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HLA phenotypes in children with Duchenne muscular dystrophy and their gene carrier mothers

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Typing of HLA A, B and C locus antigens was carried out and the frequency distribution calculated in 32 hemizygous children affected by DMD, in 11 mothers who were either obligatory gene carriers or had increased CPK activity, and in 222 healthy blood donors. For typing peripheral blood lymphocytes and the standard NIH lymphocytotoxicity test were used. The HLA-B7 antigen had a tendency to be more frequent, being 31% in the group of hemizygous children with DMD as against 13.5% in the control group ($p < 0.04$). In the gene carrier mothers the frequency of HLA–B7 was 36% ($p < 0.12$). In the group of DMD hemizygotes the HLA–Aw24 antigen showed a tendency to higher frequency ($p < 0.05$).

The association between various pathological conditions and the HLA antigens has been the subject of intensive study in the last ten years. We only refer here to the HLA and Disease Registry by Ryder et al. [1] Neither this international register nor the recent literature contain data

TABLE I

Distribution of HLA-antigens in DMD-hemizygotes

HLA–A antigens	DMD (n=29) HLA–A antigen positivity		Controls (n=222) HLA–A antigen positivity		χ^2	p
	No.	per cent	No.	per cent		
1	4/29	13.8	49/222	22.1	0.62	0.44
2	13/29	43.8	110/222	49.5	0.08	0.98
3	10/29	34.5	43/222	19.4	2.67	0.10
11	2/29	6.9	33/222	14.9	0.77	0.39
w24	9/29	31.0	32/222	14.4	4.04	0.05
25	1/29	3.40	19/222	8.5	0.35	0.60
26	5/29	17.2	24/222	10.8	0.5	0.46
28	3/29	10.3	22/222	9.9	0.07	0.99
29	3/29	10.3	11/222	4.9	0.58	0.42
w30	1/29	3.4	7/222	3.2	0.23	0.99
w31	1/29	3.4	6/222	2.1	0.14	0.99
32	1/29	3.4	13/222	5.8	0.01	0.99

TABLE II

Distribution of HLA-B antigens in DMD-hemizygotes

HLA–B antigens	DMD (n=29) HLA–B antigen positivity		Controls (n=222) HLA–B antigen positivity		χ^2	p
	No.	per cent	No.	per cent		
5	8/29	6.9	28/222	12.6	0.35	0.59
7	9/29	31.0	30/222	13.5	4.74	*0.04*
8	4/29	13.8	41/222	18.5	0.13	0.72
12	8/29	27.6	44/222	19.8	0.53	0.46
13	2/29	6.9	18/222	8.1	0.02	0.99
14	4/29	13.8	15/222	6.7	0.95	0.32
15	3/29	10.3	16/222	7.2	0.05	0.99
17	2/29	6.9	18/222	8.1	0.02	0.99
18	4/29	13.8	34/222	15.3	0.004	0.99
w21	2/29	6.9	15/222	6.7	0.13	0.99
27	4/29	13.8	29/222	13.1	0.03	0.99
w35	4/29	13.8	50/222	22.5	0.7	0.41
38	3/29	10.3	10/222	4.5	0.79	0.36
w39	1/29	3.4	10/222	4.5	0.05	0.99
37	1/29	3.4	—	—	—	—
40	4/29	13.8	31/222	13.9	0.07	0.99
Cw 2	4/22	18.2	16/124	12.9	0.11	0.71
3	4/22	18.2	18/124	14.5	0.01	0.99
4	2/22	9.1	38/124	30.6	3.35	0.053
6	1/22	4.5	—			

concerning progressive muscular dystrophy (DMD). Therefore, a study of the question has been performed.

MATERIALS AND METHODS

Frequency distribution of HLA antigens was studied in 32 hemizygous DMD child patients from 29 families and in 222 healthy blood donors as controls. Eleven mothers were available for examination; they were either obligatory heterozygous gene carriers, or had increased CPK activity. In two families where 2 and 3 children, respectively had DMD, we took into consideration the data of one child for each of these families.

HLA typing of peripheral blood lymphocytes was carried out by the standard NIH lymphocytotoxicity test [3] for 37 HLA antigens of the A, B and partly the C loci. We have omitted from the Tables those antigens which were not represented in the patient population. Evaluation was done by the χ^2 test and Yates correction at the computer centre of Szeged University.

Results

Table I shows the frequency distribution of HLA–A antigens in the DMD hemizygotes and in the control group. Table II shows the frequency of the HLA–B antigens in the aforementioned groups. It can be seen that the frequency of antigen HLA–B7 had a tendency to be higher than in the controls ($p < 0.04$), and of the HLA–A antigens the HLA–Aw24 had a tendency of being more frequent ($p < 0.05$) than in the controls.

Among the HLA antigens of the DMD gene carrier mothers HLA–A3 and B7 showed a slight tendency to be somewhat more frequent than

Table III

Distribution of HLA-antigens in DMD-gene carriers

HLA–A antigens	DMD-gene-carriers (n=11) HLA–A antigen positivity		Controls (n=222) HLA–A antigen positivity		χ^2	p
	No.	per cent	No.	per cent		
1	1/11	9.1	49/222	22.1	0.42	0.55
2	6/11	54.5	110/222	49.5	0.0003	0.99
3	5/11	45.5	43/222	19.4	2.91	0.1
w24	2/11	18.2	32/222	14.4	0.008	0.99
25	1/11	9.1	19/222	8.5	0.24	0.99
26	1/11	9.1	24/222	10.8	0.1	0.99
28	2/11	18.2	22/222	9.9	0.14	0.63
29	2/11	18.2	11/222	4.9	1.42	0.24
32	1/11	9.1	13/222	5.8	0.04	0.99
HLA–B						
7	4/11	36.4	30/222	13.5	2.75	0.12
12	2/11	18.2	44/222	19.8	0.06	0.99
13	3/11	27.3	18/222	8.1	2.65	0.09
15	1/11	9.1	26/222	7.2	0.13	0.99
17	1/11	9.1	18/222	8.1	0.2	0.99
18	2/11	18.2	34/222	15.3	0.03	0.99
27	4/11	36.4	29/222	13.1	2.96	0.11
w35	2/11	18.2	50/222	22.5	0.001	0.99
40	1/11	9.1	31/222	13.9	0.00004	0.99
39	1/11	9.1	10/222	4.5	0.0008	0.99
Cw						
2	3/11	27.3	16/124	12.9	0.74	0.37
3	1/11	9.1	18/124	14.5	0.002	0.99
4	2/11	18.2	38/124	30.65	0.27	0.63

usual ($p < 0.1$ and $p < 0.12$ respectively).

Two affected children of different sexes in a family proved to be HLA-identical while lacking the B7 antigen. In two out of three male children of another family the haplotypes inherited from the mother were identical: A3, B7; in the third the maternal haplotype was A25, B18. Their sister who was suspected to be a gene carrier, also possessed the A3, B7 maternal haplotype.

Discussion

The only investigation into HLA antigen frequency in muscle disease known to us has dealt with neurogenic myopathy and myasthenia gravis [2], finding the antigens A1, B8, and DRw3 more frequent. We have no knowledge of data concerning DMD hemizygotes. In our material, antigen B7 had a tendency to be more frequent and antigen Aw24 to be more frequent, too. In a small group of possible heterozygous gene carrier mothers A2 and B7 had a slight tendency to be more frequent. The frequency of B7 was similar in percentage in the two groups, thus somewhat supporting each other while being not significant in the statistical sense. Further examinations are needed to find out whether these or other HLA antigens might figure as genetic markers in Duchenne muscular dystrophy.

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