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On Recent Observations in the Rhesus Blood Group System

I. A Weak Expression of the Rh Antigen e
II. Finding of the Rare Rh Antigen C^x

Jürgen Henke and Marianne Basler

Institut für Rechtsmedizin der Universität Düsseldorf, Moorenstraße 5, D-4000 Düsseldorf, Federal Republic of Germany

Summary. Upon testing blood samples for medico-legal purpose, an exceptionally weak expression of the Rhesus antigen e was observed. There is evidence for the phenotype Rh_2ŕh which is rather unusual in white people. Apart from this, the low incidence antigen C^x has been found in two cases. Its mode of reaction with anti-C and anti-c sera is described.

Key words: Blood groups, e antigen, C^x – Rhesus system, weak e antigen, C^x

Zusammenfassung: Im Rahmen von blutgruppenserologischen Abstammungsbegutachtungen wurde eine sehr schwache Ausprägung des Rhesus-Antigens e beobachtet. Es wird vermutet, daß es sich hierbei um den im europiden Rassenkreis extrem seltenen Phänotyp Rh_2ŕh handelt. Daneben wurde in zwei weiteren Fällen das Rhesus-Antigen C^x gefunden. Seine Reaktionsweise mit Anti-C und Anti-c wird beschrieben.

Schlüsselwörter: Blutgruppen, e-Antigen, C^x – Rhesus-System, schwach ausgeprägtes e-Antigen, C^x

Introduction

This paper aims at giving a brief report on a weak expression of the Rhesus antigen e and on further occurrences of the Rh antigen C^x.

I. e-Problem

Material and Methods

The individual displaying a weak expression of the Rh antigen e is an alleged father (Mr. Ack.) who is white. Particularly interesting observations have been made by using the following antisera:

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Anti-e, conglutinating (Behring-Werke AG, 013417 B)
Anti-e, conglutinating (Dr. Molter GmbH, 2863)
Anti-e, conglutinating (Biotest, 111020)
Anti-e, agglutinating (Biotest, 143010)
Anti-hr^B, Bast., contributed by Dr. Shapiro
Anti-hr^S, Motaung, contributed by Dr. Shapiro

Results and Discussion

Testing the red blood cell antigens of Mr. Ack., the following results were obtained: 0, MSs, ccD.E(e), C^w-, K−k+,Fy(a−b+), Jk(a+b−), Lu(a−b+), Co(b−), P_1+. The tables summarize our further typing results:

Table 1

Cells	Dilutions (aggl. anti-e serum)					
	1:1	1:2	1:4	1:8	1:16	1:32
Ack.	3	1	0	0	0	0
R_2r-control	4	3	3	1	(1)	0
Cells	Dilutions (congl. anti-e sera)					
	1:1	1:2	1:4	1:8	1:16	1:32
Ack.	2	0	0	0	0	0
R_2r-control	4	3	1	0	0	0

Table 2

Further reactions with selected sera[a]	
Anti-C^x (Thom.)	:0
Anti-hr^B (Bast.)	:0
Anti-hr^S (Motaung)	:3
Anti-LW (contrib. by Sh. Bush)	:2
Anti-Tar. (contrib. by Canadian RC)	:0
Anti-En[a]	:4

[a] 4 = 100% agglutination; 0 = no agglutination

Dr. Tippett (London) was consulted. She confirmed our results and kindly added the following findings: V−, VS−, Be(a−), Go(a−), Evans−, $\overline{\overline{R}}^N-$, G+.

Dr. Tippett's as well as our investigations revealed, that the e antigen of the proband, Mr. Ack., is weaker than that of control R_2r cells, as judged by some anti-e sera.

The question arose whether we were dealing with an e^i. Since we were not familiar with the mode of reaction of e^i cells, Dr. Tippett was consulted. She

concluded, that Mr. Ack. had not e^i, "since he had much more e antigen than such people" (pers. comm.). Examiners have to be aware of the fact, "that cde^i behaved as cD– with most anti-e sera" [6].

Attention should be drawn to the result that Mr. Ack.'s cells reacted as e(+), hr^S+, hr^B–! There is little doubt that, like antigen D, antigen e represents a mosaic structure [3]. There is also evidence that the mosaic structure of e is much more complex in Negroes than in white people. In several cases, antibodies reacting with all e-positive (but no e-negative) red cells from white people have been found in the sera of e-positive black people.

Because both anti-hr^S and anti-hr^B were reported by Dr. Shapiro [8, 9] we must describe these antigens and the antibodies that define them in Dr. Wiener's terminology preferred by Dr. Shapiro.

Race and Sanger look on hr^S as a variant of e [6]. (Unfortunately, the superscript s was used for both e^S and hr^S in publications that came out almost at the same time, but e^S and hr^S describe different things.) Anti-hr^S was reported in 1961. It was formed by a Bantu woman (Mrs. Shabalala) whose red cells are hr″+, hr^S– [8].

Anti-hr^B was reported under similar circumstances. Shapiro et al. [9] described this antibody which defines (like anti-hr^S) another "blood factor" associated with hr″.

E or e can sometimes be replaced by the alternate antigen E^w [1, 3, 4]. Examples of a weak expression of the E antigen, perhaps due to the lack of the factor E^T, had been reported by Sanger et al. [7] and by Nijenhuis [5].

The antigens hr^S and hr^B seem to be controlled from the E/e locus, but are obviously not replacements of e [3]. Thus far, at least, e-positive bloods from Caucasians are hr^S+, hr^B+, while E+,e– bloods are hr^S–, hr^B–. Therefore, we would hazard the guess, that it seems to be quite possible, that the reported weakness of the e antigen could be attributed to the lack of the hr^B factor.

Following his discovery of hr^S and hr^B, Shapiro [8, 9] introduced some new symbols for Rh nomenclature. Since most genes that produce hr″ also produce hr^S and hr^B they continue to be described as R^0, r, R^1, etc. Genes that produce hr″ but not hr^B are identified by a dot over the top of the gene symbol. Thus, we assume that the phenotype of Mr. Ack's cells is to be described as $Rh_2\dot{r}h$ ($R_2\dot{r}$).

II. C^x-Problem

Material and Methods

The involved individuals are of German origin. One of them (Mr. Abr.) is living in the Düsseldorf area, the others in Lower Saxony. Testing Mr. Abr.'s red blood cells with anti-Jk^b sera (Fresenius, 2618; Serco, 1.31078; Biotest, 112060) strongly positive reactions were observed with the first two sera already after 5 min of incubation in a saline suspension! The bloods of the other probands were contributed by Mrs. Kneiphoff (Dipl. Biol.) who observed similar unusual reactions. The serum anti-C^x (Thom.) was kindly contributed by Dr. Bruce Chown and Marion Lewis, Winnipeg (Ontario, Canada).

Results and Discussion

Testing the red blood cell antigens of the alleged father, Mr. Abr. the following results were obtained:
0, Ms, P_1-, R_1R_1, K-k+, Fy(a−b+), Jk(a+b+), Lu(a−), Co(b−).

Apart from this, we observed unusual strongly positive reactions when using the commercially available anti-Jk^b sera 2618 and 1.31078. Further tests revealed that these sera even reacted in saline suspension with Mr. Abr.'s erythrocytes. It is evident that these sera contain a very strong complete antibody against a "low incidence" antigen.

Cells and sera were sent to Dr. Tippett to obtain further information. She and Carole Green were able to solve the problem by testing the cells against a battery of antisera to private antigens. Mr. Abr.'s cells were found to be C^x-positive! Another C^x sample was also agglutinated by the anti-Jk^b, thus it looked as though anti-C^x was the extra-antibody.

A few days later, red blood cells from probands being involved in a paternity case were sent to us by our collegue Mrs. Kneiphoff (Rotenburg/W.). The cells of both the child and the alleged father gave extraordinary strongly positive reactions with anti-Jk^b (2618). The results of our additional typings are given below:

Reactions with	Cells of		
	Child	Mother	Lover
Anti-Jk^b (112060) ind. Coombs-Test	3	3	0
Anti-Jk^b (2618; 1.31078) NaCl; 5′ inc.; R.T.	4	0	4

Reactions with	Control		Cells of		
	rr	R_1r	Child	Mother	Lover
Anti-C^x (Thom.) NaCl; 30′ inc. 37° C	0	0	2	0	3

The typings reveal that instead of being CcD.ee, the cells of the child and those of the alleged father are both C^xcD.ee!

In this case, a false typing of the lover's Kidd-phenotype did not happen, because of the lucky incident that the two specificities in the anti-Jk^b reagent reacted obviously different. The titer of the anti-C^x in both anti-Jk^b sera (deriving evidently from the same source) is 1:64 in a saline suspension.

It can also be learnt from our observations that C^x blood (if tested with anti-C and anti-c sera) may give the reactions expected of Cc blood. The antigen C^x was found in four of 3,931 individuals [6].

Rare variants or deviations within the Rhesus blood group system are suggested to exist in an amount of about 0.3% [10]. The cases described above are indeed rarities, but they illustrate situations for which the blood grouper ought to be continually on the alert. As can be learnt from the literature, as well as from these cases, one should not hesitate to consult a specialist in cases presenting uncertain results [2].

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Addendum

In the meantime, we observed a further family with C^xDe. The reactions with anti-C and anti-$\bar{c}$ sera were also in the usual CDe-manner!