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Linkage analysis of families with severe childhood autosomal recessive muscular dystrophy in Morocco indicates genetic homogeneity of the disease in North Africa

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Abstract

It has been previously shown in Tunisian and Algerian families that the locus for SCARMD maps to the proximal part of 13q, and in Algerian families that the disease is associated with deficiency of the 50 kDa dystrophin associated glycoprotein (50DAG). We have tested this linkage in six families from Morocco where this disease is also prevalent. In one family the 50DAG was tested and found to be negative in a muscle biopsy. Our results showed similar linkage in this country, with statistical tests indicating genetic homogeneity between the three Maghreb countries.

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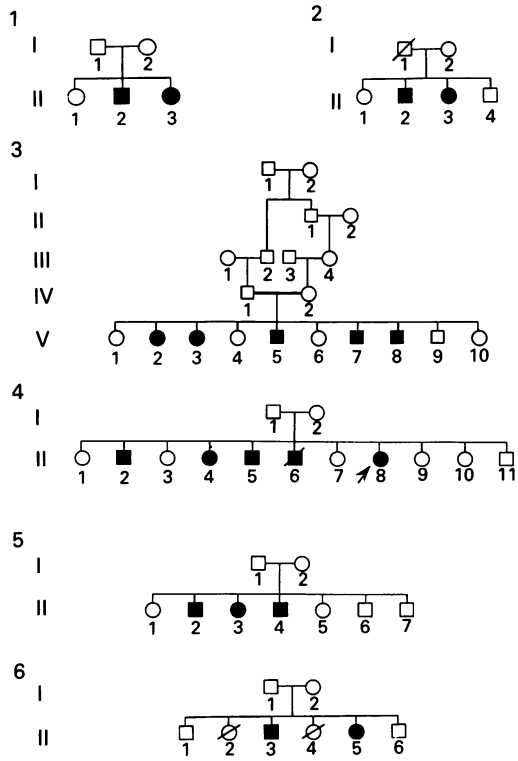
Severe childhood muscular dystrophy (SCARMD) is a Duchenne-like form of progressive muscular dystrophy affecting both sexes, first described by Ben Hamida and Fardeau in Tunisia.[1,2] This autosomal recessive disease (MIM 253700) is prevalent in Tunisia and Algeria[3,4] where it may be as frequent as Duchenne/Becker myopathies. The gene responsible has not yet been identified, but it was recently shown that: (1) in muscle specimens from Algerian patients the sarcolemmal 50 kDA dystrophin associated glycoprotein (50DAG) is absent whereas dystrophin and the other dystrophin associated proteins are normally present[5]; (2) the SCARMD locus maps to 13q12 by linkage analysis, as shown first in three Tunisian families[3] and confirmed in 13 Algerian families.[6]

Like Tunisia and Algeria, Morocco belongs to the Maghreb, a geographical region of north west Africa characterised by a common Arabo-Berberic population with a high frequency of inbreeding. Therefore SCARMD would also be expected to be prevalent in Morocco. Indeed, Duchenne-like families with affected girls are quite frequent in this country (M Yahyaoui, personal communication).

In the present study we have selected for linkage analysis six well characterised families from Morocco, comprising 18 patients (10 males and eight females) (figure). They were selected on the following obligate criteria: (1) a clinical and pathological pattern typical of SCARMD[1,2]; (2) multiplex families with at least one female affected. In addition the diagnosis was further validated by finding 50DAG deficiency by immunofluorescence analysis of one muscle specimen[5,7,8] (patient 8 of family 4, figure). The SCARMD families were genotyped using the following microsatellite markers assigned to the proximal long arm of chromosome 13: D13S221 (AFM 248wcl)[9] D13S175 (AFM2 49xbl),[9] and D13S115,[10] as described in Azibi *et al.*[6]

The cumulated two point lod scores[11] obtained with the three markers in the six families and a comparison with the data obtained in 13 families from Algeria[6] are shown in the table. A search for genetic heterogeneity among the cumulated 19 SCARMD families was carried out with the HOMOG program (version 3.31[12]) on the three sets of lod score values. No evidence for heterogeneity was found for informative families (data not shown).

The homogeneity of our linkage data in Morocco compared to those previously



Pedigrees of six families with SCARMD. Arrow indicates patient in whom 50DAG was investigated.

Cumulated lod scores in the six families with SCARMD

	θ								
Marker	*0·000*	*0·001*	*0·01*	*0·05*	*0·1*	*0·15*	*0·20*	*0·30*	*0·40*
D13S175									
Morocco*	$-\infty$	− 7·03	−3·03	−0·39	0·50	0·81	0·89	0·64	0·23
Algeria†	$-\infty$	− 9·87	−4·60	0·25	2·00	2·49	2·43	1·59	0·56
Cumulated	$-\infty$	−16·90	−7·63	−0·14	2·50	3·30	3·32	2·23	0·79
D13S221									
Morocco*	$-\infty$	− 5·31	−1·35	1·15	1·85	1·96	1·82	1·15	0·37
Algeria†	$-\infty$	− 8·85	−2·98	1·43	2·64	2·78	2·51	1·56	0·61
Cumulated	$-\infty$	−14·16	−4·33	2·58	4·49	4·74	4·33	2·71	0·98
D13S115									
Morocco*	$-\infty$	− 5·54	−0·63	2·36	3·08	3·10	2·83	1·79	0·60
Algeria†	$-\infty$	− 4·85	−1·34	1·60	2·45	2·49	2·21	1·37	0·58
Cumulated	$-\infty$	−10·39	−1·97	3·96	5·53	5·59	5·04	3·16	1·18

* This study.
† 13 families of Azibi *et al.*[6]

obtained in Tunisia and Algeria suggests that SCARMD may be the result of the same defective gene and possibly the same mutation in all three Maghreb countries. This is not surprising because of the common origin of these populations. It would be interesting to determine whether the same locus is involved in SCARMD outside North Africa,[13–15] and ultimately to define whether the 50DAG defect is primary or secondary to the gene defect.

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