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Case Report

Scoliosis Correction Surgery in Collagen Type VI Dysfunction

Babak Mirzashahi[1], Furqan Mohammed Yaseen Khan[2,*] and Rasul Gharakhan-Maleki[2]

[1] Professor, Department of Orthopedics and Spine Surgery, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran
[2] Resident, Department of Orthopedic Surgery, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran

[*]Corresponding author: Furqan Mohammed Yaseen Khan; Resident, Department of Orthopedic Surgery, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran. Tel: +98-9904177825, Email: drfurqan@outlook.com

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Abstract

Background: Collagen VI (COLVI) dysfunction results in a combination of connective tissue and muscular disorders. Spinal involvement and development of scoliosis precede loss of ambulation and respiratory deterioration in these patients. Therefore, spinal deformity correction surgery is warranted to preserve ambulation and respiratory function.
Case Presentation: A twelve-year-old girl presented with progressive scoliosis accompanying respiratory deterioration, sitting imbalance, and wheelchair-bound. The patient demonstrated an array of overlapping phenotypes related to COLVI dysfunction, including developmental delay, muscular dystrophy (MD), fatty replacement of skeletal muscles, and reduced bone mineral density to mention few. Patient was diagnosed with COLVI dysfunction caused by COLVI alpha 2 (COL6A2) gene mutation. She had severe phenotype expression similar to Ullrich congenital MD (UCMD). A Cobb angle of 85 degrees and thoracic kyphosis of 40 degrees were recorded. Surgical correction was performed in form of spinal fusion from T4 to S1 in addition to multiple level vertebral osteotomies.
Conclusions: Respiratory distress and ambulatory problems are life-endangering events in these patients. As the disease progresses and respiratory distress increases, anesthesia becomes more difficult and the risk of surgery increases. Therefore, early intervention for correction of scoliosis is warranted to support the quality of life. Surgical time has to be kept as short as possible to minimize blood loss in these patients.

Keywords: Collagen Type VI; Scoliosis; Collagen Type VI, alpha2 Chain; Mutation; Congenital

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Background

Collagen type VI (COLVI) is a unique beaded filament collagen that represents an important extracellular matrix molecule and is found in the interstitial space of many soft tissues, including muscle, tendon, skin, cartilage, and intervertebral discs (1). COLVI dysfunction results in a combination of muscular and connective tissue disorders, including weakness, laxity and contractility of joints, and abnormal skin findings (2). Mutations in COLVI alpha 1 (COL6A1), COL6A2, and COL6A3 genes that encode COLVI, cause disease expression (3). We would like to report a very unusual patient with COL6A2 mutation, presented with progressive scoliosis.

Mutation in COL6A2 causes a spectrum of overlapping phenotypes: Bethlem myopathy (BM) on the mild side of the spectrum and Ullrich congenital muscular dystrophy (UCMD) on the severe side. BM is a combination of joint contractures and proximal muscle weakness, most frequently affecting elbow, ankle, and finger flexors. Although the onset maybe neonatal or at early childhood, a fair life expectancy is obtained due to its slow progression. BM rarely involves respiratory system and the involvement appears to be related to severe form of it (4).

UCMD is characterized by congenital muscle weakness, hypotonia, proximal joint contractures, and remarkable laxity of distal joints. Some patients with UCMD independently acquire ability to walk and respire (5). Spinal involvement and development of scoliosis in UCMD are uncommon and precede loss of ambulation and respiratory deterioration; Therefore, spinal deformity correction surgery is warranted to preserve ambulation and respiratory function (6). Thus, in this patient with progressive scoliosis, surgical correction was performed. This is a valuable case to report in view of its rarity in our population and to show favorable outcome of early intervention for spinal deformity in patients with UCMD.

Case Presentation

A twelve-year-old girl presented with progressive scoliosis accompanying respiratory deterioration and barely walking. Patient exhibited an array of overlapping phenotypes related to COLVI dysfunction, including global developmental delay, obesity, atypical facial deformity, high palate, MD, joint laxity, congenital hip dysplasia, fatty replacement of skeletal muscles, generalized hypotonia, muscle weakness, myopia, reduced bone mineral density, and talipes equinovarus (TEV). At the age of four, she had a Cobb angle of 30 degrees and by the age of twelve, it had progressed to 85 degrees accompanying with thoracic kyphosis of 40 degrees (Figure 1).

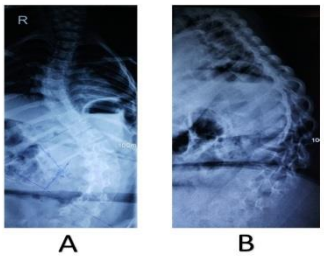

Figure 1. Pre-operative x-rays; (A) anteroposterior (AP) view, (B) lateral view

Careful preoperative planning was carried out, active involvement of anesthesiology team helped in controlling intraoperative and postoperative blood loss. Respiratory deterioration in this patient had made anesthesia challenging and surgery had to be kept as short as possible; long operative time may affect the post-operative respiratory function.

Owing to progressive spinal deformity and sitting imbalance, correction and fusion from T4 to sacrum was performed (Figure 2).

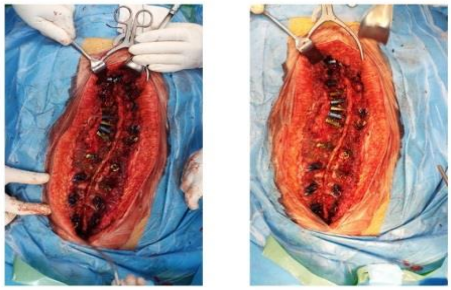

Figure 2. Intraoperative pictures showing fusion levels (A and B).

Single posterior approach along with posterior release was chosen as to shorten the operative time. Multiple osteotomies were performed due to higher Cobb angle and rigid deformity. However, performing osteotomy in such patients is challenging owing to severe osteoporosis. The patient showed good results after the operation with a balanced spine (Figure 3). As these patients are prone to developing wound dehiscence, extensive wound care was also administered, including dressing change every 12 hours and avoiding any cytotoxic substances such as iodopovidone. After surgery, respiratory function was improved and patient was able to stand with support. Chest and gait supportive physiotherapy were initiated. Figure 4 shows pre- and post-operative sitting balance. One-year follow-up showed excellent outcomes with good sitting balance and moderate ambulation with help of walking aid.

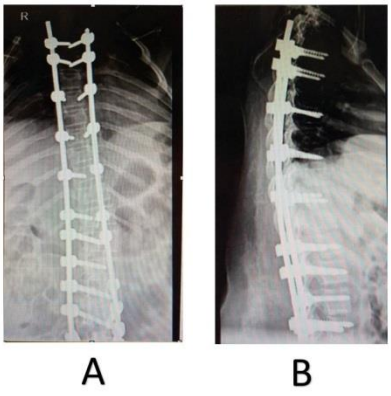

Figure 3. Post-operative x-rays; (A) anteroposterior (AP) view, (B) lateral view

Discussion

Scoliosis correction surgery in CMD has been challenging because of the primary muscular pathology and frequently-associated cardiac and pulmonary complications (7).

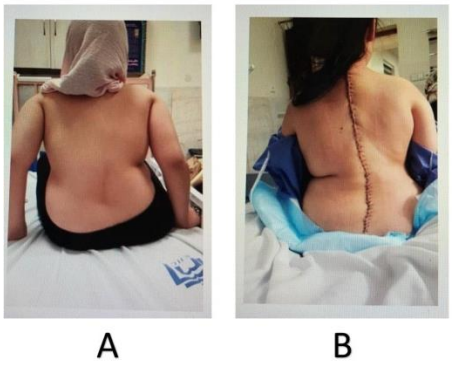

Figure 4. Sitting balance; (A) pre-operative, (B) post-operative.

We think most surgeons have been reluctant to use early interventional approach for spinal deformity in patients with various MDs until considerable curve progression or severe respiratory distress. In our patient, onset of scoliosis followed loss of ambulation; this is in contrast to usual forms of MDs, where spinal deformity sets in after patients become wheelchair-bond (8). In UCMD, scoliosis may develop even in ambulant patient and is characterized by marked progression from early stage. This pattern of progression was also pointed out by Nadeau et al. (5). Physical disability including difficulty in sitting, standing, and walking is accelerated by early-onset and rapidly-progressive spinal deformity in UCMD. More importantly respiratory function is compromised due to reduced chest wall compliance.

Okada et al. have found primary COLVI deficiency as the second most common CMD in Japan (9). This is a remarkable finding as dystrophies related to COLVI dysfunction are rarely reported in Iranian population (10). This might be attributable to non-reporting of such cases due to early death of patient or lack of diagnostic facilities in our country. Diagnosis of COLVI deficiency and its relation with UCMD in our patient was done by an European Laboratory in Germany, because such kind of advanced gene testing is currently under development in our country.

In review of COLVI-related myopathies, Bonnemann described these inter-related phenotypes with a different perspective. He defined such myopathies as muscle meets its matrix. Accordingly, among the hereditary myopathies, they are unique hybrid disorders with clinical features attributable to both muscle and connective tissue. As such, they are disorders of the 'myomatrix' (the extracellular matrix of muscle) and show the importance of the myomatrix in the functioning and maintenance of muscle (11).

Anesthesia has always been considered challenging in patients with MD. Few authors have recommended inspiratory muscle training to reduce intra- and post-operative anesthetic complications in these patients (12). There is no detailed knowledge about the risk of anesthesia in patients with UCMD; however, there were no serious complication due to anesthesia in patients with UCMD phenotype who underwent spinal deformity correction surgery (13, 14).

In our patient, we did not commence respiratory training prior to surgery. However, an echocardiography was performed to rule out cardiomyopathy that could have complicated post-surgical recovery. We did not notice any post-operative complication related to general anesthesia in our patient.

There is currently no specific treatment for UCMD;

however, better respiratory management has improved survival. Loss of independent ambulation and respiratory failure are considered as life-changing events and are associated with poor prognosis (5). Spinal deformity plays a significant role in both ambulation and respiratory function of these patients. As rapid progression of scoliosis is most certainly associated with progression of respiratory failure and loss of ambulation, we suggest early correction of spinal deformity in view of preserving these vital functions and improving life expectancy in these patients.

Conflict of Interest

The authors declare no conflict of interest in this study.

Acknowledgments

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