Fascioscapulohumeral Dystrophy

Estelita Michelle H. Jacinto and Cynthia D. Ang-Muñoz

Department of Rehabilitation Medicine,
College of Medicine and Philippine General Hospital, University of the Philippines Manila

ABSTRACT

Two Filipino sisters from Capiz presented with facial muscle weakness followed by weakness of both shoulders and arms, and scapular winging. Both presented with difficulty in performing activities of daily living. The younger sister also had bilateral lower extremity weakness with difficulty in ambulation. The results of electrodiagnostic testing in both sisters were compatible with myopathic disease. Comprehensive individualized rehabilitation addressing different functional limitations, focusing on maintaining mobility and functional capacity, and resulting improvements are presented.

Key Words: Fascioscapulohumeral dystrophy; Landouzy-Dejerine muscular dystrophy; fascioscapulohumeral disease, rehabilitation

Introduction

Muscular dystrophies (MDs) are inherited disorders characterized by progressive weakness and degeneration of the skeletal or voluntary muscles which control movement, without a central or peripheral nerve abnormality. Cardiac muscles, other involuntary muscles, and other organs are also affected in some forms of MDs. The major forms of MDs are: myotonic, Duchenne, Becker, limb-girdle, facioscapulohumeral, congenital, oculopharyngeal, distal, Emery-Dreifuss, and Fukuyama MDs.[1]

The incidence of muscular dystrophy (MD) varies depending on the specific type. Duchenne muscular dystrophy is the most common condition with an incidence of one case per 3,500 live male births.[1] It is an x-linked recessive disorder, primarily affects boys, and is the most severe type. Becker muscular dystrophy, another x-linked recessive condition, is the second most common form, with an incidence of one case per 30,000 live male births.[1] Some types of MD are more frequent in certain populations but are rare elsewhere. Autosomal dominant distal MD occurs more often in Scandinavia than elsewhere. There are more reported cases of Fukuyama MD in Japan, oculopharyngeal MD in French Canada, and several autosomal recessive limb girdle MD cases in Brazil, North America, and the Middle East.[2]

Fascioscapulohumeral dystrophy (FSHD) is the third most common MD after the dystrophinopathies and myotonic dystrophy,[3] with an estimated prevalence of 10 to 20 cases per million population.[4] The disease is named for the regions of the body most severely affected: muscles of the face (fascio), shoulders (scapula), and upper arms (humeral). Hips and legs may be affected. No definitive therapy is available for FSHD.[5] Data from the Philippine Field Health Services Information System of all rural health units and the national annual government hospital statistical reports, including the Philippine General Hospital, report no cases of FSHD from 1998 to 2007.[6]

The rarity of the disease and the absence of a known cure make this case reportable. This report aims to spark more interest for future research on FSHD, to identify more cases and to study the condition's heterogeneous clinical presentations and functional outcomes. This information can guide physiatrists and other clinicians in improving the quality of life of individuals with FSHD by maximizing performance in activities of daily living (ADL) in spite of underlying progressive impairments.

Case Report

Patient 1. A 40-year-old, right-handed female, consulted at a tertiary government hospital in April 2008 for weakness of both shoulders. Since childhood, the patient had noted weakness at the left side of the mouth and cheek resulting in asymmetrical smile and wrinkling of the forehead. At 15 years of age, she had a back injury which resulted in low back pain and difficulty in ambulation that subsequently resolved. Beginning in the third decade of life, she had difficulty raising both upper extremities (UE) and lifting heavy objects, associated with jutting out of the shoulder

---

Presented at the University of the Philippines College of Medicine – Philippine General Hospital Annual Research Week, December 1-4, 2009, Philippine General Hospital, Manila. (Finalist, Research Poster Category)

Presented at the University of the Philippines – Philippine General Hospital Department of Rehabilitation Medicine Annual Interesting Case Presentation, November 21, 2008, Philippine General Hospital, Manila. (3rd Place)

Corresponding author: Cynthia D. Ang-Muñoz, MD, MSc
Department of Rehabilitation Medicine
Philippine General Hospital
University of the Philippines Manila
Taft Avenue, Ermita, Manila, Philippines 1000
Telephone: +632 5548400 local 2403
Telefax: +632 5548494
Email: cdang@info.com.ph

blades. She could perform ADLs independently, but required more time compared with her performance of the same ADLs 10 years prior. She had difficulty hanging clothes, reaching overhead cabinets, and writing on a blackboard.

Similar signs and symptoms have been observed in an older sister, mother, maternal grandmother and uncles (Figure 1).

The patient denied history of hypertension, diabetes or cerebrovascular disease. She had a history of pulmonary tuberculosis treated with anti-Koch's medications for six months. She denied smoking and intake of alcoholic beverages.

At the time of consult, the patient was a substitute grade school teacher who lived with her two children and husband in a two-storey house. Neither of her children manifested similar symptoms or had any other remarkable medical conditions.

On consult, the patient was fairly nourished, fairly developed, and ambulatory with no gait aid. Pertinent systemic physical examination (PE) findings include facial asymmetry (Figure 2) and atrophy of both deltoids with winging of the medial border of both scapulae (Figure 3). There was no spinal deformity. Passive range of motion (ROM) in all extremities was within normal limits. There was limited active but pain-free shoulder abduction (0 to 90^0, normal 0 to 180^0) and internal rotation (0 to 50^0, normal 0 to 90^0) bilaterally. For both shoulders evaluated within available range, abductors and adductors were graded 3/5, flexors 4/5, and extensors 5/5. Both elbows were graded 4/5, and both wrists and hands were graded 5/5. Both lower extremities (LE) were graded 4/5. The left occipitofrontalis, buccinators and levator anguli oris were weakly functional (WF), while the right facial muscles were functional (normal) grade. Bilateral orbicularis oculi, corrugator supercilli, levator palpebrae superioris, procerus, levator labii superioris, orbicularis oris, and zygomaticus major were graded functional. Rest of the neurologic examination was normal. There was no dysarthria or drooling. Posture and gait analysis were normal. She obtained a Functional Independence Measure (FIM) score of 124/126 with difficulty in upper extremity dressing, eating, grooming, and bathing. A FIM score of 126 means complete independence.

The patient was diagnosed with muscular dystrophy, probably FSHD. Her total creatine phosphokinase (CPK) was 190 umol/L (normal value is 30 to 150 umol/L), 27% elevated from the upper limit. Electromyography and nerve conduction velocity (EMG-NCV) studies were compatible with myopathy.

The patient underwent out-patient physical therapy (PT) and occupational therapy (OT) twice a week for four months focusing on improving the following: active ROM in both UE; motor strength of the UE, trunk and LE; and performance of ADL. Active ROM in both shoulders increased from 0 to 180^0 on abduction and from 0 to 90^0 on internal rotation. All muscles in both UE improved to 4/5. Strength in both shoulder extensors, both wrists, and both hands was maintained at 5/5. Strength in both LE remained 4/5. She could perform ADL at a faster pace with FIM score maintained at 124/126.

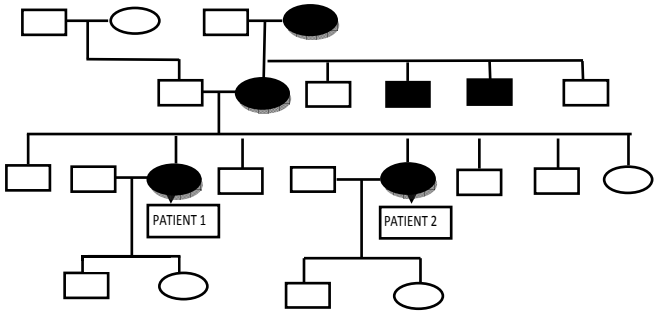

Figure 1. Family Genogram

Figure 2. Facial asymmetry in Patient 1

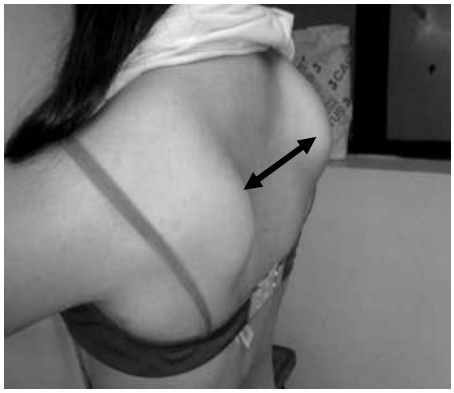

Figure 3. Winging of scapulae in Patient 1

Patient 2. A 36-year-old right-handed female, the younger sister of Patient 1, consulted in April 2008 because of weakness of both shoulders and difficulty in ambulation. She reported having facial asymmetry described as asymmetrical smile and wrinkling of the forehead in childhood. Starting from the second decade of life, she had difficulty in raising both UE, followed by weakness in both LE with limited active hip flexion, muscle cramps after exertion, and difficulty in ambulation. She could perform ADLs independently but had difficulty reaching overhead cabinets, hanging clothes, cooking, cleaning, lifting heavy water-filled containers while working in a water refilling station. She could ambulate indoors and in the community with one-man assist. She could negotiate stairs at the workplace but would require support by holding the rail. She had difficulty commuting to the workplace, experiencing easy fatigability during walking; she subsequently resigned from work.

Her past medical history was unremarkable.

At the time of consult, the patient lived with her two children and husband in a one-storey house, with one step to enter the house. Neither of her children manifested similar symptoms or had any other remarkable medical conditions. She denied smoking and intake of alcoholic beverages.

On examination, the patient was fairly nourished, fairly developed, and ambulatory with one-man assist. Physical examination revealed atrophy of the deltoids, biceps and triceps of both arms, and the quadriceps (Figure 4) and the hamstring muscles of both legs, and winging of medial border of both scapulae (Figure 5). There were no spinal, hand or foot deformities. There was limited but pain-free active ROM in both shoulders (0 to 100^0 abduction; 0 to 40^0 internal rotation) and in the right ankle (dorsiflexion 0 to 10^0, normal 0 to 20^0). The shoulder and elbow muscles of both arms were graded 3/5 within available range; both wrists 4/5; and finger flexors 5/5. Both LE were graded 3/5, except for the left knee flexors and extensors, and left toe extensors graded 4/5, and the right ankle dorsiflexors and right toe extensors graded 1/5. Facial muscles on both sides of the face were graded WF, except for the levator palpebrae superioris and orbicularis oculi which were graded functional. The rest of the neurologic examination was normal. Dysarthria and drooling were not observed. There was no postural deviation. On independent ambulation, there was hyperextension of both knees during initial contact and midstance, and waddling and steppage gait. Her FIM score was 118/126, with difficulty in feeding, grooming, bathing, UE and LE dressing, and ambulation.

The patient was diagnosed with FSHD. Total CPK was 479 umol/L, 229% higher compared with the upper limit of normal. Her EMG-NCV studies were consistent with myopathy.

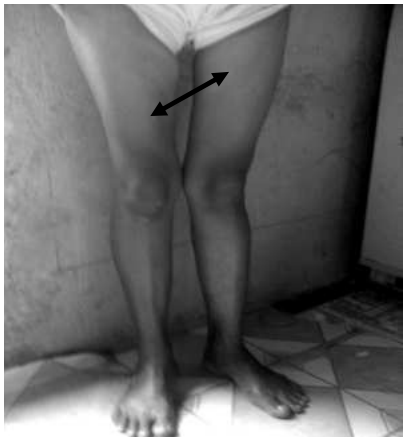

Figure 4. Atrophy of quadriceps in Patient 2

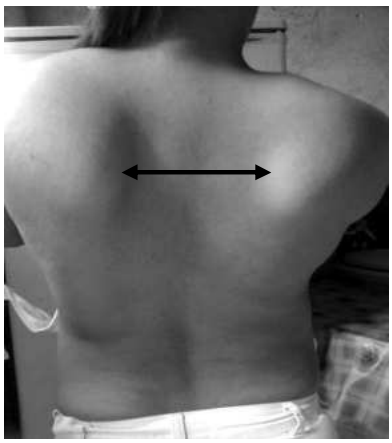

Figure 5. Winging of scapulae in Patient 2

She underwent out-patient PT and OT twice a week for four months to improve active ROM and motor strength in both UE, trunk and both LE, and endurance; and to promote safe ambulation and independence in ADL skills. Active ROM in both shoulders improved to 0 to 110^0 abduction and 0 to 80^0 internal rotation. Motor strength in both UE improved to 4/5 and both right ankle dorsiflexors and toe extensors to 3/5. Her FIM score increased to 124/126; she is now able to perform overhead activities and ambulate using a single tip cane with correction of gait deviation.

Discussion

Fascioscapulohumeral dystrophy, also known as Landouzy-Dejerine muscular dystrophy, was first described by Landouzy and Dejerine in 1884.[5] This disorder results from a deletion of a fragment of deoxyribonucleic acid (DNA) located on chromosome 4 in the region 4q35 found in 70% to 90% of patients with FSHD.[5] A greater deletion

presents with more severe manifestation.[4] This is an autosomal dominant disorder but 10% to 30% of cases are sporadic.[5] The mutation is highly penetrant but presents with varying degrees of disability,[4] severity and age of onset, even among members of the same family.[7] Fascioscapulohumeral MD usually presents between the first and third decades, and greater than 90% have demonstrable symptoms by age 20.[5] Onset during infancy or childhood is possible. Symptoms tend to be more severe with earlier onset. Patients usually present with slowly progressive asymmetric weakness and may have difficulty whistling or drinking through a straw.[7] They may experience prolonged periods of relatively stable function.[4] Progressive weakness and loss of skeletal muscle mass are observed in the face, upper arms, and shoulders with protruding shoulder blades,[4] progressing from the face caudally, starting in the orbicularis oculi, mouth, and cheek.[7] Winging of the scapula is the most characteristic sign[7], with loss of rhythmic motion of both scapulae during shoulder motion due to weakness of the scapular stabilizer muscles. The scapulae are in the elevated position due to weakness of middle and lower trapezius muscles and internal rotation of the arms.[8] Eventually, weakness of the abdominal and hip girdle muscles and tibialis anterior muscles resulting in foot drop can also appear. Extraocular and bulbar muscle involvement is typically spared and symptomatic respiratory muscle weakness is rarely seen in FSHD as exemplified in this case report.[3]

The onset of symptoms in Patient 1 was at age 30 compared to age 26 in Patient 2. Both patients presented with facial asymmetry in childhood and weakness of both shoulders. Patient 2 also developed progressive LE weakness with unilateral foot drop, gait deviation, and difficulty in ambulation. Both patients manifested loss of skeletal muscle mass and winging of scapulae.

Diagnosis of FSHD entails careful medical history, thorough physical examination, and diagnostic tests to determine distribution of symptoms, presence of disabilities and/or handicaps, and to rule out other causes of progressive weakness.[9] Family history may give important clues since all the MDs are genetic conditions, although no family history will be evident in the event of new mutations.[9] Signs and symptoms similar to those seen in the two sisters were observed in the mother, maternal grandmother and two maternal uncles. Their relatives did not seek consultation as these features were considered normal inherited traits.

Laboratory tests for FSHD include: CPK, EMG-NCV studies, muscle biopsy and genetic tests. The serum level of muscle enzyme CPK is elevated with muscle damage and may be seen in some conditions even before symptoms appear. Both sisters had elevated CPK levels which were non-specific. Myopathic changes are typically seen in skeletal muscles and seen in EMG studies as increased insertional activity, low amplitude, short duration, polyphasic motor unit potentials despite maximal recruitment.[1,10] These EMG-NCV findings, consistent with myopathy, were evident in both sisters. Traction-type injuries to the brachial plexus may occur with shoulder girdle muscle weakness; sensory symptoms may develop with distal denervation involving the hands and arms.[10] The EMG-NCV studies may then show denervation changes, positive sharp waves, and fibrillation potentials. Muscle biopsy is valuable with a negative family history to confirm myopathic etiology and to exclude other primary muscle diseases which have presentations similar to FSHD.[5] A typical muscle biopsy shows changes in the structure of muscle cells and the presence of fibrous tissue or other aberrant structures.[1] A muscle biopsy was recommended to both patients but was not performed due to financial constraints.

In 1991, an international consortium published four main diagnostic criteria for FSHD; these are: "1) onset of disease in facial or shoulder girdle muscles; sparing of extraocular, pharyngeal, and lingual muscles and myocardium, 2) facial muscle weakness to more than 50% of affected family members, 3) autosomal dominant inheritance in familial cases, and 4) evidence of myopathic disease from electromyography and muscle biopsy in at least one affected member, without biopsy features specific for alternative diagnoses."[11] Involvement of the myocardium was subsequently reported.[7,8] The clinical diagnosis of FSHD for both patients was based on the distinctive pattern of muscle involvement with an apparent autosomal dominant history, although affected family members were not evaluated. Electrodiagnostic studies of both sisters were consistent with myopathy. Diagnosis of FSHD can now be confirmed with molecular studies, obviating the need for muscle biopsy in most cases. Molecular testing can demonstrate the presence of mutated genes through DNA analysis for the 4q35 deletion, specifically "contraction of the D4Z4 repeats in one copy of 4q35".[3] Genetic testing was arranged for both patients and other family members but was not feasible due to financial and logistical constraints as most family members were living in Capiz.

No definitive treatment for FSHD is available to date.[3,5] Corticosteroids, albuterol, and creatine monohydrate have not been shown to be effective in improving strength.[3,12] Novel interventions include somatic gene therapy;[1] autologous stem cell therapy;[13] and folic acid and methionine supplementation, myostatin inhibition, and muscle stem cell therapy.[3] Although, stem cell therapy cannot correct the genetic defect, growing new nerve or muscle through stem cell therapy may significantly improve function.[4]

In spite of recent advances in molecular diagnosis for FSHD and research on potential cures, the underlying

mechanisms leading to progressive atrophy and weakness secondary to the genetic defect are still not understood. Rehabilitation medicine remains the mainstay in the management of FSHD.[14] The goals of treatment are three-fold: treatment of symptomatic impairments, prevention of secondary problems, and improvement of function and quality of life.[8] Physical therapy, particularly regular stretching, is effective in maintaining shoulder ROM limited by weakened muscles and in preventing or delaying the onset of contractures.[1] Strengthening unaffected muscle groups to compensate for weakness may be possible if the affected muscles are few and isolated. Regular, non-strenuous exercise helps maintain general good health. A 12-week moderate resistance exercise program for patients with slowly progressive neuromuscular diseases showed improvement in strength from 4% to 20% without adverse effects compared with a 12-week high resistance exercise program which showed no benefit over the former.[4] Overwork weakness was also observed in the latter group.

A recent Cochrane update published that moderate-intensity strength training for individuals with FSHD and myotonic dystrophy appeared not harmful, but there was insufficient evidence to establish its benefits.[15] Exercise to the point of exhaustion should be avoided. Other complications include increased risk for falls with ankle or knee weakness and overuse, and stretch injuries with shoulder and pericapsular weakness.[3] Both sisters improved in muscle strength, active ROM, and endurance after out-patient rehabilitation, with no reported overwork weakness or other complications. Both remained ambulatory.

Leg braces and ankle splints can prevent equinus deformity.[14] Custom molded ankle-foot orthoses (AFO) can be prescribed for foot drop. For combination of foot drop and knee extensor weakness, floor-reaction AFO (FRAFO) or knee-ankle-foot orthosis (KAFO) have been recommended.[3]

With progressive LE weakness, assistive devices such as walkers and wheelchairs[14] are necessary to facilitate independent mobility. Figure-eight braces can minimize visual scapular winging but force applied is not adequate to fix scapulae to improve shoulder ROM.[3] Compression of the brachial plexus may occur if brace is worn too tightly. Individuals with intractable shoulder pain from shoulder joint laxity may benefit from wearing figure-eight braces for a short period.[3] Abdominal supports may be recommended to patients with marked abdominal muscle weakness; wheelchair-bound patients may benefit from postural supports and environmental adaptations.[8] Patient 2, who had LE weakness, was trained to ambulate using a cane for safe mobility and ambulation. Both sisters did not require LE or shoulder braces (orthoses) or abdominal supports.

Occupational therapy assists individuals with FSHD in engaging in ADL (e.g., feeding, self-care) and instrumental ADL (IADL) (e.g., leisure activities, home-making) at the most independent level possible through use of adaptive equipment, work simplification, and energy conservation techniques. Occupational therapy can address psychosocial changes and cognitive decline which may accompany FSHD, and provides patient support and education regarding the disease.[9] Environmental modification may be necessary to improve accessibility and optimize the individual's function. Both sisters showed improved ADL skills through adaptive devices and environmental modifications.

Psychological intervention and genetic counseling are other components of the holistic, multidisciplinary management in rehabilitation of patients with FSHD. Patients may also present with other impairments: musculoskeletal pain, usually involving the shoulders and upper back, knees, lumbosacral area; hyperlordosis, scoliosis and kyphosis; high-frequency hearing loss; retinal telangiectasias; cardiac diseases; and respiratory insufficiency. Inability to maintain a smile and drooling secondary to facial muscle weakness can be a handicap. Neither of the sisters presented with these problems. Physiatric monitoring of disease progression with early identification of secondary problems or complications and prompt treatment are essential.

Some patients may benefit from surgery. Operative scapular fixation appears to produce significant benefits, although the procedure has to be balanced against postoperative immobilization and potential complications.[5] Surgery is recommended in patients with stable or slowly progressive disease, and relatively preserved upper arm strength.[3] Other surgical interventions include gold weights implanted into the upper eyelid for lagophthalmos, tendon transfer for foot drop, and plastic surgery for markedly everted lower lip.[3]

The prognosis of FSHD is variable.[5,7] An affected parent's disability from FSHD cannot accurately predict the severity of the affected child's disease.[5] Disease progression and extent of muscle loss vary; some may need a wheelchair[5] whereas others have limited difficulties in ADL. Some may have mild disease which progresses very slowly over a normal lifespan, while others may have severe muscle weakness, functional disability, and loss of the ability to walk. Cardiac and pulmonary complications may occur in most MDs, and cardiac complications may occasionally precede the clinical presentation.[4] Definitive diagnosis by molecular testing is warranted to facilitate genetic counseling, prognostication, and anticipatory management. There is an inverse relationship between residual repeat number in the deletion and age of onset and severity of disease.[5,16] Patient 1 may have better functional prognosis with later onset of disease, lesser degree of muscle weakness and ADL difficulties, and better motivation and understanding of the disorder. In contrast, Patient 2, who is more symptomatic with an earlier onset and a more

progressive disease may have more functional limitations compounded by fatigue and apprehension on the progressive disease course. Patient 2 continued to work as a teacher while Patient 1 continued to be a homemaker with less difficulty in ADL and IADL skills.

In conclusion, two sisters with similar clinical diagnosis of FSHD presented with varying degrees of impairments. Despite progressive impairments, optimal function and quality of life can be achieved through comprehensive individualized rehabilitation by not only "adding years to life" but also "adding life to years."

References

1. Do T. Muscular Dystrophy [Online]. 2008 [cited 2008 Jul]; Available from http://emedicine.medscape.com/article/1259041-overview.
2. Emery AE. Population frequencies of inherited neuromuscular diseases--a world survey. Neuromuscul Disord. 1991;1(1):19-29.
3. Tawil R. Fascioscapulohumeral muscular dystrophy. Neurotherapeutics. 2008;5(4):601-6.
4. Carter GT. Rehabilitation management of neuromuscular disease [Online]. 2010 [cited 2010 Feb]; Available from http://emedicine.medscape.com/article/321397-overview.
5. Tawil R, Forrester J, Griggs RC, et al. Evidence for anticipation and association of deletion size with severity in fascioscapulohumeral muscular dystrophy. The FSH-DY Group. Ann Neurol. 1996;39(6):744-8.
6. National Annual Hospital Statistical Reports. Department of Health 1998–2007. (Unpublished)
7. Fascioscapulohumeral Muscular Dystrophy [Online]. 2008 [cited 2008 Jul]; Available from http://www.patient.co.uk/doctor/Facioscapulohumeral-Muscular-Dystrophy.htm.
8. Pandya S, King WM, Tawil R. Facioscapulohumeral dystrophy. Phys Ther. 2008; 88(1):105-13. Epub 2007 Nov 6.
9. Griggs RC, Mendell JR, Miller RG. The muscular dystrophies [Online]. 2008 [cited 2008 Jul]; Available from http://emedicine.medscape.com/article/1176126-overview.
10. Dumitru D. Myopathies. In: Dumitru D, ed. Electrodiagnostic Medicine, 2nd ed. Philadelphia: Hanley & Belfus, Inc.; 2002. pp. 1031-117.
11. Padberg GW, Lunt PW, Koch M, Fardeau M. Diagnostic criteria for fascioscapulohumeral muscular dystrophy. Neuromuscul Disord. 1991; 1(4):231-4.
12. Rose MR, Tawil R. Drug treatment for fascioscapulohumeral muscular dystrophy. Cochrane Database Syst Rev. 2004;(2):CD002276.
13. Morosetti R, Mirabella M, Gliubizzi C, et al. Isolation and characterization of mesoangioblasts from fascioscapulohumeral muscular dystrophy muscle biopsies. Stem Cells. 2007;25(12):3173-82.
14. FSH Society Fascioscapulohumeral Muscular Dystrophy. About FSHD [Online]. 2008 [cited 2008 Jul]; Available from http://www.fshsociety.org/pages/abtWhat.html.
15. Voet NB, van der Kooi EL, Riphagen II, Lindeman E, van Engelen BG, Geurts Ach. Strength training and aerobic exercise training for muscle disease. Cochrane Database Syst Rev. 2010;(1):CD003907.
16. Lunt PW, Jardine PE, Koch MC, et al. Correlation between fragment size at D4F104S1 and age at onset or at wheelchair use, with a possible generational effect, accounts for much phenotypic variation in 4q35-fascioscapulohumeral muscular dystrophy (FSHD). Hum Mol Genet. 1995;4(5):951-8.