Facioscapulohumeral Dystrophy: Case Report and Discussion

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Abstract Facioscapulohumeral dystrophy (FSHD) is often cited as the third most common form of muscular dystrophy. Therefore, it should be considered in patients with complaints of progressive weakness. We present the case of a man with facial, truncal, and leg weakness that initially sought medical attention for lower back pain. Electrodiagnostic testing revealed findings in the trapezius, serratus anterior, biceps, triceps, pectoralis major, tibialis anterior, and gastrocnemius muscles consistent with a myopathic disorder. Subsequent genetic testing identified a FSHD allele size consistent with a FSHD deletion mutation. Therefore, confirming the diagnosis of FSHD. Unfortunately, no effective treatments currently exist for FSHD. However, supportive measures involving physical therapy and the use of orthotics may aid in improving function and mobility.

Keywords facioscapulohumeral dystrophy · FSHD · Landouzy–Dejerine disease · muscular dystrophy · telomeric deletion disease · electrodiagnostic testing

Case presentation

The patient is a 51-year-old right-handed man who presented to his primary care provider with complaints of persistent lower back pain. After noticing little improvement of his symptoms with conservative management, including the use of nonsteroidal antiinflammatory drugs (NSAIDs), the patient was referred to a physiatrist for further evaluation and electrodiagnostic testing. The majority of the primary care provider's work-up was unremarkable with the exception of magnetic resonance imaging (MRI) of the lumbar

spine that noted a broad-based central disc herniation at the L5–S1 level. In addition, an elevated creatine kinase (CK) level of 324 U/l was noted on routine serology.

While describing the history of the present illness to the physiatrist, the patient explained that he also noted some right lower extremity weakness and atrophy. The patient attributed these findings to an old racquetball injury of the right calf. Furthermore, the weakness made it difficult for him to walk properly at times. During the review of symptoms, the patient added difficulty lifting his arms overhead and a “crooked” smile to the list of complaints. The physical examination noted an asymmetric smile, minimal right lateral scapular winging, and a steppage gait. Furthermore, atrophy of the right pectoralis major, trapezius, and gastrocnemius muscles were noted. In addition, atrophy of the bilateral tibialis anterior muscles were noted as well. Manual muscle testing was 5/5 throughout the bilateral upper and lower extremities with the exception of the findings noted in Table 1. The remainder of the physical examination was unremarkable.

Electrodiagnostic testing of the upper and lower extremities resulted in a normal nerve conduction study (NCS). However, electromyography (EMG) did demonstrate findings consistent with a myopathic disorder. These results are summarized in Tables 2, 3, 4, and 5. The needle examination noted abnormal spontaneous activity in the form of fibrillation potentials and positive sharp waves (PSW) in various muscles including the right gastrocnemius and bilateral tibialis anterior muscles. Furthermore, short duration polyphasic potentials were noted in numerous muscles of the right periscapular region as well as of the bilateral lower extremities. Tracings obtained during the testing of the right tibialis anterior, such as that depicted in Fig. 1, are representative of these findings. Given that the results of the electrodiagnostic testing were consistent with a myopathic disorder, facioscapulohumeral dystrophy (FSHD) was suspected and genetic testing was ordered to confirm the diagnosis.

Genetic testing, performed at an outside facility, reported that the patient possesses a FSHD allele size measuring 35 kilobases (kb) that is consistent with a FSHD deletion mutation. However, the analysis also noted a possible benign translocation between the chromosome 4q35 and chromosome 10q26 loci that occurs in approximately 20% of the

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Table 1 Manual muscle testing

Muscle	Right	Left
Orbicularis oculi	4/5	4/5
Pectoralis major	4/5	5/5
Tibialis anterior	2/5	4/5
Peroneus longus	3/5	4/5
Extensor hallucis longus	3/5	4/5
Gastrocnemius	4/5	5/5
Hamstrings	4/5	4/5

general population. Therefore, given that the genetic testing was only suggestive and not confirmatory for FSHD, the patient was referred to a neurologist specializing in the diagnosis and treatment of muscular dystrophy.

The neurologist requested that the patient don an ankle foot orthosis (AFO) in order to aid with ambulation given tibialis anterior weakness as well as ordering physical therapy in hopes of strengthening the affected musculature. In addition, it was recommended that the genetic testing be repeated at a second facility specializing in muscular dystrophy analysis. The results of the repeat genetic testing did confirm FSHD noting that the patient has a chromosome 4q35 deletion with restriction fragments smaller than 35 kb.

Subsequently, the patient revisited with the physiatrist approximately 1 year after being diagnosed with FSHD. The patient noted improved ambulation with the use of the AFO. Furthermore, manual muscle testing noted significant improvement in the strength of the involved musculature. In addition, the CK level was 202 U/l at the time of revisit. Hence, 122 U/l less than the initial level measured by the primary care provider. Therefore, the patient was satisfied with his care and had taken the initiative to learn more about FSHD. Additionally, he was considering whether to have his four children tested for the disease as well.

Facioscapulohumeral dystrophy

In their landmark 1886 paper, French physicians, Louis Théophile Joseph Landouzy and Joseph Jules Dejerine, were

the first to describe FSHD [1]. This autosomal dominant disorder is clinically defined as progressive asymmetric muscular weakness typically of the face, scapular stabilizers, proximal arm, and leg [2]. However, clinical presentations may vary. Uncini and his colleagues report of cases in which patients presented simply with asymmetrical atrophy of the calf muscles [3]. Additionally, Van Der Kooi and his colleagues also present cases of leg weakness without any apparent involvement of facial muscles [4]. The prevalence of FSHD is estimated at approximately one in 20,000 individuals. The disorder affects men and women equally. The age of onset is variable, but 90% of sufferers notice some weakness prior to 20 years of age. However, FSHD can at times have a very insidious clinical presentation in patients during their third or fourth decades of life. These patients often note that their scapula protrudes. They may also have shoulder pain from pathology due to scapulothoracic instability. An astute clinical eye is sometimes needed to identify the abnormal scapulothoracic mechanics contributing to their symptoms. As noted above, their complaints and physical examination findings are often asymmetric. Superiorly migrating scapular winging and an inability to fluidly abduct the shoulder may be noted on inspection as illustrated in Figs. 2 and 3. The slow progression of the condition often makes it difficult to be self-aware of an individual's own deficits. Some patients learn to compensate by thrusting their arms upward and overhead to elevate the shoulder in order to perform everyday activities. In addition, given the varying degree of genetic penetrance, a history of symptoms among family members is variable as well. Unfortunately, 20% of patients will also lose their ability to ambulate on their own and eventually require wheelchair assistance [5, 6]. Furthermore, hearing and visual impairments may be associated with the disorder. Various studies demonstrate a possible genetic link between FSHD and retinal vascular abnormalities [7, 8]. Lastly, it appears that FSHD does not affect the life expectancy of individuals suffering of the disease.

Although the pathogenic mechanism of FSHD remains unclear, it is believed that the disorder characteristically results from a partial deletion of an integral number of 3.3 kb

Table 2 Nerve conduction study

Nerve conduction report: motor nerves										
Nerve	Site	Onset last (ms)	Norm onset	Amplitude	Norm amp	Duration (ms)	Seg name	Distance (cm)	Velocity (m/s)	Norm vel
L Peroneal	EDB			O–P (mV)		Full				
30.2°C	Ankle	3.84	<5.5	3.76	>2.5	7.55	AbFbHd–ankle	34.00	46.8	>40.0
	AbFbHd	11.11		3.36		8.72				
R Peroneal	EDB			O–P (mV)		Full				
29.9°C	Ankle	5.34	<5.5	3.60	>2.5	5.81	AbFbHd–ankle	32.00	46.1	>40.0
	AbFbHd	12.28		3.34		11.86				
L PostTib	AbdHal			O–P (mV)		Full				
30.3°C	Ankle	3.61	<6.0	7.19	>3.0	11.39	Knee–ankle	46.00	46.7	>41.0
	Knee	13.45		5.84		9.00				
R PostTib	AbdHal			O–P (mV)		Full				
30.6°C	Ankle	3.19	<6.0	9.67	>3.0	11.02	Knee–ankle	37.00	44.1	>41.0
	Knee	11.58		8.62		11.95				

Table 3 Nerve conduction study

Nerve conduction report: sensory nerves

Nerve	Site	Onset lat (ms)	Norm onset	Peak lat (ms)	Amplitude	Norm amp	Duration (ms)	Seg name	Distance (cm)	Velocity (m/s)	Norm vel
LS Peron 30.0°C	Ankle				O–P (μV)		Neg				
	Latleg	2.31		2.91	20.58		1.47	Latleg–ankle	10.50	45.4	
RS Peron 30.2°C	Ankle				O–P (μV)		Neg				
	Latleg	2.09		2.84	18.46		–	Latleg–ankle	11.00	52.5	
L Sural (30.0°C)	LatMal				O–P (μV)		Neg				
	Calf	2.09		2.88	20.28		–	Calf–LatMal	10.50	50.1	
R Sural 30.1°C	LatMal				O–P (μV)		Neg				
	Calf	1.88		2.69	20.64		1.38	Calf–LatMal	10.00	53.3	

Table 4 Nerve conduction study

F/H report

Nerve	Muscle	Lat1 (ms)	Lat2 (ms)	Lat2–Lat1 (ms)	Amplitude (μV)	Temp (°C)
L Peroneal F	EDB	50.63		50.63		30.0
R Peroneal F	EDB	53.44		53.44		30.0
L Tibial F	AHB	49.53		51.09		30.7
R Tibial F	AHB	49.53		49.53		30.5

Table 5 Electromyography

Side	Muscle	Nerve	Root	INS	FIBS	PSW	FAS	AMP	DUR	Configuration	PAT	REC INT	Comment
L	MedGastroc	Tibial	S1–2	Nml	0	0	0	Nml	Nml	Di/Tri phasic	Full	Normal	
L	TibAnt	Peroneal	L4–5	Nml	0	2+	0	Inc	Short	Inc Polys	Myopath	Normal	
R	1stDorint	Ulnar	C8–T1	Nml	0	0	0	Nml	Nml	Di/Tri phasic	Full	Normal	
R	Biceps	Musc	C5–6	Nml	0	0	0	Nml	Nml	Di/Tri phasic	Myopath	Normal	
R	FlexCarRad	Median	C6–8	Nml	0	0	0	Nml	Nml	Di/Tri phasic	Full	Normal	
R	GluteusMax	InfGlu	L5–S2	Nml	0	0	0	Nml	Nml	Di/Tri phasic	Full	Normal	
R	LowTrapezius	Spin	C3–4	Nml	0	0	0	Nml	Nml	Inc Polys	Myopath	Normal	Incr short duration MUAP
R	MedGastroc	Tibial	S1–2	Nml	2+	2+	0	Nml	Short	Inc Polys	Myopath	Normal	Very atrophic
R	Pect Major	Ant Thor	C 7 – 8 T1	Nml	0	0	0	Nml	Short	Inc Polys	Myopath	Normal	Severely atrophic
R	Rhomboids	DorsS	C5	Nml	0	0	0	Inc	Nml	Inc Polys	Full	Normal	
R	SerratAnt	LnTho	C4–6	Nml	0	0	0	Nml	Nml	Inc Polys	Myopath	Normal	Incr short duration MUAP
R	TensFaseLata	SupGlut	L5–S1	Nml	0	0	0	Nml	Nml	Di/Tri phasic	Full	Normal	
R	TibAnt	Peroneal	L4–5	Nml	2+	2+	0	Nml	Short	Inc Polys	Myopath	Normal	Very atrophic
R	Trapezius	Spin	C3–4	Nml	0	0	0	Nml	Short	Inc Polys	Myopath	Normal	Very atrophic
R	Triceps	Radial	C6–7–8	Nml	0	0	0	Nml	Short	Inc Polys	Myopath	Normal	Very atrophic
L/R	RectFemoris	Femoral	L2–4	Nml	0	0	0	Nml	Nml	Di/Tri phasic	Full	Normal	
L/R	VastusMed	Femoral	L2–4	Nml	0	0	0	Nml	Nml	Di/Tri phasic	Full	Normal	Very atrophic

Fig. 1. Electromyography tracing of the right tibialis anterior

polymorphic repeats, identified as D4Z4, within the subtelomeric region of chromosome 4q [9, 10]. Whereas healthy individuals normally have *EcoRI* digestion fragments of D4Z4 consisting of 11 to 150 U, sufferers of FSHD have fragments of 1 to 10 U. However, Upadhyaya and his colleague note that, although molecular diagnosis of the disease is often cited to be 98% accurate, the search for the gene during testing is sometimes hampered by sequence homologies between the suspected 4q35 region and other chromosomal regions [11].

In addition to genetic testing, the work-up for suspected FSHD often includes serology and electrodiagnostic testing. CK levels tend to be elevated in patients with FSHD. Furthermore, electromyography may reveal myopathic potentials. Podnar and his colleague note a high sensitivity of multimotor unit potential (MUP) analysis confirming myopathy in patients suspected of FSHD [12]. However, they stress that the evaluation of three MUP parameters, thickness, amplitude, and duration/area, is needed for maximal sensitivity. In addition, Stübgen explains that quantitative EMGs in patients with FSHD often reveal findings consistent

Fig. 2. Scapular winging related to facioscapulohumeral dystrophy

Fig. 3. Scapular winging related to facioscapulohumeral dystrophy

with a mild, slowly progressive myopathy [13]. Furthermore, the author notes that the most sensitive indicators of early muscle disease are MUP duration on motor unit analysis and MUP area on MacroEMG. However, given the characteristic slow progression of the disorder, EMGs may often reveal no or few fibrillation potentials or positive sharp waves throughout the involved musculature. In such studies, myopathic motor unit recruitment or the presence of short duration motor units may be the sole electrodiagnostic finding.

In cases in which the clinical suspicion remains high despite nonconfirmatory genetic or electrodiagnostic testing, a muscle biopsy may be performed. Dystrophic features are often noted on muscle biopsy of patients with FSHD. Reed and his colleagues note that the pathophysiology of FSHD includes novel changes in the organization of the sarcolemma and its association with nearby contractile structures, suggesting that the integrity of the sarcolemma may be compromised [14].

Despite the various methods available to diagnose FSHD, no effective treatment is currently available for patients with the disease. Various studies examine the possible role of beta2-adrenergic agonists, such as albuterol, in treating FSHD. It is hypothesized that the use of such medications may exert anabolic effects on muscles and prevent atrophy after a variety of insults. Kissel and his colleagues explain that, although the use of albuterol does not improve overall strength or function in patients with FSHD, the medication may improve muscle mass [15]. However, a Cochrane Database System Review of medical literature from 1966 to 2003 concludes that there is no evidence from randomized controlled trials to support any drug treatment for FSHD [16]. Therefore, treatment often involves supportive measures to aid in improving the patient's function. Orthotics, such as an AFO, may be used to aid in improving ambulation. In addition, exercise and physical therapy may result in less fatigue and increased mobility. Olsen and his colleagues note that a 12-week low-impact aerobic program improves maximal oxygen intake and workload without further damaging muscles [17]. Future treatments, however, may involve the use of stem cells in order to possibly treat FSHD at the cellular level. Morosetti and his colleagues

discuss the possible use of autologous mesoangioblasts from the patient's own healthy muscle to limit damage within the diseased musculature [18]. Vilquin and his colleagues offer a similar suggestion as they discuss the possible use of autologous myoblasts in order to treat FSHD [19]. Although these treatments involving cellular transplantation offer promise, they are years from being able to impact the lives of patients with FSHD. Finally, experts highly recommend genetic counseling for individuals with FSHD who are planning to have children [20].

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