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Case report
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RESOLVING BLOOD GROUP DISCREPANCY IN A PATIENT WITH ACUTE MYELOID LEUKEMIA – A CASE REPORT

PREVAZILAŽENJE SMETNJI KOD ODREĐIVANJA KRVNE GRUPE U SLUČAJU BOLESNIKA SA AKUTNOM MIJELOIDNOM LEUKEMIJOM – PRIKAZ SLUČAJA

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Summary

Introduction. The ABO blood group antigens are determined by genes located at three separate genetic loci. Loss or weakening of ABO antigens is often associated with hematological malignant diseases, but also solid tumors in the body. A change in the expression of ABO antigens leads to discrepancies when determining the patient's blood group and carries the risk of incompatible transfusions. **Case Report**. During the blood typing of a 27-year-old female patient with a diagnosis of acute myeloid leukemia, there were discrepancies in the interpretation of the ABO blood group. Since the confirmation blood group indicated that it was blood group O, when determining the reverse blood group, the reading showed the absence of the expected agglutination of group A_1 and B red blood cells. By examination of the patient's records, as well as confirmation genotyping, the blood group A was established. After the patient entered the remission phase of the disease, the A Rhesus D positive blood group was determined, without discrepancies during testing. **Conclusion.** Changes in blood groups can occur even before the diagnosis of hematological malignant disease is established. For this reason, it is extremely important to thoroughly examine any discrepancy during blood typing in order to provide patients with safe blood.

Key words: Leukemia, Myeloid, Acute; ABO Blood-Group System; Rh-Hr Blood-Group System; Risk Factors; Blood Grouping and Crossmatching; Blood Group Antigens

Sažetak

Uvod. Antigeni ABO krvnogrupnog sistema determinisani su genima smeštenim na tri nezavisna lokusa. Gubitak ili slabljenje ekspresije ABO antigena često je povezan sa hematološkim malignim bolestima ali i solidnim tumorima u organizmu. Promena ekspresije ABO antigena dovodi do smetnji prilikom određivanja krvne grupe pacijenta i nosi rizik od inkopatibilnih transfuzija. **Prikaz slučaja.** Tokom određivanja krvne grupe pacijentkinji staroj 27 godina, sa dijagnozom akutne mijeloidne leukemije, pojavile su se smetnje u interpretaciji ABO krvne grupe. S obzirom da je konfirmaciona krvna grupa ukazivala da se radi o O krvnoj grupi, prilikom određivanja reverzne krvne grupe očitavanje je pokazalo izostanak očekivane aglutinacije sa test-eritrocitima A_1 i B. Uvidom u dosije pacijentkinje, kao i potvrdnom genotipizacijom, ustanovljena je A krvna grupa. Nakon što je pacijentkinja ušla u remisionu fazu bolesti, određena joj je A krvna grupa, bez neusaglašenosti prilikom testiranja. **Zaključak.** Promene krvne grupe mogu da se dogode i pre nego što je uspostavljena dijagnoza hematološke maligne bolesti. Zato je izuzetno važno da se svaka neusaglašenost prilikom određivanja krvne grupe temeljno ispita kako bi se pacijentima obezbedila bezbedna krv.

Ključne reči: akutna mijeloidna leukemija; ABO krvno grupni sistem; Rh krvno grupni sistem; faktori rizika; krvne grupe i ukrštanje; krvnogrupni antigeni

Introduction

The ABO blood group system was the first and most important human blood group system to be discovered that uses red blood cells (RBCs) and has the greatest clinical significance. The determination of ABO blood groups is the most significant test in transfusion medicine, since ABO incompatible transfusions carry the risk of inducing hemolytic transfusion reactions with potentially fatal outcomes in the recipients.

The ABO antigens are carbohydrates by their biochemical composition and are inherited as Mendelian characteristics in a codominant autosomal fashion. Three groups of genes are responsible for the formation of ABO blood group antigens: ABO, fucosyltransferase gene 1 (FUT1) and fucosyltransferase gene 2 (FUT2) [1]. The ABO genes are located on the chromosome 9 (9q34.1-q34.2), they consist of seven exons and introns, and encode specific glycosyltransferase enzymes (GTs) that attach different monosaccharides to the H substance (H antigen): N-acetyl-D-galactosamine which determines the blood group A and D-galactose which determines the blood group B [1, 2]. The FUT1, located on the chromosome 19q13.3, encodes α1,2-fucosyltransferase that catalyzes the final step in the synthesis of the H antigen (H/h, H/H), and the gene FUT2 ("secretor" gene), located in the same locus, indirectly encodes a soluble form of the H antigen (Se/se, Se/Se) which is found in bodily secretions [2, 3].

In the serum of all healthy adults with A, B and O blood groups, anti-A and/or anti-B antibodies are found almost inevitably. These antibodies are often called

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Abbreviations

ABO – ABO blood group system
RhD – Rhesus D
RBC – red blood cell
FUT – fucosyltransferase gene
GTs – glycosyltransferase enzymes
Ig – immunoglobulin
AL – acute leukemia
AML – acute myeloid leukemia

"natural" and their creation starts around the third month after contact with bacteria and viruses in the bowels that are chemically similar to A and B antigens [4]. In persons with A and B blood groups, these antibodies are primarily class M immunoglobulin (Ig), although small amounts of class G Ig are present. In persons with blood group O, the dominant class of antibodies is IgG.

The RBC antigens are hereditary characteristics and, as such, their expression is constant throughout the life of an individual. Blood type can change due to bone marrow transplant or as a result of certain types of cancers and infections. An acquired change in ABO antigen is often expressed as an acquired "B" antigen, which occurs due to the enzymatic modification of normal A_1 into an antigen similar to the B antigen, caused by bacteria, e.g. Escherichia coli, Clostridium tertium, Proteus vulgaris and Bacteroides fragilis [3]. It also appears in connection with the pathology of the gastrointestinal tract, e.g. intestinal malignancies, obstruction or severe infection/sepsis. The bacteria produce an enzyme that chemically modifies N-acetyl-D-galactosamine to D-galactosamine [3, 5]. Since the terminal sugar of the "B" antigen is galactose, the anti-B antibody will cross-react with the B-like D-galactosamine antigen. The condition is transient and resolves when the infection is cured and poses no transfusion risk other than creating a mismatch in ABO typing. Changes can also occur during malignant diseases of hematopoietic tissue. According to the literature data, changes in antigen characteristics of RBCs most often occur in acute leukemia (AL) which is characterized by clonal proliferation, accumulation of abnormal cells in the bone marrow and insufficient hematopoiesis [5].

Anemia and inclination towards bleeding and infections, conditioned by pancytopenia, are the most significant manifestations of AL [6]. Patients often need blood transfusions and blood components. The problem occurs when transfusion must be postponed because irregularities and discrepancies occur during the determination of the patient's blood group.

We are therefore describing a case of a change in the ABO antigen during an acute leukemic phase in a patient with acute myeloid leukemia (AML), in whom, after remission of the underlying disease, a recurrence of ABO antigen expression occurred.

Case Report

Due to the need for administering blood components, determination of the ABO/Rhesus (RhD) blood group type was performed in a female 27-year-old patient with the diagnosis of AML. The serological testing was performed by gel agglutination using an automated immunohematological analyzer (Diaclon ABO/D+ reverse grouping, BioRad, DiaMed-ID Micro Typing System, IH-1000). The reverse gel card showed the following results of the serum and RBCs test: anti-A negative, anti-B negative, anti-D positive, with erythrocytes A_1 negative, with erythrocytes B positive, so the result could not be interpreted due to the lack of expected agglutination. The confirmation gel card with monoclonal antibodies showed anti-A negative, anti-B negative, anti-D positive from which it could be concluded that the blood group is O RhD positive. After checking the patient's medical file, it was determined that the patient was A RhD positive.

Before new tests were performed, the possibilities of technical errors (incorrect identification of the sample/documentation, incorrect marking, incorrect results entered in the operation protocol/information system, machine/reagent errors, reading/interpretation errors) were eliminated.

After receiving a new sample, determination of the blood group was performed using the test-tube technique, where the same results were obtained. Antibody screening by using the technique of gel agglutination (ID-DiaCell Pool, IH-1000, Bio Rad) was negative. The direct antiglobulin test and auto-control were also negative. After completing the serological processing of the sample, genotyping based on the polymerase chain reaction was performed using a sequence specific primer RBC Ready Gene ABO kit (Inno-Train Diagnostik GmbH, Kronberg, Germany). By genotyping, it was confirmed that it was blood group A.

After the patient had completed the therapy and entered remission of the disease, the blood group testing was repeated. There were no discrepancies during the remission phase in determining the blood group, it was confirmed that it was an A RhD positive patient.

Discussion

Changes in RBC antigen expression are associated with malignancies, when ABO blood group antigens are most often subject to change. Van der Hart et al. described these changes in ABH antigens in malignant hematopoietic tissue diseases back in 1962, describing a very weak expression of B antigens in patients with leukemia that had normal antigen expression before the aforementioned disease [7]. As in our case, after the therapy was completed, when the disease entered the remission phase, the strength of antigen expression was restored. There are no written data in Serbia on the change of blood group in patients suffering from leukemia (except for the changes that occur during bone marrow transplantation). There have been occasional case reports in world literature about ABO blood group antigen change in malignant conditions.

Nambiar et al. reported two cases of blood group change, where one patient, 14 years of age, with an AML diagnosis, resolved the problem of determining

the blood group after successful therapy [8]. Sarwer Jahan et al. described the case of a patient who was diagnosed with AML on admission, and due to a case of anemia, after determining the blood group, received a transfusion of the blood group O. After the therapy of the underlying disease was discontinued, the blood group A was determined. The blood group A was confirmed by multiple testing and the patient continued receiving blood products of the corresponding blood group [9].

The loss of antigen expression in hematological diseases is mainly the result of mutations which affect the production of antigens in the stem cells. Therefore, in the erythrocyte progenitor arising from the changed stem cell, a complete or partial loss of antigen expression occurs. In contrast, erythrocytes that are created by stem cells which are not affected by these changes have a normal expression of erythrocyte antigens [10, 11].

It is considered that there are two mechanisms which cause changes in antigen expression. The first mechanism is the inactivation of the A and/or B transferase, which leads to the inhibition of attaching immunodominant sugar to the H antigen. At the same time, decrease in the expression of the A and B antigens occurs increasing the H antigen, because it is not converting into the A and B antigen. The literature describes that such a change in AML can be the consequence of translocation between 9 and 22 (Philadelphia) chromosomes. The gene that encodes A and B transferases is located on chromosome 9q34 [7, 12, 13].

The second mechanism is the inactivation of H transferase (coded on chromosome 19q13) that inhibits addition of L-fucose to the precursor oligosaccharide chain. Inactivation of H transferase leads to a decrease in H substance and consequently the reduction of A and B substances [14].

In many cases, loss or weakened expression of ABO antigen is associated with hematological malignant diseases, often as the first sign that points to the existence of a malignancy. Likewise, the results that indicate the return to normal expression of ABO antigen indicate a favorable treatment outcome. Antigen loss can also be seen in cancers of organs such as the stomach, colon, ovary, pancreas [15]. Unlike changes that are happening in hematological diseases, here tumors secrete large amounts of soluble A and/or B substance which neutralize the reagents for blood typing. This problem can be overcome by erythrocyte washing before determining the blood group to remove plasma that contains a soluble substance of the blood type [16].

Deviations revealed when determining the reverse and confirmation blood group must be recorded and resolved because otherwise they may lead to problems related to transfusion of blood components.

Conclusion

Changes in blood groups are rare and most often associated with hematological malignancies, although this may also occur in patients with tumors of solid organs. Changes can also happen before the diagnosis of the underlying disease is established. For this reason, it is extremely important that any discrepancy in determining the blood group is thoroughly examined to prevent transfusion of blood components of an inadequate blood type.

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