Before Scoliosis Surgery Look at the Eyes and Face of the Child

Scoliosis in children, defined as lateral curvature and rotation of the vertebrae, can be congenital, syndrome-related, idiopathic, neuromuscular, or due to secondary causes.[1] Diagnostic workup is based on patient history, physical examination, and imaging, whereas the management is based on the age of the patient, nature of the curve, and risk of progression.[2]

Neuromuscular scoliosis (NMS), which is usually identified in early childhood, constitutes the second-most prevalent spinal deformity after idiopathic scoliosis.[3] Compared with idiopathic scoliosis, conservative and surgical treatment of NMS is more complex and has a higher complication rate.[4] This is because of the associated medical comorbidities and the presence of deformed spinopelvic anatomy.[5]

NMS is classified as neuropathic and myopathic types. Neuropathic type can be due to upper motor neuron lesions (e.g., cerebral palsy, spinal cord trauma, and syringomyelia), or diseases of the lower motor unit,[6] including the anterior horn cells (e.g., poliomyelitis and spinal muscular atrophy)[7] and the peripheral nerves.[8] Myopathic types include arthrogryposis multiplex congenita, muscular dystrophy, and other forms of myopathy.[9]

Charcot-Marie-Tooth neuropathy type 4 (CMT4), a group of progressive motor and sensory axonal and demyelinating neuropathies inherited as autosomal recessive, usually starts in early childhood and have more severe progression compared to the autosomal-dominant varieties.[10] They are more common in the Arabian Peninsula and North Africa due to the high rate of consanguinity. Apart from the progressive weakness of the distal muscles in the feet and hands, some of them have associated facial weakness, which helps in recognizing the clinical entity. Scoliosis is a prominent feature in three of these, namely Charcot-Marie-Tooth disease type 4B1 (CMT4B1), Charcot-Marie-Tooth disease type 4C (CMT4C), and Charcot-Marie-Tooth disease type 4E (CMT4E).

The causative gene of CMT4B1 (the first identified autosomal recessive CMT gene) was found in the families of Italian and Saudi Arabian ancestries.[11-13] The disease usually starts before the age of 4 years with progressive distal weakness leading to pes cavus foot deformity, followed by proximal weakness of the lower limbs, and death may occur as early as the end of the second decade.[14] Facial and vocal cord pareses are known to be associated together with chest deformities and diaphragmatic weakness. Hence, special precautions need to be assured when performing surgery in these patients.

CMT4C is characterized by a relatively mild childhood or adolescent-onset demyelinating sensorimotor neuropathy associated with early-onset, severe, and rapidly progressing scoliosis. Other known associations include facial weakness, cranial nerve involvement, and deafness.[15]

CMT4E presents with neonatal hypotonia and delayed motor development accompanied by distal limb muscle weakness and atrophy due to a hypomyelinating form of peripheral neuropathy. Other features of the disease include facial weakness and cranial nerve involvement, scoliosis, and respiratory insufficiency due to neuropathy. The disease is caused by homozygous mutation in the EGR2 gene.[16]

Myopathic types of NMS associated with facial weakness include Ullrich congenital muscular dystrophy caused by mutations in the genes encoding collagen VI. The presence of round face with mild weakness and prominent ears are known features of the disease together with neonatal hypotonia, torticollis, kyphosis of the spine, hip dislocation, proximal joint contractures, and distal joint hyperlaxity.[9]

Congenital myasthenic syndromes (CMS) are heterogeneous disorders caused by impaired neuromuscular transmission resulting from genetic mutations of neuromuscular junction molecules. Currently, mutations in more than thirty genes were identified, causing autosomal dominant or autosomal recessive CMS. The autosomal recessive forms are more common in the Arabian Peninsula and North Africa. One of the first identified families with ALG2 gene mutation was from Saudi Arabia,[17] and the second identified family with MUSC mutation was from Sudan.[18]

Symptoms of CMS may present *in utero* with reduced fetal movements. Mutations in the AChR delta subunit or RAPSN may present at birth with arthrogryposis multiplex congenita.[19] Childhood manifestations of CMS include fatigable ptosis and extraocular muscle weakness (ophthalmoparesis), associated with bilateral facial weakness with tenting of lips.

According to the location of genetic dysfunction, symptoms, therapy, and contraindicated drugs vary in CMS. Symptoms of CMS caused by a mutation in the COLQ gene worsen after the use of acetylcholinesterase inhibitors, as documented in a large cohort, including Saudi patients.[20] Prominent scoliosis requiring surgery is a known complication of COLQ gene mutations.[21] Other causative aberrant genes of CMS associated with scoliosis include the VAMP1 gene, which encodes for a presynaptic protein and CHRNE gene encoding for the epsilon subunit of the acetylcholine receptor.[22] Patients with CHRNE gene mutations have been reported from Saudi Arabia,[23] and a common founder mutation c. 1293insG has been identified in North African populations.[24] Anesthetic management of CMS should be designed guided by each genotype to avoid drugs that could worsen or trigger the symptoms of CMS, and judicious respiratory care is required after the surgery.[25]

Another disorder in which progressive scoliosis is associated with ocular findings is horizontal gaze palsy with progressive scoliosis (HGPPS) characterized by the lack of voluntary horizontal eye movements and progressive scoliosis developing in childhood, often requiring surgical intervention early in life. The defective gene (inherited as autosomal recessive) was first mapped to chromosome 11q23-q25 in patients from Saudi Arabia (two Saudi and Indian families).[26] Mutations in the ROBO gene were later identified to be causative,[27] and lead to noncrossing of selected axonal paths in the central nervous system.[28]

Progressive scoliosis is a known complication of two diseases characterized by myotonia associated with facial and eye abnormalities. These are myotonic dystrophy type 1 (DM1), abbreviated DM1, and previously known as Steinert's disease, and Schwartz–Jampel syndrome.[9] DM1 is caused by a heterozygous dominant expansion of a set of CTG trinucleotide repeats, which may manifest in childhood with diffuse facial weakness, associated with tenting of the upper lip, difficulty smiling, and ptosis. Complications include pulmonary impairments such as decreased forced vital capacity and cardiac conduction disturbances, which need to be observed during scoliosis surgery.[29]

Schwartz–Jampel syndrome is a rare myotonic syndrome with osteoarticular deformities, inherited as autosomal recessive and is more frequent in the Arabian Peninsula and North Africa.[30,31] Patients present with generalized myotonia, muscular hypertrophy, and osteochondrodysplasia. They have mask-like facies, microstomia, and blepharophimosis (narrow palpebral fissures). Caution should be taken during surgery to avoid suxamethonium and volatile anesthetic agents since the risk of the development of malignant hyperpyrexia and hyperkalemia has been reported.[32,33]

Patients with myopathies caused by RYR1 gene mutations are at the risk of developing malignant hyperthermia during scoliosis surgery if they were exposed to the volatile inhalational anesthetic agents and the muscle relaxant succinylcholine.[34] They can manifest as minicore myopathy with external ophthalmoplegia (OMIM #255320),[35] a recessively inherited disease characterized by muscle weakness, amyotrophy, the involvement of extraocular muscles, ptosis, and other variable features including facial diplegia, scoliosis, kyphosis, and joint contractures.[36]

Another minicore-like myopathy, which can manifest with scoliosis, ptosis, and facial weakness, is Salih myopathy (OMIM # 611705), a recessively inherited disease described in consanguineous families of Arab descent, and caused by homozygous or compound heterozygous mutation in the gene encoding titin.[37] Titin is a giant muscle protein expressed in the cardiac and skeletal muscles. Patients with Salih myopathy are known to have cardiac septal defects and develop progressive dilated cardiomyopathy with rhythm disturbances. Cardiac surveillance is required beginning at the age of 5 years, and cardiac conduction disturbances need to be observed during surgery.[38] Ibuprofen (Brufen®) should be given with care in those with evidence of cardiomyopathy and should be avoided in those with congestive heart failure.[37]

In conclusion, before scoliosis surgery look at the eyes and face of the child to avoid unpleasant surprises.

Mustafa A. Salih

Division of Pediatric Neurology, College of Medicine, King Saud University, Riyadh, Saudi Arabia

Address for correspondence: Prof. Mustafa A. Salih,
Division of Pediatric Neurology, College of Medicine, King Saud University, Riyadh, Saudi Arabia.
E-mail: mustafa@ksu.edu.sa

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