Case Report

Combined Group I and III ABO Discrepancies in Multiple Myeloma with IgG-Lambda Type: A Case Report

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Abstract

Objective: To report a case with unusual ABO discrepancies caused by coexistence of the loss of anti-B isoagglutinin and rouleau formation. Clinical Presentation and Intervention: A 79-year-old female diagnosed as having multiple myeloma (MM) with monoclonal IgG-λ type showed rouleau formation in peripheral blood smear. The ABO and Rh blood type before the diagnosis of MM was A+, but the following ABO grouping was interpreted as AB+. The ABO genotype revealed the subtypes A102 and O101, which confirmed her ABO phenotype as A+. Conclusion: This was a case of combined group I and III ABO discrepancies mimicking blood group AB.

Introduction

The ABO blood group is the most important blood type system in human blood transfusion, which exists as 4 allelic forms of AB, A, B, and O. Notwithstanding the modern laboratory technologies and reagents developed, ABO discrepancies still occur, which means the unexpected pattern of antigen on the cell and the opposite antibody in the serum. ABO discrepancies may be arbitrarily divided into 4 major categories: briefly, group I is associated with unexpected reactions in the reverse typing due to weakly reacting or missing antibodies, whereas group II is associated with unexpected reactions in the forward typing due to weakly reacting or missing antigens. Group III is caused by protein or plasma abnormalities and results from rouleau formation or pseudoagglutination. Finally, group IV is due to miscellaneous problems such as polyagglutination [1, 2]. The purpose of this report was to describe a case with unusual ABO discrepancies caused by coexistence of the loss of anti-B isoagglutinin and the rouleau formation in a patient diagnosed as multiple myeloma (MM) with monoclonal gammopathy of the IgG-λ type.

Case Report

A 79-year-old female with type 2 diabetes mellitus was admitted to Daejeon St. Mary’s Hospital for the evaluation of right-sided chest pain with no associated injuries. Contrast-enhanced computed tomography revealed multiple fractures at the right 4th to 10th ribs. In the peripheral blood smear, rouleau formation was promi-
nent. Laboratory findings showed white blood cell count of 8,500/mm³, hemoglobin of 6.7 g/dl, platelet count of 142,000/mm³, IgG of 6,648 mg/dl, IgA of 90 mg/dl, IgM of 20.4 mg/dl, κ light chain of 48.26 mg/l (serum, reference 3.3–19.4) and 138.36 mg/l (urine, 0–32.71), λ light chain of 1,259 mg/l (serum, 5.71–26.30) and 1,195.40 mg/l (urine, 0–4.99), blood urea nitrogen of 101.4 mg/dl, and creatinine of 3.62 mg/dl. Serum and urine immunofixation showed monoclonal gammopathy of the IgG-λ type reflecting an abnormal albumin-to-globulin ratio. Patient red blood cells (RBCs) were evaluated for reactivity of the forward typing with Novaclone anti-A and anti-B murine monoclonal reagents (Dominion Biologicals Ltd., Dartmouth, N.S., Canada) and of the reverse typing with Affirmagen A1 and B RBC cell reagents (Ortho Clinical Diagnostics, Pencoed, UK). The ABO and Rh blood type before the diagnosis of MM had been A+ in previous medical records, but the following ABO grouping showed A+ in red cells but not anti-B in serum by a conventional tube test. A repeated ABO test by the microtube column agglutination technique using the Diamed-ID LISS/Coombs gel card containing anti-IgG and anti-C3d within the gel matrix (DiaMed GmbH, Cressier, Switzerland) was interpreted as AB+ (the forward type: A cell 4+, B cell 2+; the reverse type: ab-). The washing technique rids the RBC membranes of the paraproteins and frees the RBCs in the case of rouleau formation in the reverse grouping. In true agglutination, red cells will continue to clump after washing with normal saline [3].

Meanwhile, group I ABO discrepancies can also occur when patients have depressed antibody production or cannot produce the ABO antibodies. Weak agglutination reactions may be obtained with reagent RBC cells and are a result of weak expression of anti-A and anti-B in the serum. Group I ABO discrepancy should be suspected because RBC and serum grouping reactions are normally very strong. IgM is the predominant isotype found in blood group A or B individuals, although small quantities of IgG antibody can be detected. In blood group O serum IgG is the major isotype for anti-A and anti-B [2]. Therefore, the severe deficiency of IgM would be responsible for group I ABO discrepancies in MM with blood group A or B [2].

### Discussion

This was a case of combined group I and III ABO discrepancy caused by coexistence of the loss of anti-B isoagglutinin and the rouleau formation in MM with monoclonal gammopathy of the IgG-λ type. Several Korean cases had been reported with MM [3, 4] or with other diseases [5–8] about group I ABO discrepancies due to the loss of isoagglutinins only (table 1). An ABO incompatibility reaction such as acute hemolytic reaction or fatal complication can occur in our patient if she receives the wrong type of AB+ RBC transfusion instead of true type A+.

M protein produced by MM cells is a common cause of group III ABO discrepancies resulting from elevated levels of globulin. Abnormally elevated paraproteins cause the rouleau formation which is stacks or aggregations of RBCs due to reduction in ‘zeta potential’ (charge on RBC membrane) [2]. It could be mistaken for agglutination by medical technicians in the forward grouping. The washing technique rids the RBC membranes of the paraproteins and frees the RBCs in the case of rouleau formation in the reverse grouping. In true agglutination, red cells will continue to clump after washing with normal saline [3].

| Sex/age | Diagnosis | ABO discrepancy (forward/reverse) | Discrepancy cause | Discrepancy category | ABO genotype | IgG, mg/dl | IgA, mg/dl | IgM, mg/dl | Ref. |
|---------|-----------|----------------------------------|-------------------|----------------------|--------------|------------|------------|------------|------|
| F/79    | MM with IgG (λ) | A/A → AB/AB | Loss of anti-B and rouleau formation | Groups I and III | ABO* A/O | 6,648 | 90 | 20.4 | This study |
| F/56    | MM with IgG (κ) | A/AB | Loss of anti-B | Group I | n.d. | 4,970 | <29.9 | <26.4 | 3 |
| F/60    | MM with λ | B/AB | Loss of anti-A | Group I | n.d. | 382.8 | <28.5 | <29 | 3 |
| M/52    | MM with IgG (λ) | B/AB | Loss of anti-A | Group I | n.d. | 5,243 | <28.5 | <29 | 3 |
| F/78    | MM with IgA (κ) | B/AB | Loss of anti-A | Group I | ABO* B/O | 236 | 4,430 | <20 | 4 |
| F/13    | Idiopathic agammaglobulinemia | B/AB | Loss of anti-A | Group I | n.d. | <33.3 | <6.7 | <4.2 | 5 |
| F/30    | Gallbladder abscess | O/B | Loss of anti-B | Group I | ABO* O/O | 39 | 46 | <5 | 6 |
| F/55    | Liver cancer | O/B | Loss of anti-B | Group I | ABO* O/O | 63 | 65 | 12 | 6 |
| M/20    | Common variable immunodeficiency | O/B | Loss of anti-B | Group I | ABO* O/O | 104 | <13 | <15 | 7 |
| M/16    | Acute osteomyelitis | O/B | Loss of anti-B | Group I | ABO* O/O | 770 | 244 | 13.5 | 8 |

*MM = Multiple myeloma; n.d. = not done.*

DOI: 10.1159/000450579

Table 1. Laboratory findings of our patient and reported cases showing ABO discrepancy in literature review

### Notes

- ABO is the major isotype for anti-A and anti-B
- Weak agglutination reactions may be obtained with reagent RBC cells and are a result of weak expression of anti-A and anti-B in the serum
- Group I ABO discrepancy should be suspected because RBC and serum grouping reactions are normally very strong
- IgM is the predominant isotype found in blood group A or B individuals, although small quantities of IgG antibody can be detected
- In blood group O serum IgG is the major isotype for anti-A and anti-B
- Therefore, the severe deficiency of IgM would be responsible for group I ABO discrepancies in MM with blood group A or B

**ABO Discrepancies in Multiple Myeloma**

Med Princ Pract 2017;26:90–92
Recently, Kaur et al. [9] reported that a few (0.06%, 28/44,425) blood group discrepancies were observed in 44,425 blood groups. Among them, 20 subgroups of A and B were a main sample-related problem of ABO discrepancies. In order to resolve the ABO discrepancy and to provide compatible blood for transfusion, it is necessary to obtain relevant historical information from the patient and to provide medical and technical expertise as well as education for the blood bank technologist in transfusion medicine-related testing, practice, risks, and related areas [2]. ABO genotyping can also be done with a high level of accuracy for the resolution of ABO serological discrepancies [10].

**Conclusion**

This was a case of combined group I and III ABO discrepancies mimicking blood group AB in MM with monoclonal IgG-λ type. ABO genotyping was very useful to resolve this unusual ABO discrepancy.

**Disclosure Statement**

There is no conflict of interest.

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