# Facioscapulohumeral disease

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*Chapter 1*

# Historical notes

In the middle of the nineteenth century most physicians held the opinion that chronic muscular atrophy was caused by anterior horn cell disease. Hypertrophy of some muscles in patients with atrophy of other muscles was such an intriguing finding that it drew the attention of many clinicians. To Duchenne goes the credit of having presented the first lucid description of the disease that now bears his name. In a series of articles in the "Archives Générales de Médicine" of 1868 he published his "Recherches sur la paralysie musculaire pseudo-hypertrophique ou paralysie myo-sclérosique". There he presented arguments for the myopathic nature of the condition based on the electrical examination and the histology of muscles. Since he never had an opportunity to do post-mortem studies, he cited the only published autopsy report at that time, in which Eulenburg and Cohnheim had shown the brain and the spinal cord to be unaffected. The muscle hypertrophy remained a puzzling finding. Duchenne discussed the possibility of a trophic influence of the autonomous nervous system but concluded (page 571) that "en somme, la pathogénie de la paralysie pseudo-hypertrohique est très obscure".

A large part of Duchenne's articles was concerned with the differential diagnosis of pseudohypertrophic muscular paralysis which included two syndromes: these were "la paralysie atrophique graisseuse de l'enfance" and "l'atrophie musculaire graisseuse progressive de l'enfance". The former started with fever in most cases and had a rapid course. These patients probably suffered from poliomyelitis. The latter consisted of a FSH syndrome and probably was what we now would call FSHD. In his summary Duchenne observed that "l'atrophie musculaire graisseuse progressive de l'enfance débute vers l'âge de cinq à sept ans par la face où elle atrophie quelques muscles, principalement l'orbiculaire des

lèvres et les zygomatiques. Après une période stationaire de plusieurs années (de deux à trois ans) elle envahit les membres et le tronc, où elle marche de la même manière que chez l'adulte, c'est-à-dire, qu'elle suit une marche descendente, en attaquant d'abord des muscles des membres supérieurs et ceux du tronc en ne s'étendant aux membres inférieurs que dans une période assez avancée".

This description constitutes the essence of the FSH syndrome and would fit FSHD perfectly. The lack of muscular hypertrophy, the descending course of muscular involvement and the facial weakness distinguished progressive fatty muscular atrophy of infancy from pseudohypertrophic muscular paralysis. The infantile and the adult form of progressive fatty muscular atrophy were both considered to be anterior horn cell diseases. The description of the infantile form served only to provide the differential diagnosis of pseudohypertrophic muscular paralysis. Duchenne did not comment specifically on spinal cord involvement in progressive fatty muscular atrophy of infancy although that seemed a logical possibility since he quoted Cruveilhiers' "mémoire sur la paralysie musculaire atrophique" published in the "Bulletins de l'Académie de Médicine" of 1852-1853. This quotation referred to Cruveilhiers' third observation of a man with progressive muscular atrophy with facial and lingual muscle involvement who on post-mortem examination was found to have an extreme atrophy of the spinal anterior roots and of the hypoglossal nerves. Duchenne mentioned this case to illustrate that involvement of the facial muscles could occur late in the course of the adult form of progressive fatty muscular atrophy. But Duchenne did not comment upon Cruveilheirs' second observation. This concerned an 18-year old man with a severe FSH syndrome who had died in 1848 of variola and on whom autopsy showed the brain, spinal cord and the periferal nerves to be unaffected. This probably represented the first autopsy of FSHD, but it passed by unnoticed. It apparently required quite a few more years for the concept of primary muscle disease to mature.

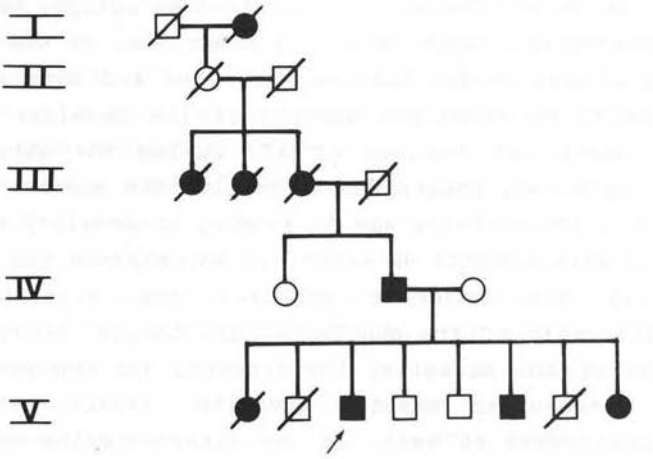
By the time Landouzy and Dejerine made their observations, the scientific climate had changed. In 1884 Erb wrote "Uber die

juvenile Form der progressiven Muskelatrophie und ihre Beziehungen zur sogenannten Pseudohypertrophie der Muskeln", and Vulpian presented a summary of Landouzy's and Dejerine's work at a meeting of the "Académie des Sciences" on January 17th. One year later (1885), Landouzy and Dejerine published their first article in the "Revue de Médicine" about "La myopathie atrophique progressive; myopathie sans neuropathie débutant d'ordinaire dans l'enfance, par la face". There they described an autopsy on a man who died of tuberculosis when he was 24 years old. At the age of three, atrophy of the facial muscles was noted and this was his only symptom until he developed atrophy of the shoulder girdle and upperarm muscles at the age of 17. During the subsequent years the atrophy slowly progressed to involve the muscles of the trunk and pelvic girdle. There was no sensory abnormality and the tendon reflexes were absent. He never had experienced any muscle pains. Landouzy and Dejerine stressed the clinical and histological integrity of the muscles of the tongue, pharynx and larynx and also of the masseter, the temporal and the pterygoid muscles. The extraocular muscles and the levator palpebrae muscles were unaffected as well. At the viscerocranium only the facial muscles were involved. (When they mentioned "facial muscles" they referred to the muscles innervated by the seventh cranial nerve. The terms "facial muscles" and "facial weakness" will be used in this text in the same sense). At post-mortem examination they found no abnormalities on the brain, spinal cord, periferal nerves and intramuscular nerve endings. Muscles which were clinically affected, but had not completely disappeared, showed "atrophie simple du faisceau primitif, avec sclérose et adipose très légères".

Landouzy and Dejerine's patient had a younger brother and sister who were similarly affected. The pedigree (Figure 1.1.) showed a definite autosomal dominant pattern of inheritance. It is interesting to see that the disease seemingly skipped the second generation. Of course it is quite possible that the woman at issue in the second generation might have represented an abortive case. Further more, if one realizes that the father of the proband developed muscle atrophy in the shoulder girdle at

the age of 26 and noted facial involvement when he was 32 years old, all the potential pitfalls involved in the diagnosis of FSHD are already obvious from the first published pedigree.

**FIGURE 1.1: FAMILY L (LANDOUZY-DEJERINE, 1885)**




The proband fitted the description of Duchenne's "infantile form of progressive fatty muscular atrophy". Landouzy and Dejerine assumed that Duchenne's and their own descriptions were about the same disease and that they had proven its myopathic nature. The proband's father and similar familial and sporadic cases described in subsequent articles (1885-1886), led Landouzy and Dejerine to adjust the diagnostic criteria of the disorder they had named facioscapulohumeral type of progressive myopathy. The age of onset was said not necessarily to be in infancy. Furthermore, they stressed that the disease did not always start with involvement of the facial muscles. In such cases shoulder girdle weakness was the presenting symptom, some never developing facial weakness. Landouzy and Dejerine described the autopsy of a case that had lacked clinical involvement of the facial muscles but showed microscopical abnormalities, suggesting a myopathy on examination of these muscles. Although these additions brought the ideas of French authors about the myopathies somewhat closer

to the German views on this matter, the gap was not closed to the satisfaction of Erb, who had formulated and defended (1884) his unifying concept of "dystrophia muscularis progressiva". Erb was convinced that all myopathic syndromes were different manifestations of one disease, because he had seen intermediate forms between all the known clinical syndromes and because he had found the histological changes in the muscles to be essentially the same in all these cases. He did not believe that "la myopathie atrophique progressive" was different from his "juvenile Muskelatrophie". In order to minimize the clinical differences he stated (1891) that he personally never had observed involvement of the facial muscles to be the first and most prominent symptom. To prove the contrary, Remak (1884) wrote an article "Uber die gelegentlichen Betheiligung der Gesichtsmuskulatur bei der juvenilen Form der progressiven Muskelatrophie" as did Mossdorf (1886): "ein zweiter Fall von Betheiligung der Gesichtsmuskulatur bei der juvenalen Muskelatrophie".

Although the concept of a primary muscle disease as a cause of a slowly progressive muscular atrophy was finally accepted by the end of the nineteenth century, the discussion about the classification of the human myopathies had only just begun. The introduction of genetical criteria proved to be very useful. Weitz (1921) was the first to recognize the possibility of autosomal dominant, autosomal recessive and X-linked recessive modes of inheritance of the myopathies. Davidenkow (1930) studied 554 cases of what he called dystrophia musculorum progressiva. Most of the cases were collected from the literature. Davidenkow was the first to recognize abortive cases of FSHD. He also drew attention to the fact that some affected members of families with FSHD failed to demonstrate facial weakness. Sjövall (1936) investigated 103 families with 161 affected persons in Sweden but his material did not include families with an autosomal dominant FSH syndrome, probably because, as Becker (1953) suggested, he had collected his cases from nursing homes and hospitals where "one rarely sees FSHD as this is a relatively benign disease". Another explanation could be that there is a large geographical

variation in the occurrence of FSHD. Julia Bell (1942, 1943) studied 1228 cases of muscular dystrophy from the literature and 113 records from the National Hospital, Queen Square, London and concluded that all three modes of inheritance seemed to occur. She divided the clinical material into three groups based on two criteria, pseudohypertrophy and facial involvement, hoping to find a certain pattern of inheritance for each group. Her first group consisted of all cases exhibiting pseudohypertrophy of muscles but cases with facial involvement were excluded. The second group contained all cases that had unaffected facial muscles and no pseudohypertrophy. The third group included all cases with weakness of the facial muscle with or without hypertrophy of muscles. Bell could not ascribe a single pattern of inheritance to each group, perhaps due to the ease with which she accepted the diagnosis of reported cases as definitely established and to the fact that in many instances the families were not completely examined, as Tyler and Winthrobe (1950) argued. This argument is of particular relevance with respect to FSHD as all Bell's 337 cases of group 3 were collected from the literature because in the 14-year period covered by the study no such cases were seen in the National Hospital.

Pseudohypertrophy and facial involvement continued to be decisive criteria in other attempts at classification of the muscular dystrophies, because the age of onset was considered too difficult to establish in many cases. Levison (1951) started from clinical criteria and concluded from eight families which he had examined personally that the FSH type of muscular dystrophy had an autosomal dominant mode of inheritance. He stressed that he had not seen patients with marked atrophy or paresis of the orbicularis oculi muscles as described by Landouzy and Dejerine (1885). He also distinguished a scapulohumeral type of muscular dystrophy that was sporadic in five families and present in two brothers of another family. Finally, he discerned an intermediate type between the FSH and scapulohumeral type in which the facial muscles were only slightly involved. The six cases of this type were all sporadic ones. However it is not stated how extensively the families were examined.

Stevenson (1953) thought an autosomal recessive mode of inheritance to be present in his families with facial involvement and included these families in his group of "autosomal recessive limb-girdle muscular dystrophy", as he judged weakness of the facial muscles an insufficient criterium for separation into two different diseases. Stevenson's examination of the families is certainly open for criticism, as will be discussed later. His view did not harmonize with the experience of many clinicians who had become accustomed to find an autosomal dominant mode of inheritance in most families with muscular dystrophy and involvement of the facial muscles. Therefore, Walton and Nattrass (1954) encountered little objection when they defined the pattern of inheritance of FSHD being usually autosomal dominant and only occasionally autosomal recessive. These authors were impressed by the occurrence of abortive cases, that can obscure the true pattern of inheritance in many families. Walton and Nattrass (1954) stressed that "the question of minor facial involvement is of the greatest importance and may well be a reason for confusion in published work since many cases which were truly FSH may have been classified as scapulohumeral".

The classification of the muscular dystrophies given by Walton and Nattrass has proven to be very successful and formed the basis of all other attempts at classification thereafter. It ended several decades of confusion about FSHD.