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Facioscapulohumeral muscular dystrophy

Synonyms: Landouzy-Dejerine muscular dystrophy, facioscapuloperoneal muscular dystrophy

What is facioscapulohumeral muscular dystrophy?[1]

Facioscapulohumeral muscular dystrophy (FSHD) is a common type of adult muscular dystrophy and is divided into types 1 and 2 based on genetic mutation. Both FSHD types often show asymmetrical and progressive muscle weakness affecting initially the face, shoulder and arms followed by the distal then proximal lower extremities.

Genetically, FSHD is associated with a macrosatellite array consisting of tandem D4Z4 repeats at the distal end of chromosome region 4q35. This array is typically highly compacted, limiting transcription but in FSHD there is a 'decompaction,' resulting in a more open state.

- In FSHD1 (95% of cases), this occurs due to a contraction of the D4Z4 repeats to between 1 to 10 copies.
- In FSHD2 (5% of cases), the region opens up due to mutations in epigenetic modifiers such as SMCHD1 and DNMT3B.

How common is facioscapulohumeral muscular dystrophy? (Epidemiology)

Facioscapulohumeral muscular dystrophy (FSHD) is one of the most common types of muscular dystrophy, affecting approximately 1 in 8000 individuals.[1]

Gene penetrance in women is believed to be lower than in men, and, on average, women are diagnosed at an older age and are often less severely affected.[2]

Symptoms of facioscapulohumeral muscular dystrophy (presentation)[1]

FHSD is characterised by progressive, asymmetrical muscle atrophy that typically affects the face, upper limb and shoulder skeletal muscles and later, the lower limbs.

Symptoms can emerge anywhere from childhood to adulthood, but typically manifests in the 2nd or 3rd decade of life. Disease severity is very variable as roughly 20% of mutation carriers are asymptomatic, while 20% eventually require a wheelchair.

In a rare, early-onset form of FSHD in which symptoms emerge by 10 years of age, severity is higher with most showing childhood facial weakness and more frequent wheelchair dependence.[3]

Both FSHD types 1 and 2 are clinically similar, characterised by:[4]

- Often marked side to side asymmetry. Muscle pain is frequent and often appears at an early stage.
- Facial weakness seen as inability to squeeze the eyes shut or furrow the brow, a transverse smile, or flattening when puckering the lips.
- Shoulder weakness often with scapular winging and flattening of the clavicles.
- Arm weakness including the biceps and triceps often with forearm sparing.
- Asymmetric abdominal weakness.
- Usually distal lower extremity weakness before proximal, starting with a foot drop.

Associated non-skeletal muscle manifestations include high-frequency hearing loss as well as retinal telangiectasias, both of which are rarely symptomatic.[5]

Differential diagnosis

Asymmetry and selective muscle group involvement help to distinguish this condition from other muscular dystrophies. Extraocular muscles, bulbar muscles, deltoids and respiratory muscles are usually spared.

- Amyotrophic lateral sclerosis.
- Chronic inflammatory demyelinating polyradiculoneuropathy.
- Congenital muscular dystrophies.
- Congenital myopathies.
- Dermatomyositis/polymyositis.
- Diabetic neuropathy.
- Endocrine myopathies.
- Inherited metabolic disorders.
- Limb-girdle muscular dystrophy.
- Scapuloperoneal dystrophy.

Investigations

- Elevated serum creatine kinase (CK).
- Imaging studies show a selective destructive process involving the anterior compartment muscles of the leg.
- Gene testing: one of the genes has been localised to chromosome band 4q35. Molecular diagnosis has 98% accuracy.[6]
- Electrodiagnostic studies may reveal myopathic potentials.
- Muscle biopsy is important to rule out other possible differential diagnoses if genetic testing is negative.

Prenatal diagnosis

Molecular diagnostic techniques are available for prenatal diagnosis.

Management of facioscapulohumeral muscular dystrophy

- No definitive therapy is available.[7] However, defining the genetic and molecular defects offers the potential for therapeutic intervention in the future.[8] [9]
- There is no strong evidence of significant benefit with operative scapular fixation. Any benefit as shown in some observational studies has to be balanced against postoperative immobilisation, need for physiotherapy and potential complications.[10]
- There is no evidence from randomised controlled trials to support any drug treatment.[11] However, both strength training and albuterol (equivalent to salbutamol) appear safe with limited benefit on muscle strength and volume. The consequences of long-term use are currently unknown.[12]
- The effectiveness of simple analgesia combined with anti-inflammatory agents for muscle pain is variable.
- A reported association with heart rhythm disorders in some cases suggests that a cardiovascular review every few years (looking particularly for ECG abnormalities, hypertension and heart muscle thickening) is important.
- A periodic eye check may also be appropriate. If troublesome inflammation of the eyes occurs as a result of them remaining open at night, surgery to bring the eyelids closer can be offered if artificial tears alone are insufficient. Research on involvement of the retina may give clues to the pathogenesis of the muscle dysfunction.[13]
- Driving licences, especially LGV or PCV, may be issued for a limited duration, with renewal subject to a satisfactory medical examination.

Complications of facioscapulohumeral muscular dystrophy

- Coats' syndrome: retinal vasculopathy with telangiectasia, exudation and retinal detachment. Seen in 49-75% of affected individuals. If detected early, retinal photocoagulation may prevent serious consequences.[14]

- Hearing loss: sensorineural deafness, which may be unilateral or bilateral. [14]
- Mental impairment and epilepsy: either or both may be seen in those patients with early onset.
- Hypertension.
- Cardiac complications: a single case report found ECG abnormalities - eg, bundle branch block, as well as left ventricular myocardial thickening. [15] [16]

Prognosis

- As many as 20% of patients eventually become wheelchair-bound. [17]
- However, up to one third of patients remain unaware of symptoms at least into old age but may have subtle detectable clinical signs. The majority of affected people come between these two extremes.
- Males tend to develop symptoms earlier and more severely at a given age than females. By age 30 virtually all males with FSHD exhibit symptoms but only two thirds of females do.
- Life expectancy is not affected, except perhaps in the most severe cases with greatly impaired mobility and consequent greater risk of chest infections.

Further reading

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