Distribution of C3 and BF Phenotypes in HIV-seropositive Patients

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SUMMARY

The paper reports on the distribution of C3 (Complement Factor 3) and Bf (Properdin Factor B) in serum samples from HIV-seropositive patients. The gene frequencies of the C3-system are similar to those in healthy persons. In the Bf-system we found unusual features of distribution. Problems of interpretation are discussed.

INTRODUCTION

In 1987 *Eales* et al. reported on a strong association between AIDS and the GC-system (D-binding protein). They suggested that individuals with the GC*1F subtype were at greater risk of HIV-infection and to develope AIDS. It was also suggested that the homozygous type GC*2 may render a relative protection. In the meantime several reports did not confirm these observations.
However, *Eales*'s report 'has created considerable concern'. Examining plasma protein polymorphism seems to be useful. In principle studies on genetic polymorphism gain further importance in connection with a possible correlation between genetic markers and various diseases and the resulting selective advantages.
In this pilot study we investigated the distribution of C3 (β_{1C}-globulin, 3rd component of human Complement) and BF (glycine-rich beta-glycoprotein, C3 proactivator, Properdin factor B) phenotypes in a sample of 86 HIV-seropositive patients.

MATERIALS & METHODS

Blood samples were taken from 86 patients treated in the Institute of Blood Coagulation and Transfusion Medicine at the *Heinrich-Heine*-University. For this pilot study we restricted us to only one marker: HIV-seropositive. Therefore the collective included individuals that were HIV-seropositive only, patients with ARC (AIDS related complex), with AIDS and with *Kaposi*- sarcoma.
We compared this group with other spot checks. The BF-control group contained 500 obviously healthy persons.

RESULTS AND DISCUSSION

C3 system Since *Wieme* and *Demaulenaere* , *Alper* and *Propp* and *Azen* and

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Smithies demonstrated a genetically determined polymorphism of the third component of Complement by using technics of agarose and starch gel electrophoresis, numerous investigations have been reported. Most of them were based on population genetics - additional on differences between Caucasians and coloured people. Hereditery defiency states of one and another of the Complement components have been documented in experimental animals and man.
Especially C3 and its conversion products (β_{1A}-globulin etc.) were examined in detail. Emphasis is placed on the fact that the Complement cascade can be triggered not only by activation of the components C1 etc. but also by activating C3 by an alternative pathway. *Whitehead* et al. and *Teisberg* et al. reported assignement of the gene for C3 to chromosome 19. The physiological function of the Complement reactions contains cell lysis, neutraliztion and lysis of virus. Therefore this study of genetic markers in HIV-seropositive individuals includes the C3 system, the Complement component with the highest serum level in man.
In a total of 86 HIV-seropositive patients we observed 3 known C3 alleles: C3*S, C3*F and C3*S^{06}. Our results of C3 phenotypes provide a satisfactory correlation to the *Hardy-Weinberg*-equilibrium. Small differences between the observed and the expected values may be due to the small number in the collective. We found the following gene frequencies (calculated by gene counting): C3*S .814, C3*F .180 and C3*Var .0060.
The results seem to be in accordance with the results obtained by other authors in Germany.
Therefore we conclude that this pilot study results in a normal distribution of C3 phenotypes in HIV-seropositive persons. Because of the small number in the collective and the restriction to only one marker (HIV-seropositive) this examination will be extended to cover the reported results.
If one sees AIDS to have originated in Africa one would expect, if an association can be assumed, a high frequency of C3*S. If one excludes the possibility of a gene drift our study does not demonstrate an association between AIDS and the distribution of the C3 system.

BF system BF - also known as C3 proactivator, C3 PA, factor B, glycine-rich glycoprotein, GBG - as one of the major participants in alternative pathway of Complement activation is coded by an locus on chromosome 6. The BF locus is closely linked to the major histocompatibility complex and it is placed between HLA-B and HLA-D. Because of this linkage the BF marker is suitable for use in the study of association between genetic susceptibility and diseases. *Bertrams* et al. described association between BF and Insulin-dependent diabetes mellitus. A possible linkage between BF and SLE (systemic lupus erythematodes) as examined by *Klemp* et al. could not be proved. *Papiha* et al. found a striking association between a special BF allele and glomerulonephritis.
However, the glycoprotein BF (mol.w. 90.000) is known as an acute phase reactant during acute inflammatory episodes.
The genetic polymorphism of the BF system was first described by *Alper* et al.. There are two common alleles BF*F and BF*S, two less common alleles BF*F_1 and BF*S_1, and rarer alleles.

Table 1 DISTRIBUTION OF BF-PHENOTYPES IN HIV-SEROPOSITIVE PATIENTS

	observed		*expected*	
Phenotype	*n*	*%*	*n*	*%*
S	53	61,63	46.15	53.66
F	11	12.79	4.65	5.41
FS	16	18.61	29.31	34.08
FVar*	2	2.32	1.40	1.63
SVar	4	4.65	4.40	5.12
Var	0	0	0.11	0.10
total**	86	100	86	100

*The following values contain variants including F1 and S1 (S 07)
**values rounded up

Table 2 DISTRIBUTION OF PHENOTYPES IN THE BF-SYSTEM CONTROL GROUP

	observed		*expected*	
Phenotype	*n*	*%*	*n*	*%*
S	100	62.50	99.23	62.02
F	7	4.38	6.60	4.13
FS	50	31.25	51.18	31.99
FVar*	1	0.62	0.61	0.38
SVar	2	1.24	2.37	1.48
Var	0	0	0.01	0.01
total	160	100**	160	100

*The following values contain variants including F1 and S1 (S 07)
**values rounded up

Gene frequences: F .1840, S .7980, Var .0180

The BF allele gene frequencies are different in distinct ethnic groups. The gene frequence of BF*F is significantly higher in Negroes than in Whites. Therefore and because of its physiological role in inflammatory processes and linkage to the HLA system it seemed to be meaningful to check fora hypothetical association between the BF system and HIV infection.
We examined a sample of 86 HIV-seropositive patients. The distribution for the BF system found in this collective is shown in table 1. Surprisingly we found no satisfying agreement between the observed and the expected numbers of phenotypes. Meanwhile the nonconfirming of the S type may be due to the small number of the collective. The nonagreement of the homocygous F type and the heterocygous BF*FS regarding to the expected numbers of cases is statistical significant. Comparing with a control group of obviously healthy individuals resulted in confirmation. The gene frequencies found in this group are similar to those reported by other authors on German collectives. An increasing gene frequency of BF*F in a southerly direction can be noted.

In our opinion caution is advised in interpretation of the results. Nevertheless the results are interesting because of the strong linkage between BF and the HLA system. Also frequencies in Negroes may be recalled.
One specific mark of our HIV-seropositive group - patients have been treated with 'autovaccination' - couldn't - in our opinion - influence the results. Other marks like homosexuality etc. must be itemized in further studies.
We are extending our investigations into more patients with the aim to create sufficient subgroups including different stages of disease. Nonetheless this paper reports the preliminary results because it might be impossible for only one research group to examine enough patients for definite decision on association or non-association.

REFERENCES

See: Huckenbeck W, Bonte W, Kuntz BME, Brüster HTH (1989) *Plasmaprotein-Polymorphismen bei HIV-seropositiven Probanden: GC- und TF*C-Subtypen, PI-, C3- und BF-System*
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