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Rare ABO Discrepancy in Multiple Myeloma: An Immunohematologic Challenge with Critical Transfusion Implications : Case report

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Case Report

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Abstract

INTRODUCTION:

Multiple myeloma is a malignant hematologic disorder characterized by clonal proliferation of plasma cells, leading to excessive production of monoclonal protein and humoral immunodeficiency due to decreased normal immunoglobulins. This condition may interfere with ABO blood grouping and result in discrepancies between forward (cellular) and reverse (serum) typing. We report a rare case of ABO discrepancy identified during a pre-transfusion workup in a patient with light-chain multiple myeloma. This case underscores the importance of integrating clinical and immunohematologic data to accurately interpret blood grouping anomalies and ensure transfusion safety.

CASE PRESENTATION:

A 61-year-old man, followed for kappa light-chain multiple myeloma, presented with symptomatic anemia requiring blood transfusion.

ABO and RhD typing showed: Anti-A (−), Anti-B (−), Anti-D (+), control (−), A cells (+), B cells (−).

DISCUSSION:

This profile is consistent with blood group A associated with a deficiency of isoagglutinins, without alteration of the erythrocyte phenotype, corresponding to a type I ABO discrepancy related to severe hypogammaglobulinemia secondary to multiple myeloma. Any discrepancy between forward and reverse typing indicates an anomaly classified into four types: weak or missing antibodies (group I), weak antigens (group II), protein abnormalities with rouleaux formation or pseudoagglutination (group III), or miscellaneous causes (group IV). Type III discrepancies, frequently observed in multiple myeloma, result from excess paraproteins promoting rouleaux formation. In the presence of an ABO discrepancy, testing should be repeated after red cell washing and, if necessary, confirmed on a new sample.

CONCLUSION:

A rigorous serological approach, based on clinical data and close clinicobiological collaboration, generally allows resolution of ABO discrepancies—particularly in multiple myeloma—and ensures transfusion safety.

INTRODUCTION

Multiple myeloma (MM) is a malignant plasma cell disorder characterized by clonal proliferation within the bone marrow, resulting in excessive production of monoclonal paraprotein (M protein), bone destruction, and suppression of other hematopoietic cell lines. MM accounts for approximately 10% of hematologic malignancies and predominantly affects adults, with a median age at diagnosis of 60 years (1). The disease is generally progressive and presents with end-organ damage summarized by the CRAB

acronym: hypercalcemia, renal insufficiency, and anemia (2). Light chain multiple myeloma (LCMM) is a less common subtype of MM, characterized by a more aggressive clinical course and poorer prognosis. It is defined by the inability of malignant plasma cells to produce heavy chains, resulting in exclusive production of free light chains (3).

From an immunohematologic perspective, MM is associated with excessive M protein production and decreased synthesis of normal polyclonal immunoglobulins. This immune dysregulation may manifest as an ABO discrepancy, defined as a lack of concordance between forward (cellular) grouping and reverse (serum) grouping—two complementary tests that serve as internal validation of one another (4).

We report the case of a patient with MM in whom pre-transfusion testing, including blood typing and antibody screening, revealed a discrepancy between forward and reverse ABO grouping. This case underscores the importance of integrating clinical and immunohematologic data to accurately interpret blood grouping anomalies and ensure transfusion safety.

CASE PRESENTATION

A 61-year-old man with a known diagnosis of light chain multiple myeloma (LCMM) was under regular clinical follow-up, with no notable personal or family medical history. Serum protein electrophoresis demonstrated profound hypogammaglobulinemia at 1.8 g/L (Figure I). Serum immunofixation revealed a monoclonal band corresponding to kappa light chains (Figure II). Additionally, Bence Jones protein analysis identified a monoclonal band consisting of free kappa light chains. Quantitative immunoglobulin testing showed marked suppression of all three immunoglobulin classes (IgG, IgA, and IgM), confirming severe humoral immunodeficiency.

Figure I: Serum protein electrophoresis demonstrating profound hypogammaglobulinemia.

Serum protein electrophoresis showing profound hypogammaglobulinemia, indicative of impaired polyclonal immunoglobulin synthesis due to clonal plasma cell proliferation.

Figure II: Serum immunofixation showing a monoclonal kappa light chain band.

Serum immunofixation identifying a monoclonal kappa light chain, supporting the diagnosis of light chain multiple myeloma and underlying humoral immune dysregulation.

Due to severe anemia, blood transfusion was indicated. A blood sample was sent for ABO typing, which was performed using both the slide agglutination method and the gel card method (DiaClon, BioRad, Switzerland).

Forward grouping demonstrated agglutination with anti-A and no reaction with anti-B, confirming the presence of antigen A and absence of antigen B, consistent with a group A phenotype. However, reverse grouping showed no agglutination with either A cells (absence of anti-A, as expected) or B cells, indicating the absence of detectable anti-B antibodies (Figure III). Since individuals of blood group A are

expected to possess anti-B isoagglutinins, this finding revealed a Group I ABO discrepancy, characterized by weak or missing antibodies.

Figure III: ABO discrepancy on gel card testing showing discordance between forward and reverse grouping.

Gel card ABO typing demonstrating a discrepancy between forward (group A) and reverse grouping, characterized by absence of anti-B isoagglutinins, consistent with a Group I ABO discrepancy in the setting of hypogammaglobulinemia.

DISCUSSION

ABO blood grouping is fundamental in transfusion medicine. Forward and reverse typing constitute complementary tests that allow cross-verification of results. ABO discrepancies arise when forward grouping does not concord with reverse grouping (5).

ABO discrepancies are classified into four groups (6):

- **Group I**: Weak or missing antibodies (reverse grouping abnormality)
- **Group II**: Weak or missing antigens (forward grouping abnormality)
- **Group III**: Plasma protein abnormalities causing rouleaux formation or pseudoagglutination
- **Group IV**: Miscellaneous causes such as warm or cold autoantibodies, cold alloantibodies, or Bombay phenotype

In our patient, the serological profile is consistent with blood group A associated with a deficiency of isoagglutinins secondary to decreased production of normal polyclonal immunoglobulins. This does not represent a modification of the erythrocyte phenotype, but rather an absence of circulating natural anti-B antibodies. This situation corresponds to a group I discrepancy, related to a marked immunoglobulin deficiency—particularly IgM—commonly observed in the setting of hypogammaglobulinemia, especially in malignant hematologic disorders such as multiple myeloma (MM), as well as in elderly individuals (7).

Group II discrepancies are characterized by weak or mixed-field reactions in forward grouping with strong reverse grouping reactions (2). Group III discrepancies are the most frequently reported in MM. Elevated paraproteins—whether intact immunoglobulins or free light chains—reduce the red blood cell zeta potential (the electrostatic force maintaining erythrocyte separation under physiological conditions), leading to rouleaux formation and false-positive reactions in reverse grouping (1, 2, 3, 6).

Arumugam et al. reported that 4% of ABO discrepancies were Group III and emphasized that the tube method is more effective than gel column techniques for resolving rouleaux. Group III discrepancies may also occur in Hodgkin lymphoma, cord blood samples, or following administration of plasma expanders such as dextran or polyvinylpyrrolidone (8). Pseudoagglutination due to rouleaux may be misinterpreted as true agglutination by inexperienced personnel. Resolution requires repeated saline washing of red

blood cells to remove membrane-bound proteins and disperse rouleaux. In contrast to pseudoagglutination, true agglutination persists after saline washing (9).

When an ABO discrepancy is identified, testing should first be repeated on the same sample after red cell washing. If the discrepancy persists, a new sample should be obtained. In most cases, careful serologic evaluation resolves the discrepancy without the need for advanced testing (8).

This case underscores the importance of integrating clinical context and associated disease states in the interpretation of ABO discrepancies, which should be systematically investigated (10).

A limitation of our study is the absence of the use of proteolytic enzymes such as papain or bromelain, which could have helped detect very low concentrations of agglutinating antibodies in the patient's serum. These enzymes reduce the zeta potential by cleaving erythrocyte membrane glycoproteins, thereby decreasing the surface electrical charge and promoting closer interaction between antigens and antibodies. This process enhances the sensitivity of hemagglutination reactions by facilitating antigen–antibody binding on the red cell surface.

CONCLUSION

Multiple myeloma can interfere with ABO blood grouping, requiring rigorous typing methods and an adapted transfusion strategy. Any ABO discrepancy warrants careful evaluation, including integration of clinical data, repeat testing after saline washing, and a clear understanding of the underlying immunohematologic mechanisms. Increased vigilance by immunohematology laboratory personnel is essential to prevent misinterpretation and avoid potentially life-threatening transfusion errors. This case emphasizes the importance of correlating clinical and laboratory findings to ensure accurate interpretation of blood group discrepancies and transfusion safety.

PATIENT PERSPECTIVE

The patient reported being informed of his diagnosis of light chain multiple myeloma and the need for regular follow-up and transfusion support. He demonstrated an understanding of the chronic nature of the disease and the importance of close laboratory monitoring to ensure transfusion safety. The transfusion was well tolerated, with no adverse events reported. He also expressed reassurance after being informed of the ABO discrepancy and the measures taken to ensure compatible blood transfusion. He remained adherent to follow-up and expressed confidence in the overall management plan.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the institutional ethics committee.

Consent to publish

Written informed consent was obtained from the patient for participation in this study.

Data availability

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

H.F. wrote the main manuscript text. Y.B. and A.C. prepared the figures and tables. M.S. supervised the work and critically revised the manuscript. H.F., Y.B., M.S., A.C., F.O., J.E.B., and A.B. contributed to the study conception and design. All authors reviewed and approved the final manuscript.

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Figures

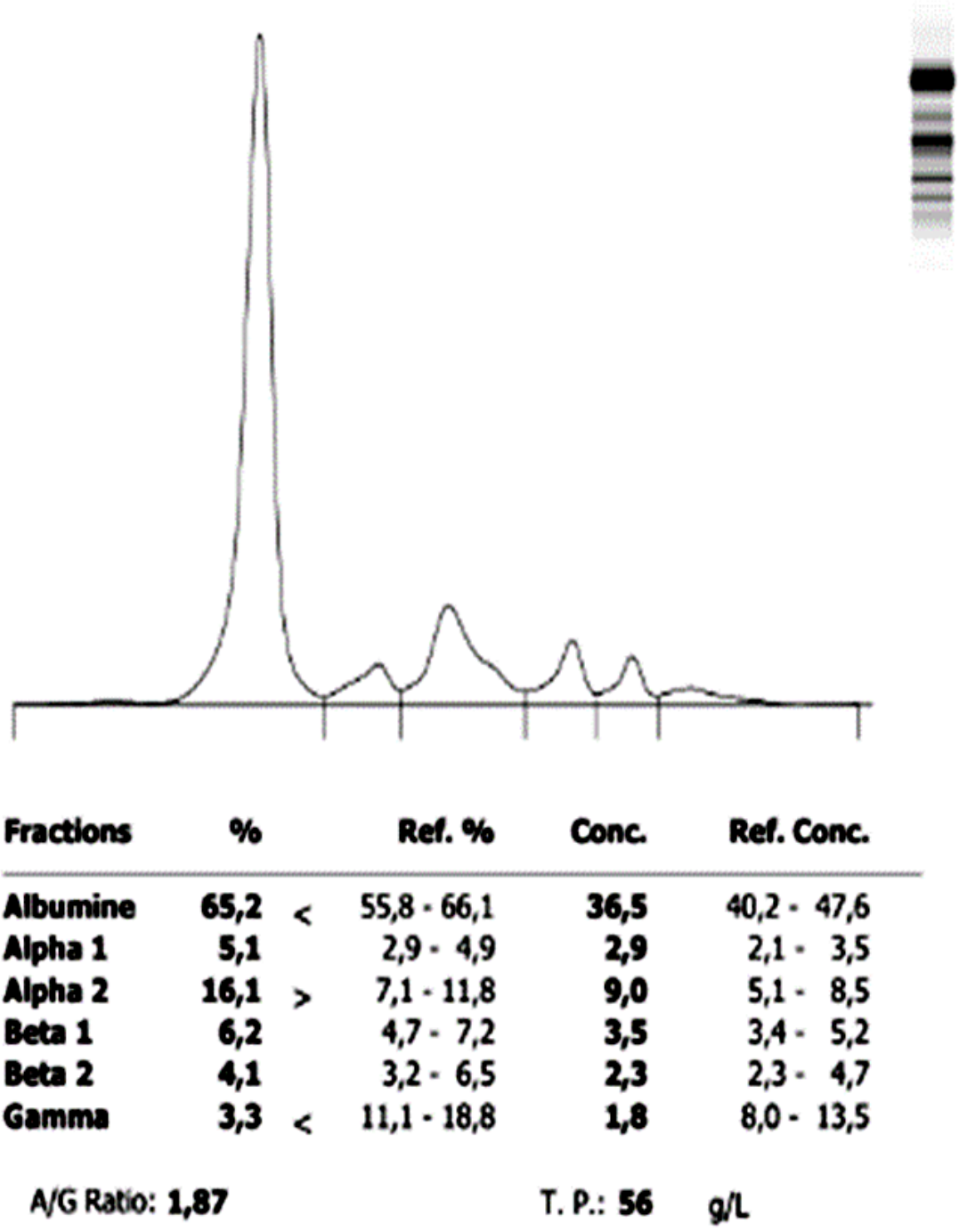


Figure 1

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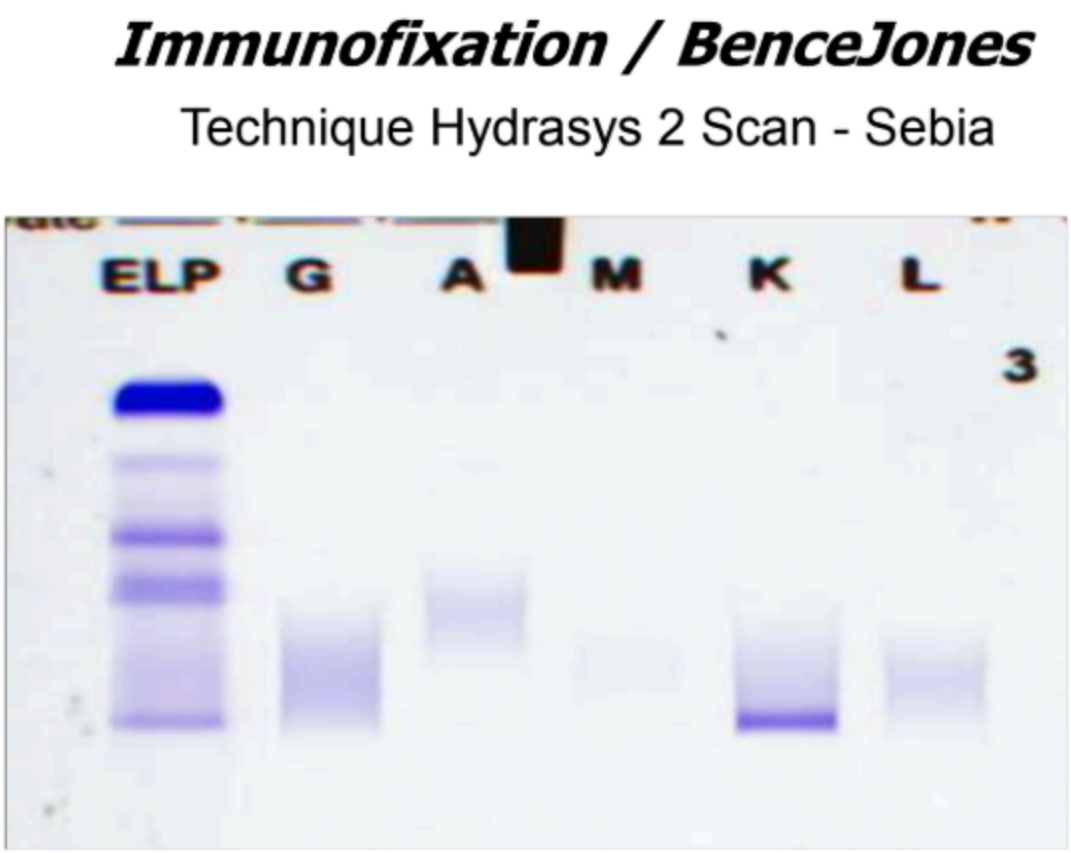


Figure 2

Serum immunofixation showing a monoclonal kappa light chain band.

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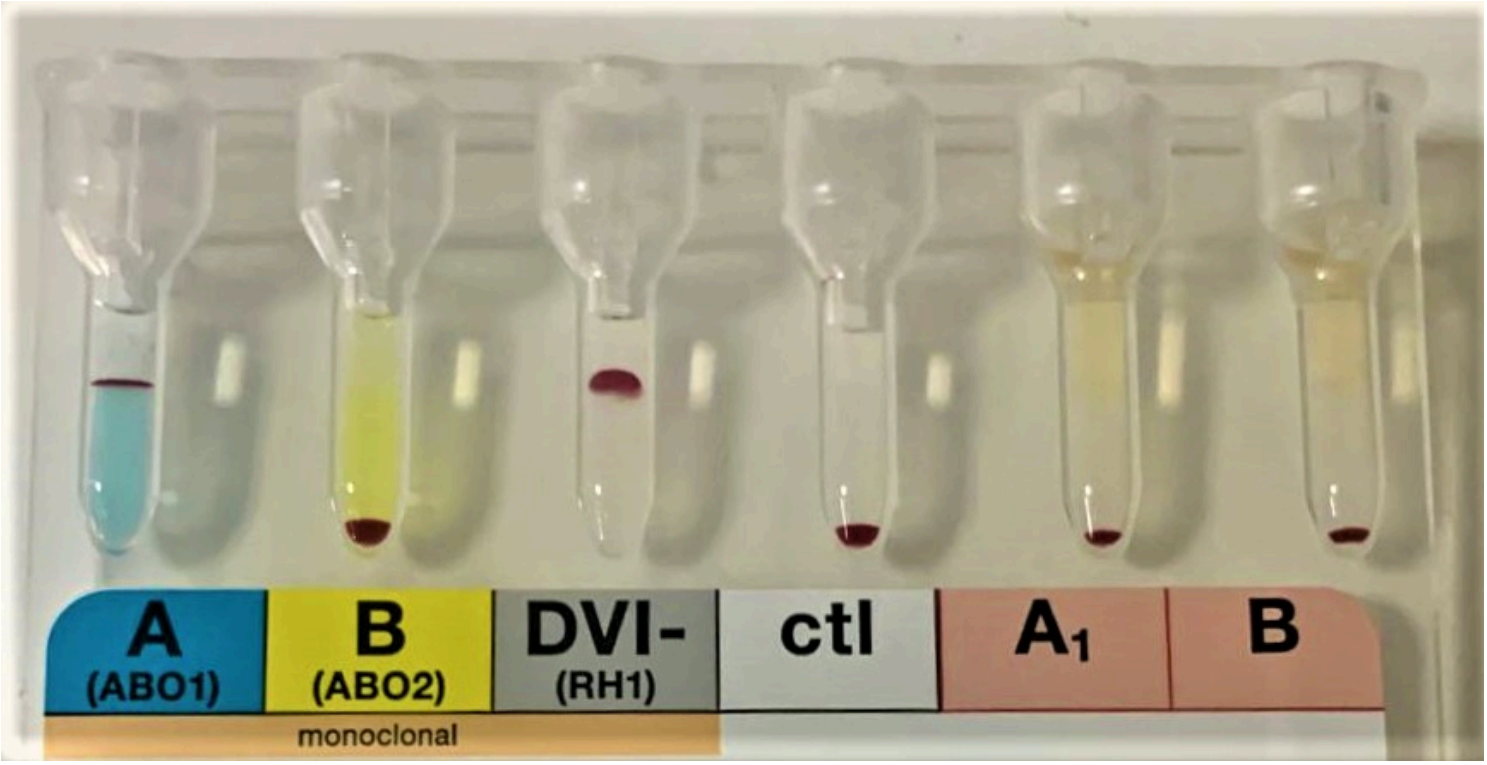


Figure 3

ABO discrepancy on gel card testing showing discordance between forward and reverse grouping.

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