Schwartz-Jampel Syndrome in Saudi Children

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Schwartz-Jampel syndrome (SJS) or chondrodystrophic myotonia is a rare disorder of unknown pathogenesis characterized by multiple skeletal deformities, limited joint mobility, muscular hypertrophy and stiffness, generalized myotonia, facial dysmorphism, and growth retardation.1-4 This syndrome was first described by Catel5 in 1951G, and subsequently by Schwartz and Jampel, whose names have been labeled the syndrome.1,6 The inheritance pattern was presumed to be autosomal recessive, though the possibility of an autosomal dominant mode has been suggested in a few cases.3,7 Case reports of SJS have been described in patients of all major racial groups worldwide.1-10

We have had the opportunity to study five Saudi children with almost identical clinical findings of SJS. These cases are presented in order to draw the attention of the practicing clinicians to the existence of this rare syndrome in a country where consanguineous marriage is common.

A clinical diagnosis of Schwartz-Jampel syndrome was established in five children (two females and three males) derived from four families. The ascertained proband and all first degree relatives underwent a standardized symptom review and clinical examination. The patient's laboratory evaluation included a complete blood count, serum calcium, phosphorus and magnesium, blood glucose, renal and liver function profiles, serum creatinine phosphokinase (CPK) and aldolase, thyroid function tests, growth hormone assay, serum immunoglobulins, urinalysis, urine screen for mucopolysaccharides and amino acids, chest and skeletal radiographic studies, computed tomography (CT) scan of the brain and electrocardiogram (ECG). Nerve conduction and electromyographic (EMG) studies, electroencephalogram (EEG) and muscle biopsy were performed on those children whose parents gave consent. The salient clinical data of our five cases are summarized in the table.
Table: Salient clinical findings in the five cases with Schwartz-Jampel syndrome.

<table>
<thead>
<tr>
<th></th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
<th>Case 5</th>
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<tr>
<td>Age of onset/evaluation</td>
<td>9M/6Y</td>
<td>6M/6Y</td>
<td>6M/6Y</td>
<td>4M/5½Y</td>
<td>3M/2Y</td>
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<td>Consanguinity</td>
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<tr>
<td>Fixed face</td>
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<tr>
<td>Short neck</td>
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<td>Pectus carinatum</td>
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<tr>
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<td>Increased muscle enzymes</td>
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</table>

+=present; -=absent; ND=not done.

Case Report

Case 1:

This six-year-old female, the descendent of consanguineous parents, was born after a normal term pregnancy and uneventful delivery. At nine months of age, she began having poor sucking and later difficulty in swallowing fluids and solid food. Later, she began choking with cold drinks. Her early psychomotor development was normal. From two years of age onwards, the parents noticed unusual changes in her facial features that were slowly progressive. Her gait became progressively stiff and she began walking on the tips of her toes. Language and speech development were normal but the voice was nasal and high-pitched. One female sibling with similar phenotypic appearance died at the age of three years and the remaining six siblings were normal.

On physical examination, she weighed 14.8 kg (below 5th percentile) and measured 95 cm (below 5th percentile). Head circumference was normal. She was a shy girl and sensitive about her unusual appearance; her facial expression was fixed and frozen, giving the appearance of sadness. There was slight ptosis of the right eye.
with blepharophimosis, blepharospasm, small and puckered mouth, high arched palate and micrognathia. The ears were low set and rotated slightly counterclockwise. She had a short neck, pectus carinatum, hyperlordosis, slight hirsutism and a protuberant abdomen with a small umbilical hernia. Her limb muscles were mildly hypertrophic and firm to palpation. Percussion of these proximal and distal muscles did not evoke any clinically evident myotonic response. Because of the contractures, passive movements met resistance and were limited in their extreme degree. Tendon reflexes and muscular strength, while difficult to evaluate, appeared decreased. The gait was laborious and stiff.

Laboratory investigations revealed a serum CPK of 2202 u/L (normal 30-232 u/L) and serum aldolase was 25 u/L (normal up to 7.6 u/L). The results of the remaining laboratory investigations were normal. Radiographic studies revealed mild osteoporosis of the long bones, kyphoscoliosis of thoracolumbar spine, and bilateral coxa valga. The bone age and CT scan of the brain were normal. The EMG showed no electric silence at rest, but a continuous myotonic activity, with frequent bursts after voluntary contraction, muscle percussion, and needle movements, accompanied by a "dive bomber" sound. The EEG and motor and sensory nerve conduction velocities were normal.

Light microscope examination of a muscle biopsy of the quadriceps revealed mildly to moderately myopathic alterations with variability of muscle fiber size and vacuoles were found in the center of a few fibers. Electron microscopy revealed increase of subsarcolemmal sarcoplasm, vacuoles between bundles of myofibrils and abrupt loss of filaments, together with disarray of the Z disks. The parents and other siblings were normal by clinical and electromyographic examinations. The treatment of our patient with phenytoin and procainamide for about six months showed no significant improvement.

Cases 2 and 3:

These six-year-old male twins were born at term after normal pregnancy and uneventful delivery to consanguineous parents. At the age of six months, the parents noticed that both twins had peculiar facial appearance, notably narrow palpebral fissures with visual difficulty. Since then, their facial appearance has become more and more peculiar, and contractures of several muscle groups have appeared. Psychomotor development appeared normal during the first three years of life. Progressive muscular weakness and difficulty in walking started during the fourth year. Then they developed an increasingly evident awkward gait associated with frequent falls, generalized muscular stiffness and hindrance in running and climbing stairs. One of the twins underwent surgical repair of a right inguinal hernia at the age of two years. The family history was negative for similar illness, neuromuscular diseases and skeletal deformities. Both parents and seven siblings were normal.
On physical examination, the twins were severely growth retarded with both weight and height below the 5th percentile, but the head circumference was normal. Their faces were pinched and expressionless. The palpebral apertures were markedly narrow, the eyes were deeply set and the ears were prominent. The mouth was pursed, the palate was highly arched, and the chin was small in both twins (Figure). There was pectus carinatum deformity of the chest and the abdomen was protuberant with no visceromegaly. Both twins had bilateral undescended testicles. They had percussion myotonia in the thenar muscles and action myotonia after hand grasping and eye closure. Their limb muscles were hypertrophied and their strength appeared reduced. There was resistance to passive motion at all their joints, and mild contractures were present at the elbows and knees. The tendon reflexes were apparently hypoactive. They walked with a waddling gait.

Laboratory investigations revealed markedly elevated serum CPK (1324 u/L for twin A and 1620 u/L for twin B) and serum aldolase (576 u/L for twin A and 676 u/L for twin B). The results of the other laboratory studies were normal. Radiographic studies revealed abnormality of the chest (pectus carinatum) and spine (mild thoracolumbar scoliosis with platyspondyly). The EMG of both twins showed persistent electrical activity of constant frequency at rest. High frequency discharges that continued for several minutes with myotonic bursts were elicited by movement of the needle electrode, muscular percussion and voluntary contraction. Muscle biopsy in either twin was not granted by the parents.

Case 4:

This 5-1/2-year-old male was the product of a normal term pregnancy and uneventful vaginal delivery to consanguineous parents. At the age of four months, difficulty in opening his mouth and eyes was noted and his face was described as immobile. He was slow in feeding and had difficulty swallowing fluids and solid food. He walked with an unsteady stiff gait at the age of 15 months, but psychomental development was normal for his age. Both parents and two siblings were normal.
On physical examination he was growth retarded with a height of 100 cm (below 5th percentile), a weight of 14.2 kg (below 5th percentile) and a normal head circumference of 50 cm. His facial appearance was peculiar with blepharophimosis, bilateral ptosis, small pursed mouth and puckered chin. The forehead was narrow with low anterior hairline insertion. He displayed marked sad expression. The palate was highly arched. The ears were normal but the neck was very short. The chest was narrow with marked pectus carinatum deformity. There was a left inguinal hernia. The limb muscles were stiff and firm to palpation and showed extreme difficulty in relaxing. He had limitation of active and passive movements at the elbows, hips and knees and his gait was stiff and unsteady. Percussion myotonia of the thenar muscles was easily elicited.

Laboratory investigations revealed a serum CPK of 444 u/L and a serum aldolase of 334 u/L. The results of the other laboratory studies were normal. Radiographic studies revealed only the chest deformity of pectus carinatum, osteoporosis and thoracolumbar scoliosis. The EMG study and muscle biopsy were not granted by the parents.

Case 5:

This two-year-old female was born after a normal term pregnancy and uneventful vaginal delivery to nonconsanguineous parents. At the age of three months, stiffness of the joints was noted by her parents. Her motor impairment resulting from generalized muscular stiffness did not improve with early implementation of physiotherapy. She walked with an unsteady stiff gait at the age of one year. At this time, the mother noticed small eye slits and immobility of the facial muscles; these unusual facial features were progressive. The abnormalities of motor impairment became more evident with the passing of time. Both parents and four siblings were normal. There were three cousins with similar illness on both maternal and paternal sides.

On physical examination she weighed 9.5 kg (below 5th percentile) and measured 78 cm (below 5th percentile). Her head circumference was normal. The hair was inserted low on the forehead and there was marked narrowing of the palpebral fissures with blepharospasm. There was a high arched palate, a flat nasal bridge and low insertion of the ears. The chin was receding and the mouth was pursed. The neck and chest were normal. The abdomen was protuberant with no visceromegaly. There was resistance to passive motion at all joints, notably the knees and hips. The limb muscles were firm to palpation and their strength appeared to be normal. Percussion of muscles evoked clinically evident myotonic response.

All laboratory studies were normal except serum CPK and aldolase, which were 1764 u/L and 12 u/L, respectively. The EMG and muscle biopsy were not performed due to refusal by the parents.

Discussion

There has been slight variability in the clinical expression of the SJS; the somatic signs are strikingly similar in the reported patients who would seem to belong to the same family. Patients with this syndrome have been described as being generally normal at birth with the characteristic clinical features only becoming apparent as they grow older. The clinical symptoms and signs are initially noted in the first two to three years of life, as illustrated in the present cases reported herein, and thereafter the disorder shows a stationary or slowly progressive course. In most reported cases, skeletal abnormalities appear before facial changes. The spectrum of skeletal anomalies includes hip dysplasia, kyphoscoliosis, talipes equinovarus, epiphyseal alterations of the long bones, coxa vara or valga, platybasia, flattened vertebral bodies and pectus carinatum. Some of these osteoarticular deformities have been noted in our cases.

The five patients described in this report presented typical oculofacial features of the SJS. These features consist primarily of mask-like facies, blepharophimosis, blepharospasm and small pursed mouth with frozen smile. The characteristically pinched face is mainly due to the constant state of contraction of facial muscles. Other frequently occurring features are myopia, ptosis, prominent bushy eyebrows, irregular eyelashes, low-set ears, receding chin, highly arched palate and low position of the hairline on the forehead and neck. These oculofacial abnormalities were demonstrated in our cases, but they were not detected before the age of six months.

Dwarfism has been described as a consistent feature of the SJS and is noted in most cases by three years of age; the findings of this report in which all our patients fell below the 5th percentile in height and weight confirm the presence of growth retardation. The head circumference has been reported to be normal, as in our cases. Intelligence has been considered normal in this syndrome, but several cases with mental retardation have been reported. All our patients were neurodevelopmentally normal. Motor developmental delay is primarily in ambulation. Patients with SJS have progressive limitation of movements of their large joints and contracture of these joints results in their typical crouched stance; there is increased lumbar lordosis and kyphosis and the arms are held across the trunk with semiflexion of the elbows, hips and knees. The gait has been noted to be stiff and waddling. Muscular hypertrophy tends to be proximal and more obvious in males. The muscles are stiff and the power is
generally normal. The muscle tone is increased and the tendon reflexes are diminished. Generalized hirsutism, short neck, protuberant abdomen, umbilical and inguinal hernias and high pitched or nasal voice have been reported in patients with SJS. 3,8,13

The diagnosis is based upon recognition of the characteristic clinical features and abnormal nonspecific electromyographic and radiologic findings. In agreement with the data of others, 2,4,7,13,14 the findings of the laboratory evaluation of our cases were normal with the exception of increased concentration of serum CPK and aldolase, which may be explained as a consequence of persistent muscular contraction and hypoxia. In the present report as in others, 3,8,15 a continuous, spontaneous, high frequency activity has been observed on EMG studies and these electric discharges increase with movement of the needle, on percussion of the muscle and following voluntary contraction. Although abundant spontaneous EMG activity has been documented in all reported cases of SJS, opinions differ as to its character and origin. 3,16 Myotonic discharges with waxing and waning have been described in some cases, 2,6,17 but have not been reported in others. 3,16,18 Recently, atypical complex repetitive discharges have been observed as the principal spontaneous activity. 3,16,19 There are conflicting reports with respect to the persistence of the spontaneous electrical activity in SJS. In some reports, the spontaneous activity never disappeared during routine EMG recording, 7,11,16 though others have reported finding periods of silence. 17,19 Case 1 demonstrated most of the salient features of SJS with the exception of myotonia clinically, probably because the muscles were continuously and unceasingly contracted; however, the EMG was clearly myotonic. A number of authors have reported patients with SJS in whom myotonia remained undetected clinically. 4,11,20

Light and electron microscope and histochemical examinations of muscle biopsy specimens have demonstrated multiple minor nonspecific abnormalities in some cases 3,11,13 and have been reported normal in others. 6,9,16 These histologic abnormalities include variation in fiber size and shape, proliferation of internal nuclei, and diffuse and focal fiber atrophy. Electron microscopy has shown swelling of the sarcoplasmic reticulum, mitochondrial enlargement appearing as fine vacuoles in muscle fibers, Z band staining and dense homogeneous material in the terminal cisternae of the sarcoplasmic reticulum. 3,16

The SJS must be distinguished from a number of disorders in which myotonia or skeletal deformity is a prominent feature. The clinical picture of this syndrome is clearly different from that of the three known types of myotonic syndromes, which include myotonia congenita, paramyotonia congenita, and myotonic dystrophy. 12 In clinical differential diagnosis, the Freeman-Sheldon and Marden-Walker syndromes should be taken into account. 4,12 The former is characterized by the whistling face, puckered lips with microstomia, a long philtrum, dimpled chin, blepharophimosis, ulnar deviation of the hands, and flexion of the fingers. Marden-Walker syndrome is a congenital multiple anomaly disorder consisting of immobile facies, blepharophimosis, ptosis, multiple congenital joint contractures, failure to thrive, and mental retardation. 12 Other disorders to be considered are some mucopolysaccharidoses and various first visceral arch syndromes in which abnormalities of the facial skeleton and stunted growth are present. 4

Isolated case reports have associated SJS with selective deficiency of IgA, 21 complex immunodeficiency, 22 bilateral carpal tunnel syndrome, 15 von Willebrand disease, 10 compressive myelopathy, 23 and malignant hyperthermia. 24 The latter is a potentially lethal complication that may arise during anesthesia.

The nature of the basic defect in SJS has not yet been identified although a metabolic disturbance of bone and muscle during fetal development is suggested. 13 Recently, Lehmann-Horn et al 25 proposed that a sodium channel defect may be responsible for the hyperexcitability and the associated slowed relaxation of muscles. A more definite answer, however, could be provided by further study of cases with SJS.

References

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