In the present time there is the opinion that FSHD is a disease genetically heterogeneous, but homogeneous from a clinical point of view: “…clinical, genetic and epigenetic features of facioscapulohumeral muscular dystrophy (FSHD) allowed the identification of two forms of FSHD, the classical autosomal dominant FSHD type 1, and the FSHD type 2 characterized by an identical clinical phenotype but associated with a different (epi-) genetic defect” (1) and “Of the 33 patients with FSHD2 … the initial symptom was scapular weakness in 61%, foot dorsiflexor weakness in 27%, facial weakness in 10%, and hip girdle weakness in 3%”(2).

These authors, as many others, supposed that the facio-scapulo-peroneal topography of muscle weakness (early involvement of facial, shoulder girdle and tibialis anterior muscles) is the specific sign of both FSHD forms, at the beginning stage of the disease.

During years 1969-1971 the patterns of 67 bilateral muscles involvement were analyzed in 200 patients with FSHD, called FSLD, at different stages of the disease (3-5).

Of these, 145 cases were from the world literature while 55 were under Kazakov’s personal observation. Seventy-eight of them (31 personal cases and 47 from literature, 59 hereditary and 19 sporadic) had developed a descending Facio-Scapulo-Limb Dystrophy (FSLD2) with a jump type, 38 patients a FSP or FSP(H) phenotype and 40 patients a final FSPFGH [facio-scapulo-peroneo-femoro (posterior thigh muscles)-gluteo (gluteus maximus)-humeral (biceps brachial)] or FSPHFG phenotype. The “pure” FSP phenotype was clinically observed at an average age of 11-16 years. The diagnosis of FSHD (or FSLD2) in patients personally followed, was confirmed by molecular analysis in 1996 (6).

On the other hand, 60 out of 200 patients – 47 hereditary and 11 sporadic cases from the world literature and 2 Kazakov’s personal cases – had developed a FSLD1 gradually descending type. Among these, 31 presented with the FSHGF phenotype and 29 with the final FSHGFP phenotype. In the last group, pelvic girdle and thigh muscles were more severely affected when compared with peroneal muscles, except for some cases in which the peroneal muscles were similarly affected.

The existence of FSLD1 is also confirmed by the fact that in many Handbooks on Nervous Diseases and Handbooks on Muscle Diseases, FSHD is described as a “gradually descending muscular dystrophy (i.e. the FSLD1) with the affection of pelvic girdle and hip muscles as well as of peroneal muscles (in some patients) during 20-30 years after the involvement of the face, scapular, humeral and trunk muscles”.

In addition, we cannot ignore the publications of many authors who described the FSHD gradually descending type (i.e. the FSLD1). Furthermore, it’s necessary to remark that the famous discussion between Erb and Landouzy-Dejerine dealt with the priority of recognition (and description) of the FSHD as a descending type with a “jump” (i.e. the FSLD2); however both had to admit the priority of Duchenne in describing FSHD as a gradually descending type (i.e. the FSLD1) (7).

Therefore, because both FSLD1 and FSLD2 are diseases clinically and historically well documented, FSLD (or FSHD) must be considered a disease not only genetically but also clinically heterogeneous.

The FSLD2 descending type, with a “jump” and an initial FSP phenotype may develop as FSHD1 or FSHD2 clinical phenotypes. As both forms are linked to chromosome 4q35, what is the FSLD1 gradually descending type, with initial FSH phenotype?

In our opinion FSLD1 occurs very rarely and is limited to definite geographical areas. Two hypotheses can be advanced: 1. FSLD1 and FSLD2 recognize a same gene mutation but present a different phenotype, under the action of different modifier genes; 2. FSLD1 has a different gene defect, not linked to chromosome 4q35.

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References


