Development of Anti-G, Anti-C and Anti-Jk(b) in a 22-Year-Old Mother during Her Fourth Pregnancy

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Keywords
Anti-G · Pregnancy · Antibodies · HDN

Summary
Background: Anti-G antibodies are rarely found since anti-D, in combination with anti-C, are difficult to discriminate from anti-G antibodies in routine testing. Case Report: A 22-year-old, gravida-3, para-1, woman with blood group A Rh D neg ccddee and known antibody anti-Jk(b), gave birth to her second child. While anti-Jk(b) could not be detected at birth, a new anti-C was found. Antibody screening tests (IAT) were performed using gel cards and rare G positive rGr erythrocytes. Genotyping for RHD and RHCE was performed using PCR-SSP. Results: The child’s blood group was A Rh D neg Ccddee. Genotyping revealed Cde/cde haplotypes. The erythrocytes of the new-born showed a positive direct antiglobulin test with IgG; anti-D and anti-C could be eluted. Erythrocytes with the rare phenotype rGr were reactive with the serum of the mother. Conclusion: The presence of anti-D and anti-C in the eluate from new-born’s Ccddee erythrocytes proved anti-G or anti-G in combination with anti-D. When anti-C and anti-D are seen during a pregnancy, possibly anti-G is present. This observation is of relevance since women with anti-G can still develop anti-D and require rhesus prophylaxis.

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Introduction
The rhesus G antigen (Rh12) is encoded within the RHD and RHCE genes, more precisely, within the latter in the C encoding gene. G is not expressed when serine is replaced by proline on position 103 of either protein, as characterized by Faas et al. [1, 2]. Rhesus G was first described in 1958 by Allen and Tippett [3]. The authors found that erythrocytes bearing the C and/or D antigen exhibit the G antigen. It was also discovered that erythrocytes that do not carry either antigen usually do not express the G antigen. Expression of G is at maximum when both D and C antigens are present [4]. In accordance to the frequency of C and D antigens, G is present in 84% of all Caucasians. Anti-D and anti-C as well as anti-G antibodies have been reported in pregnancies of Rh D neg (ccddee) women and can also lead to severe haemolytic disease of the new-born (HDN) [5–10]. Additional clinical relevance can arise when rhesus prophylaxis is not administered such as in case that anti-G is erroneously considered to be anti-C in combination with anti-D [10]. However, all of these women are still able to form anti-D.

Material and Methods
Rhesus antigens Ccddee were determined using Mono-Type® monoclonal antibodies in tube test with two different clones (Medion-Grifols, Langen, Germany). The clones are anti-C: MS-24, MS-273, anti-c: MS-33, MS-35; anti-E: MS-258, MS-12, and anti-e: MS-62, MS-16/MS-21. Indirect antiglobulin test (IAT) and direct antiglobulin test (DAT) were performed in a gel card system ID System® (DiaMed-Diagnostika, Munich, Germany). Elution was performed using chloroform technique. Anti-G was confirmed using G-expressing erythrocytes with the rare phenotype rGr. Rh genotyping was performed using a commercial PCR-SSP system (RBC READY GENE CDE®-SSP, Inno-Train Diagnostik GmbH, Kronberg/Ts., Germany).

Case Report
A 22-year-old gravida-3, para-1, woman with blood group A Rh D neg ccddee and known anti-jk(b) was monitored for antibody titre before giving birth to her second child. During her third pregnancy in 2008 anti-D
Conclusion

Anti-D and anti-C are frequent antibodies. In a recent Danish study, anti-D accounted for 46% of all pregnancy-related antibodies and anti-C for no more than 1%. However, of all 122 multiple cases with antibody combinations, the majority (52, i.e., 43%) accounted for a combination of anti-D and anti-C [11]. Both are known to cause severe HDN [12, 13]. Since both antibodies often occur in combination, identification of an anti-G that comprises both epitopes on the D and C antigen is often unrecognised [5, 7, 10]. Even combinations of anti-C and anti-G, in the absence of anti-D, are found to cause severe HDN [8, 9]. However, little data exists on the presence of anti-G on its own during pregnancies [6]. This antibody is rarely diagnosed and may occur more often in pregnancies due to the high frequency of C and D in the population. However, women that present anti-G antibodies can develop additional anti-D. An accurate differentiation between anti-C plus anti-D and anti-G is of high importance in pregnancies. When anti-D is absent, rhesus prophylaxis must be administered.

Disclosure Statement

The authors declare no conflict of interest.
References


