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Serum alpha-galactosidase activity in children with Duchenne-type muscular dystrophy and in gene carriers

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Serum alpha-galactosidase activity was studied in 21 control children, 15 children with Duchenne muscular dystrophy, and in 8 gene carrier mothers. In both the DMD hemi- and the heterozygous groups a significant increase of alpha-galactosidase activity was demonstrated.

Lack or minimal activity of alpha-galactosidase (AG), which belongs to the group of lysosomal enzymes of serum, is a commonly known genetic feature of Fabry's disease with X-linked heredity [5]. The gene site of AG is located on the long arm of the X-chromosome (X_q 22–24) [9]. The elevated serum level of lysosomal enzymes is indicative of membrane destruction [8].

An attempt has been made to establish whether in Duchenne-type muscular dystrophy (DMD), AG was suitable to characterize the homo- and heterozygous condition of the disease.

Materials and Methods

AG activity was studied in the sera of 15 hemizygous 5–18-year-old children and 8 gene carrier mothers of families suffering from DMD as well as in 21 children free from genetically determined myopathy, using the fluorimetric method with 4-methyl-umbelliferyl-beta-D-galactopyranoside (Koch–Light Ltd.) as substrate [4].

Enzyme activity is expressed in nmol/ml/h according to the quantity of decomposed substrate. The creatine kinase (CK) level of the DMD patients and their gene carrier mothers is shown in Table I. The clinical severity of DMD was marked with 2–4 points. Two points indicated the patients who had no noticeable difficulty of gait except when walking uphill; those marked with three points had serious difficulty in walking, and those marked with 4 points were unable to walk. We calculated the correlation coefficient between AG activity and CK activity as well as between the degree of clinical severity and the AG level in the group of hemizygotes with DMD and the gene carriers.

Results

Table I shows the AG level of the control group, that of the DMD patients (hemizygotes), and that of the gene carriers with DMD. The value of serum AG activity was 3.21 nmol/ml/h in the control group; in the group of hemizygotes with DMD the mean activity was 9.99 nmol/ml/h significantly higher than in the control group. The AG level of DMD patients, compared with the degree of clinical severity showed a statistically significant positive correlation. At

TABLE I

Alpha-galactosidase values of DMD patients, DMD gene carriers and controls

Case No.	DMD patients		
	Degree of clinical severity	AG nmol/ml/h	CK mU/ml
1	3	11.9	132
2	2	5.8	756
3	2	8.0	280
4	2	8.3	178
5	3	14.1	74
6	4	11.9	1000
7	4	7.9	300
8	3	9.3	78
9	3	8.9	340
10	3	6.1	1000
11	3	7.6	158
12	2	3.9	3160
13	3	7.7	1530
14	4	22.6	95
15	4	16.9	268

Mean: 9.99
S.D.: ±4.71
$p = 0.0001$
Correlation coefficient between clinical severity and AG: 0.64
$p = 0.0089$
Correlation coefficient between AG and CK: −0.46
$p = 0.08$

the same time, AG activity and CK activity showed a nearly significant correlation in the DMD patients. AG activity of the DMD gene carriers was also significantly increased in comparison with the control group, but 50% of the cases examined showed an overlap; in the remaining 50% a marked increase could be observed.

In the heterozygotes, the CK and AG activities failed to show a significant correlation.

DISCUSSION

Dennis et al. [2] discussed the use of CK for detecting severe X-linked muscular dystrophy carriers. Nicholson et al. [7] investigated the effect of age on carrier-detection rates with CK: the detection rate with a standard CK assay was 53%, in the daughters of known carriers it was 45% after correction for age. A much higher detection rate, about 90% may be obtained in young carriers and thus seems to be suitable for differentiation between carriers and non-carriers.

There is evidence that in carriers of the relatively benign type of X-linked muscular dystrophy the serum CK level decreases with age [11]. This may also be true, though to a lesser extent, in carriers of DMD [6].

Table 1 (continued)

Case No.	DMD gene carriers	
	AG nmol/ml/h	CK mU/ml
1	4.0	223
2	25.5	15
3	7.9	228
4	15.7	40
5	17.4	149
6	5.8	59
7	6.2	56
8	7.2	5.9

Mean: 11.21
S.D. ±7.52
Correlation coefficient between AG and CK: −0.42
$p = 0.29$
Controls (n=21)
AG, nmol/ml/h
Mean: 3.21
S.D.: ±1.64

Information on the serum CK level of the normal daughters of a consultand might be helpful in counselling [10]. A modification was given of the original density function formula of Emery and Morton for estimating heterozygosity in X-linked DMD [3] which takes into account the CK level in the normal sisters and normal daughters of a suspected carrier in families where there is only one affected male.

As in the literature available we have found no report on AG activity examination in DMD patients, the present report seems to be the first to demonstrate the significant increase in AG activity in the serum of hemizygotes and of possible gene carriers for DMD.

Although a negative correlation was found between CK and AG activity, at the same time the AG activity corresponds better to the degree of clinical severity; there seems to be a positive correlation between them.

It is well-known that the serum CK activity is increased in not more than two thirds of the gene carriers. Thus genetic guidance is difficult since one third of the carriers cannot be detected. Still, investigation of the AG activity may provide further clues concerning the gene carriers.

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