On Nosological Place of Facioscapuloperoneal (Or Facioscapulolimb, Type 2) 4q35-Linked Muscular Dystrophy: Report of Cases

Valery Kazakov, Alexander Skoromets, Dmitry Rudenko, Vladislav Kolynin and **Tima Stuchevskaya**

Department of Neurology, First Pavlov State Medical University, St. Petersburg, Russia

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We observed the pattern of muscle weakness in 28 patients from 13 families with 4q35-linked EcoRI/BlnI DNA fragment size 13-30 kb facioscapuloperoneal muscular dystrophy (FSPMD) (Table). Thirteen patients (8 men and 5 women) from these families were re-examined by V.K.: after 27-29 years (4 patients: F5, IV-7, aged 52; F8, II-13, aged 88 and III-25, aged 55; F13a, III-1, aged 45), after 36-37 years (5 patients: F2, III-7, aged 73, III-10, aged 73 and VI-8, aged 42; F8, VI-17, aged 41; F13, III-8, aged 63), after 43 years (1 patient: F20, IV-2, aged 61), after 48 years (1 patient: F15, IV-3, aged 68) and after 49 years (2 patients: F18, III-3, aged 67; F9a, IV-1, aged 74) (Table).

In the first examination the next phenotypes of muscle weakness were found: facio(scapular) [F(S)] (3 patients), (facio)scapular [(F)S] (1), facioscapular (FS) (1), (facio)scapuloperoneal [(F)SP] (5), (facio)scapuloperoneal-(femoral) [(F)SP(F)] (1), scapuloperoneal (SP) (1), and facioscapuloperoneal-(humeral) [FSP(H)] (1) (Table).

On re-examination (V.K.) these patients after 27-49 years the next phenotypes of muscle weakness were found: facio-scapulo-peroneal-femoro (posterior thigh muscles)-gluteo (gluteus maximus) (FSPFG) (3 patients), facio-scapulo-peroneal-femoro (posterior thigh muscles)-gluteo (gluteus maximus)- (humeral; biceps brachii) [FSPFG(H)] (4 patients), facio-scapulo-peroneal-humero (biceps brachii) - femoral (posterior thigh muscles)-gluteal (gluteus maximus) (FSPHFG) (2 patients), (facio) scapuloperoneal [(F)SP)] (2 patients), facioscapuloperoneal (FSP) (1 patient) and facioscapuloperoneal-(femoral) [FSP(F)] (1 patient) (Table). Thus, in nine patients their phenotypes of muscle weakness were transferred in final ones: in FSPFG or FSPFG(H) in seven patients and in two other patients – in FSPHFG phenotypes in who the biceps brachii muscles were severe affected after involving of tibialis anterior muscles. However, in all patients with final phenotypes the interscapular and peroneal group muscles were more severely affected than posterior group of thigh and gluteus maximus muscles. Three patients (F2, III-10, aged 73 and VI-8, aged 42; F8, III-25, aged 55) on re-examination after 37, 36 and 27 years, respectively, had the same pure facioscapuloperoneal phenotype and in one patient (F8, VI-17) after 36 years the FSP phenotype predominated as well but with slight involvement of posterior thigh muscles.

Beside this, in two patients (from F2) having clinical pure FSP phenotype on MRI of lower limb muscles the severe involvement of some posterior thigh muscles and rectus femoris was found. Thus, in all discussed patients the disease began with initial involvement of the face (in minimal/slight degree) and shoulder girdle muscles and some time later of the peroneal group (anterior tibial) muscles. However, the dystrophic process gradually was extended to the thigh muscles (posterior group, namely; the quadriceps were preserved in 13 patients), pelvic girdle muscles (gluteus maximus, namely; the gluteus medius were preserved in 13 patients) and not always on upper arm muscles (biceps brachii, namely; slightly weakened on the one side in four from 13 patients; in two patients these muscles were severe affected). In the patients having the last phenotype the muscular strength were included after warmth of the peroneal gathering muscles and the expanded lumbar lordosis because of shortcoming of stomach what's more, gluteus maximus muscles however not the erector trunci ones was watched.

Our present clinical and MRI data, as well as our earlier investigations (1969-2009), allow us to suggest that the facioscapuloperoneal muscular dystrophy (FSPMD) is probably an independent form with "hard" static and dynamic pattern of muscle involvement and a mild course of the disease (1-3). All discussed patients including those at the age of 68, 73, 73 and 74 years old could walk independently and climb the stairs with the aid of a railing excluding two patients (F13, III-8, aged 63 and F8, II-13, aged 88) who could walk with aid of a stick on short distances only. However, in first patient the FSPMD associated with aortic aneurism and in second one - with diabetic polyneuropathy. On other 8 symptomatic patients who were reexamined (V.K.) after 3-20 years the similar final FSPFGH (2 men), FSPFG(H) (1 man), FSPHFG (3 men), FSPFG (1 man) and (F)SP(FG) (1 man) phenotypes were found and only 2 patients had FSP and FSP(F) phenotypes after reexamination (V.K.) via 7 and 15 years, respectively (Table).

In conclusion, in our opinion, the term "facioscapulolimb muscular dystrophy, type 2 (FSLD2), descending with a "jump" with initial FSP phenotype, Erb, Landouzy and Dejerine type" would be more correct. The FSP or (F)SP phenotype constitutes merely a stage in the development of FSLD2. We suppose that classical AD FSPMD (or FSLD2, a descending with a "jump" with initial FSP phenotype) is different from the classical AD FSHD1 (which we called as a facioscapulolimb muscular dystrophy, type 1 (FSLD1), a gradually descending with initial FSH phenotype,

Duchenne de Boulogne type) although these both diseases probably are connected with the same 4q35 chromosomal deletion but the different phenotypes due to the action of the different modifier genes. However, it can be also suggested that FSLD1 is connected with the basic gene other than FSLD2 and is not linked to the chromosome 4q35.

№F	DFS Kb	№P in ped.	Age ex.	Ph1	D.S.1	DLWD1	Re ex. yrs	Age reex.	Ph2	D.S.2	DLWD2
2	27/24	III-7	36h	(F)SP	Mod	2	(37)	73	FSPFG(H)	Sdd	3
		III-10	36	(F)SP	Sdd	2	37	73	(F)SP	Sdd	2
		VI-8	6	F(S)	Pr	1	36	42	FSP	Modd	2
5	25/22	IV-7	23	(F)SP(F)	Sdd	2	29	52	FSPFG(H)	Sdd	3
		V-4	1,5	Norma			22.5	24	(F)SP	Pr	1
8	23/20	II-13	60	(F)SP	Sdd	2	28	88	(F)SPFG(H)	Sdd	4
		III-25	28	(F)SP	Pr	1	27	55	(F)SP	Mdd	1
		VI-17	5.5	F(S)	Pr	1	36	41	FSP(F)	Sdd	2
18	27/24	III-3	18h	F(S)	Mdd	1	(49)	67	FSPFG(H)	Sdd	3
20	16/13	III-5	73	FSP(F)	Sdd	2	7	80	FSPFG(H)	Sdd	3
		III-10	62	FSPH(FG)	Sdd	2	3	65	FSPHFG	Sdd	3
		IV-2	18h	FS	Mdd	1	(43)	61	FSPFG	Sdd	3
19	20/17	III-4	47h	F(S)	Mdd	1	(8)	55	(F)SP(FG)	Sdd	2/3
		IV-2	19h	(F)SP	Mdd	1	(20)	39	FSPFGH	Sdd	3/4
16	23/20	III-5	45	FSP	Sdd	2	13	58	FSPFG	Sdd	3
		IV-6	21	FSP	Mod	2	15	36	FSP(F)	Modd	2/3
		IV-10	17	FSPH(FG)	Sdd	2	18	35	FSPHFG	Sdd	3/4
21	17/14	II-6	49	FSP	Mdd	1	11	60	FSPHFG	Modd	3
		LLJ-5 III-6	25 14	FSPFG (F)SP	Sdd Pr	3 1	14 12	39 26	FSPFGH (F)SP	Sdd Pr	4 1
22	23/20	III-1	42	FSP	Mod	2	7	49	FSP	Sdd	2
13a	26/23	III-1	18h	(F)SP	Pr	1	(27)	45	FSPFG	Sdd	2
9a	16/13	IV-1	25h	(F)S	Pr	1	(49)	74	(F)SPFG	Sdd	3
13	28/25	III-8	26h	FSP(H)	Sdd	2	(37)	63	FSPHFG	Sdd	4
15	24/21 33/30 33/30	IV-3 V-10 V-17 VI-10	20h 10 15 16	SP S (F)S (F)SP	Pr Pr Pr Pr	1 1 1 1	(48) 24 24	68 34 39	(F)SPHFG (F)S(P) (F)S(P)	Sdd Pr Pr	3/4 1 1

Table Dynamic of myogenic phenotypes and degree of severity disease in 28 patients from 13 families with different EcoRI/BLnI DFS

List of the abbreviations used in the Table

№F = number of family; DFS kb = EcoRI/BLnI DNA fragment size (kilobas); №P in ped. = number of patient in pedigree; Age ex. = age of patient in first examination; 18h, 47h and other = age of patients in which the myogenic status was take from the case history; Ph1 = patient's phenotype which in the first examination; D.S.1 = the degree severity of disease in first examination: Pr – presymptomatic, Mdd – mild degree of disease, Modd – moderate degree of disease, Sdd- severe degree of disease (see Acta Myol. 2000; vol. XIX, p.71); DLWD1 = daily-life work disability in first examination (see Acta Myol. 2000; vol. XIX, p. 72); Age reex. = the patient's age in which he was re-examined; Reex. yrs = after what years the patient was re-examined by Dr. Kazakov V.; Ph2 = patient's phenotype after re-examination; D.S.2 = the degree severity of disease after re-examination; DLWD2 = daily-life work disability after re-examination. Phenotypes: FS = facioscapular; S = scapular; SP =scapuloperoneal; FSP = facioscapuloperoneal; FSPFGH = facio-scapulo-peroneal-femoro (posterior group muscles)-gluteo (gluteus maximus muscle)-humeral (biceps brachii muscle); FSPFG = facio-scapulo-peroneal-femoro (posterior group muscles)-gluteal (gluteus maximus muscle); FSPHFG = facio-scapulo-peroneal-humero (biceps brachii muscle)-femoro (posterior group muscles)-gluteal (gluteus maximus muscle). (F) = slight atrophy and weakness of upper or lower half of orbicularis oris muscle and slight weakness of orbicularis oculi muscles (orbital part); (S) = slight atrophy of lower part of trapezius muscle; (H) = slight atrophy or slight weakness, (grade 4) of biceps brachii muscle; (F) = slight weakness of posterior thigh muscles; (FG) = slight weakness of posterior thigh and gluteus maximus muscles; (P) = slight weakness of tibialis anterior muscles (the patient cannot stand up on his heels / or one heel). The patient's phenotypes who were re-examined over 27-49 years marked by rich black color.

References

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