. Written informed consent was obtained from the patient and his parents for publication of this case report and any accompanying images. No identifiers are included in this article relating to patient identity.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

S.B. is the primary author of the manuscript. C.W. and J.X. supervised revision and final approval. Submission statement was signed by all the authors.

Availability of Data and Material

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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