A SILENT ALLELE OF PROPERDIN FACTOR B POLYMORPHISM (BF*QO) IN FIVE FAMILY MEMBERS:

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Introduction

Only three families with an apparently silent allele of the properdin factor B polymorphism (BF*QO) have been described until now (1-3). We found another family with altogether five BF*QO carriers during a disputed paternity case by a seemingly inverse homozygosity of the BF alleles S and F between mother and child (4).

Material and Methods

BF typing was performed by thin layer agarose gel electrophoresis and immunofixation with BF-specific antisera (5) (Atlantic Antibodies) and in addition by a hemolytic overlay after isoelectric focussing of BF allotypes (6). Factor B protein concentration was measured by radial immunodiffusion, functional levels of factor B by radial diffusion hemolysis (7). HLA-A,B,C,DR typing was performed by the standard lymphocytotoxicity technique (8). C2,C4 and GLO typing was done as previously discribed (9-11).

Results

The apparent inverse homozygosity of BF alleles S and F between mother (II-4) and child (III-2) is clearly demonstrated in Fig. 1 and could also be shown by the hemolytic overlay after isoelectric focussing of BF allotypes.

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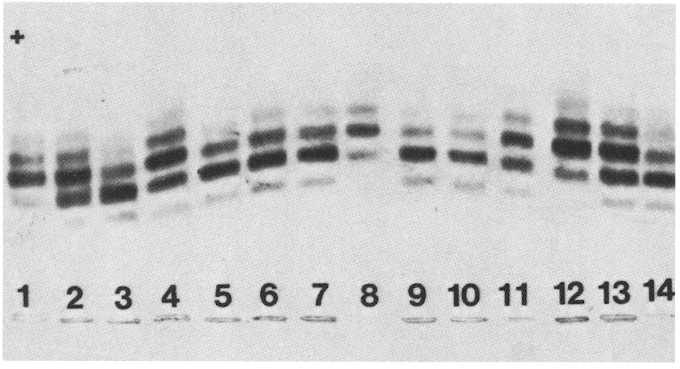

Fig.1 BF phenotypes after agarose gel electrophoresis and specific immunofixation: 1=control BF FF, 2=control BF FS, 3=control BF SS, 4=grandmother I-2, BF FS, 5=brother II-2, BF S(QO), 6=sister II-3, BF SS, 7=sister II-1, BF S(QO), 8=son III-2, BF F(QO), 9=son III-1, BF S(QO), 10=mother II-4, BF S(QO), 11=father II-5, BF FS, 12=control BF FF, 13=control BF FS, 14=control BF SS

In the pedigree of this family, given in Fig.2, heterozygous factor B deficient individuals are indicated by half black symbols. Haplotypes of the MHC region are marked by letters a,b,c,d,e,f. The given order of MHC loci is HLA-A, HLA-C, HLA-B, C4A, C4B, Bf, C2, HLA-DR, GLO.

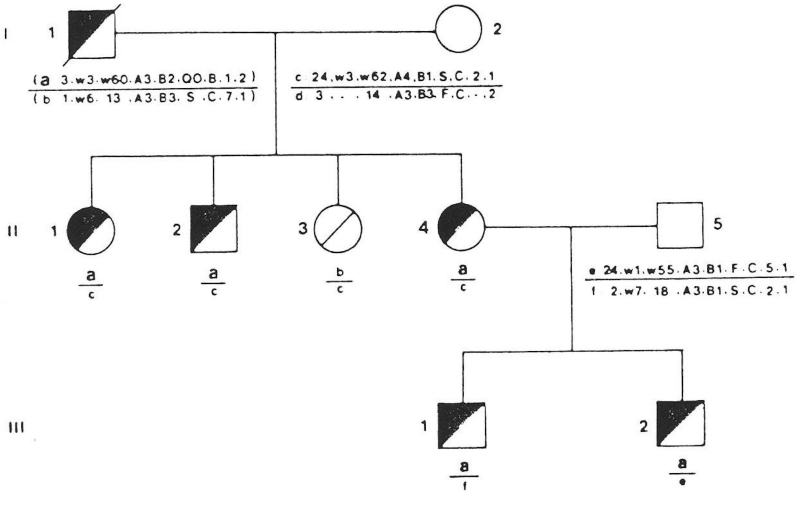

Fig.2 Pedigree of the family with five BF*QO carriers

The BF*QO allele is carried by haplotype a. As shown in the pedigree the silent BF allele came from the deceased grandfather (I-1) and existed in altogether five individuals (II-1, II-2, II-4, III-1, III-2).

Immunochemical levels of factor B protein and factor B hemolytic activity (relative and absolute) are given in Table 1.

Table 1. Immunochemical and functional levels of factor B

Family member	BF-type	Factor B protein (mg/l)[a]	Factor B hemolytic activity	
			relative (U/mg)	absolute (U/l)
I-2	FS	113.7	1.218	138.5
II-1	SQO	68.6	1.914	131.3
II-2	SQO	97.5	1.222	119.1
II-3	S	126.5	1.095	138.5
II-4	SQO	85.3	1.581	134.9
II-5	FS	115.7	1.067	123.4
III-1	SQO	80.9	1.570	127.0
III-2	FQO	68.1	1.435	97.7

[a] Normal range 170–420 mg/l

While the protein level was markedly decreased in the five BF*QO carriers, the absolute hemolytic activity of factor B was normal in four out of them. Obviously the lack of an expressed BF gene is compensated by the functionally normal BF*S of BF*F allele on the other chromosome. This compensating effect is documented by the relative increase of hemolytic activity in the heterozygous BF deficient individuals.

An association of BF*QO with special alleles of other MHC loci, as described for rare alleles of the BF system (12), does not seem to exist (Table 2).

Table 2. BF*QO MHC haplotypes

Loci									Reference
HLA-A	HLA-C	HLA-B	C4A	C4B	BF	C2	HLA-DR	GLO	
3	n.t.	7	n.t.	n.t.	QO	n.t.	n.t.	2	Weidinger et al. (1979)
2	w3	15	n.t.	n.t.	QO	B	4	1	Suciu-Foca et al. (1980)
w24	w1	w54	3	6	QO	C	w8	2	Tokunaga et al. (1984)
3	w3	w60	3	2	QO	B	1	2	This study

n.t. = not tested

It is of interest, however, that BF*QO may possibly be associated with rarer alleles of the C4B locus (C4B*2, C4B*6) and the C2 locus (C2*B).

Since among numerous cases of single or combined complement component deficiencies complete factor B deficiency has not

been reported, nonexpression of B obviously acts as a lethal factor. All hemizygous deficient individuals of this family were apparently healthy. Thus BF heterozygous deficiency seems to be without any disease risk.

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