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LETTER TO THE EDITOR

Facio-scapulo-humeral muscular dystrophy and its connection with facio-scapulo-peroneal muscular dystrophy 4q35-linked: some historical remarks

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.

Valery Kazakov, Dmitry Rudenko,
Vladislav Kolynin and Tima Stuchevskaya
Department of Neurology, Pavlov State Medical University St. Petersburg, Russia

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