Distribution of Adenosine Deaminase (EC 3.5.4.4) Phenotypes in a Series of HIV-Seropositive Patients

W. Huckenbeck, B. Jacob, B.M.E. Kuntz, H.T. Brüster

Institute of Legal Medicine, Heinrich-Heine-University Düsseldorf,FRG*

INTRODUCTION

Adenosine deaminase (ADA) takes its role in physiological pathway in deamination of adenosine to inosine. The enzyme was found in human erythrocytes and tissues. Three common phenotypes - ADA*1, ADA*2-1, ADA*2 - can be separated by electrophoresis. Rarer alleles (ADA^0, ADA^3, ADA^4, ADA^5, ADA^6) have also been described. The ADA* polymorphism is coded by chromosome 20. This enzyme seems to be of interest for immunology, too. The homocygous ADA0 type is associated with the SCID syndrome (severe combined immune defiency) (8,9). Several authors reported on increased ADA levels in HIV-infected patients (1,2,3,4,7,13, 14).

MATERIAL & METHODS

Blood samples were taken from 226 HIV-seropositive patients treated in the Institute of Blood Coagulation and Transfusions Medicine at the Heinrich-Heine-University. This series thus includes individuals that were only HIV-seropositive, patients with ARC (AIDS related complex), with full blown AIDS and with Kaposi-sarcoma. We compared this group with obviously healthy persons spot checked otherwise..
Electrophoresis was carried out on Cellogel electrophoresis membranes using electrophoresis buffer Biotest (dilution 1:10): 250 Volt, 15 mA, 50 min. Staining was performed with 15mg Adenosine, 5 mg MTT, 5 mg PMS, 25 µl nucleoside and 25 µl xanthine oxidase.

RESULTS & DISCUSSION

The ADA system takes a role in immunological reactions. The silent ADA gene ADA 0 is associated with the SCID syndrome. Several authors reported increased ADA levels in HIV-infected patients (1,2,3,4,7,13,14). For this study we examined the distribution of the ADA*phenotypes in a series of 226 HIV-infected persons. The distribution found is shown in table 1. We observed only the common three phenotypes ADA*1, ADA*2-1 and ADA*2. The results provide a satisfactory correlation to the Hardy-Weinberg-equilibrium
(Chi2: $0.045<3.841;df=1;\alpha=0.05$).
In table 2 the results of other studies on ADA*polymorphism in Germany are listed. Small differences between the gene frequencies may be due to the small volume and to the heterogeneity of the HIV-group - large clinical catchment area.
The differences are not significant and there is no association between the ADA*system and HIV-infection detectable.

* and Institute of Blood Coagulation and Transfusion Medicine

Advances in Forensic Haemogenetics 4
Edited by Ch. Rittner and P. M. Schneider

TAB.1 ADA-PHENOTYPES IN HIV-SEROPOSITIVE PATIENTS

Phenotype	observed		expected	
	n	%	n*	%*
1-1	195	86.28	194.21	85.93
2-1	29	12.83	30.63	13.55
2-2	2	0.89	1.21	0.54
total	226	100	226	100

* values rounded up

gene frequencies: ADA1 : 0.9269 ; ADA2 : 0.0731

TAB.2 OTHER STUDIES ON ADA-POLYMORPHISM IN GERMANY

Country	ADA*1	ADA*2	n	Reference
Lower Rhine region	0.9447	0.0553	262	Scheil et al.
Düsseldorf region	0.9366	0.0634	500	Scheil et al.
South Western	0.9238	0.0762	302	Tariwerdian et al.
Hamburg	0.9355	0.0645	861	Goedde et al.
Hessen	0.9499	0.0501	579	Renninger et al.
Berlin	0.9420	0.0580	500	Lefevre and Niebuhr
This study	0.9269	0.0731	226	

REFERENCES

1) Casoli, C., Magnani, G., Barbuti, S., Barchi, E.(1989) Erythrocyte Adenosine Deaminase (ADA) Expression in AZT-treated Aids Patients.Abstract, V. International Conference on AIDS, June 4-9, Montreal
2) Clotet, B., Sirera, G., Pastor, C., Romeu, J., Tural, C., Jou, A., Foz, M.(1989)Adenosine Deaminase (ADA) Values in Cerebrospinal Fluid of Asymptomatic HIV Infected Patients.Abstract, V. International Conference on AIDS, June 4-9, Montreal
3) Eto, K., Tsuboi, I, Saneyoshi, Y., Yoshioka, H., Yokoyama, M.M.(1989)Adenosine Deaminase (ADA) Levels in Tears of AIDS Patients and AIDS Carriers.Abstract, V. International Conference on AIDS, June 4-9, Montreal
4) Ferrazzi, M., De Rinaldis, M.L., Pezzella, M., Caprilli, F., Bozzi, A., Strom, R.(1989)Determination of Erythrocyte Adenosine Deaminase Activity in Anti-HIV Seronegative Homosexual Men with Latent HIV Infection.Abstract, V. International Conference on AIDS, June 4-9, Montreal
5) Goedde, H., Benkmann, H.G., Christ, I., Singh, S., Hirth, L.(1970)Gene frequencies of red cell adenosine deaminase, adenylate kinase, phosphoglucomutase, acid phosphatase and serum a1-antitrypsin (Pi) in a German population.Humangenetik 10: 235-243
6) Levevre, H., Niebuhr, R.(1970)Polymorphismus der Adenosindesaminase. Untersuchung an einer Stichprobe aus der Berliner Bevölkerung.Humangenetik 10: 88-90
7) Palomba, E., David, O., Gabiano, C., Tovo, P.A.(1989)Increased ADA Activity in Children with Perinatal HIV Infection.Abstract, V. International Conference on AIDS, June 4-9, Montreal
8) Prokop, O., Göhler, W.(1986)Die menschlichen Blutgruppen Gustav Fischer Verlag Jena

9) Spielmann, W., Kühnl, P.(1982)Blutgruppenkunde.Georg Thieme Verlag Stuttgart New York
10) Renninger, W., Bimboese, C.(1970)Zur Genetik der Erythrocyten-Adenosin-Desaminase.Humangenetik 9: 34-37
11) Scheil, H.G., Fiedler, K.P., Huckenbeck, W.(1991) Untersuchungen zur Phänotypen-Häufigkeit einiger hämogenetischer Polymorphismen am Niederrhein (Bereich Kleve, Goch, Kalkar).
Anthrop. Anz. 1/2: 137-144
12) Tariwerdian , G., Ritter, H.(1969)Population genetics of adenosine deaminase (EC:3.5.4.4): gene frequencies in Southwestern Germany.Humangenetik 7: 179
13) Valls, V., Ena, J., Figueredo, I., Roca, V. De Salamanca R.E.(1989)Adenosine Deaminase (ADA) Levels in Sera of Patients with HIV-1 Infection.Abstract, V. International Conference on AIDS, June 4-9, Montreal
14) Yokoyama, M.M., Tsuboi, I.(1989)Adenosine Deaminase in Retrovirus Infected Diseases.Abstract, V. International Conference on AIDS, June 4-9, Montreal