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CASE REPORT

Unexpected Identification of Anti-Di^a During Routine Pretransfusion Testing

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ABSTRACT

Background: **Anti-Di^a is a clinically significant alloantibody directed against a low-prevalence antigen in the Diego blood group system. While rare in most populations, its prevalence is notably higher among East Asian and indigenous South American groups. Detection is often challenging due to the limited presence of Di^a (+) cells in routine antibody screening panels.**
Methods: **We describe a case involving a 62-year-old male inpatient at Asia University Hospital who was evaluated for symptomatic anemia. Routine pretransfusion testing using an automated analyzer revealed a positive antibody screen with a sparse and non-congruent reaction pattern. Subsequent manual repeat testing and serologic work-up with an 11-cell panel showed reactivity limited to Di^a-positive cells. The presence of anti-Di^a was confirmed by testing the patient's plasma against Di^a-positive red blood cells obtained from the local blood center. After confirming compatibility using the manual polybrene method, the patient received a safe transfusion of leukocyte-reduced red blood cells without adverse reactions.**
Results: **This case underscores the importance of recognizing atypical reactivity patterns that may indicate a low-incidence antibody. It highlights the need for a rapid pathway to selected cell testing and reference support for accurate antibody identification. While Di^a (-) units are readily available, appropriate LIS documentation, clear clinical communication, and staff awareness are essential to ensure safe and timely transfusion care.**
Conclusions: **This case demonstrates the value of a structured workflow for identifying rare antibodies like anti-Di^a and reinforces the need for proactive laboratory protocols to safe and effective transfusion practice.**
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KEYWORDS

anti-Di^a, Diego blood group system, low-frequency antigen, pretransfusion testing

INTRODUCTION

The Diego blood group system currently comprises 22 antigens organized across 16 distinct antigenic sites on the band 3 glycoprotein, an integral membrane protein of red blood cells [1]. The system includes two well-known antithetical pairs: Di^a/Di^b and Wr^a/Wr^b. Among these, Di^b and Wr^b are commonly found, whereas Di^a and Wr^a are considered low-incidence antigens [2,3]. Alloantibodies against Di^a and Di^b are clinically important and have been implicated in hemolytic transfusion

reactions and hemolytic disease of the newborn [4,5]. Di^a is classified as a low-prevalence antigen in the Diego system. It is rarely found in individuals of Caucasian descent but occurs more frequently in certain populations, particularly among East Asians such as Chinese, Koreans, Taiwanese, and Japanese, where its prevalence ranges from 3% to 10%, and in South American Indians, with reported rates as high as 7% to 54% [6-11]. A retrospective study conducted in southern Taiwan between 2015 and 2017 reported a red blood cell alloimmunization rate of 3.29%, with anti-Mi^a, anti-E, and cold antibodies being the most frequently detected. The findings underscore the importance of Rh-ee phenotype matching to enhance transfusion safety in this population [12].

Although the Di^a antigen is generally rare in most donor populations, its higher prevalence among certain East Asian groups means that laboratories in our region may occasionally encounter anti-Di^a during routine type-and-screen procedures. Despite its low frequency, anti-Di^a is clinically significant, having been associated with both hemolytic transfusion reactions and hemolytic disease of the fetus and newborn (HDFN). As one of the most relevant low-incidence antigens in the Diego blood group system, Di^a warrants careful detection and documentation in transfusion practice [13]. In everyday practice, the primary challenge is recognizing the antibody when reactivity is limited to one or two Di^a-positive reagent cells on a panel, and subsequently communicating efficient, safe transfusion guidance to the clinical team. We report a concise case from our blood bank and outline a stepwise approach that other laboratories can adopt.

CASE PRESENTATION

A 62-year-old male inpatient at Asia University Hospital was evaluated for symptomatic anemia, accompanied by nausea and vomiting. Laboratory findings revealed anemia with a hemoglobin level of 8.5 g/dL, an RBC count of 2.95 x 10^6/μL, and a hematocrit of 25.1%. The patient also had an elevated RDW of 17.5%, suggesting a population of red blood cells with varying sizes. Other parameters included a WBC count of 10.4 x 10^3/μL, a platelet count of 311 x 10^3/μL, and normocytic indices (MCV 85.0 fL, MCH 28.8 pg, MCHC 33.9 g/dL). Inflammatory marker hsCRP was elevated at 3.2 mg/dL, and mild hyponatremia was noted (Na 131 mmol/L). ABO/RhD typing identified the patient as blood type B, RhD positive. Based on clinical symptoms, the clinical team requested two units of leukocyte-reduced packed red blood cells (LR-PRBCs) to manage his chronic anemia.

Routine type-and-screen using the ORTHO AutoVue Innova yielded a positive antibody screen with a sparse and non-congruent pattern: SI 0.5+, SII 0, SIII 3+ (Figure 1). Given the limited reactivity and atypical pattern on the initial screen, a repeat manual polybrene test was performed for confirmation. The results confirmed selective reactivity: SI and SII were negative, while SIII showed 2+ reactivity, supporting the presence of a low-incidence antibody, later identified as anti-Di^a. An 11-cell antibody identification panel revealed reactivity exclusively with Di^a-positive red blood cells, while all Di^a-negative cells were non-reactive. Common alloantibodies - including those from the Rh, Kell, Duffy, Kidd, and MNS systems - were excluded based on standard rule-out criteria. No agglutination was observed during the immediate spin (IS) or 37°C incubation phases. However, a 2+ reaction was noted in the anti-human globulin (AHG) phase with $Di(a^+)$ cells. The autocontrol was negative. This pattern supports the presence of a clinically significant alloantibody directed against the low-frequency Di^a antigen. Selected-cell testing was performed using Di^a-positive leukocyte-reduced red blood cells sourced from the local blood center. The patient's plasma demonstrated reactivity with Di^a-positive red blood cells, confirming the antibody's specificity. No reactivity was observed with Di^a-negative cells from the reference panel, and no additional alloantibodies were identified.

DISCUSSION

This case underscores three operational priorities for transfusion services. First, maintain a rapid pathway to selected-cell testing for low-incidence antigens. Because many commercial antibody panels contain few or no Di^a-positive red blood cells, ready access to a reference laboratory or a small in-house rare-antigen mini-panel can significantly shorten turnaround time and reduce repeated, inconclusive investigations. Once anti-Di^a was suspected, compatibility was confirmed using the manual polybrene method. This allowed us to identify suitable leukocyte-reduced red blood cell units efficiently, without the need for rare donor inventories or advanced serologic testing, thereby minimizing transfusion delays. Third, strengthen staff training.

CONCLUSION

Anti-Di^a is rare but clinically significant. In this 62-year-old man, automated screening, manual polybrene confirmation, and selected-cell testing established the diagnosis. The patient was safely transfused with leukocyte-reduced red blood cells without adverse events. When antibody screening reveals sparse and non-congruent reactivity, a low-incidence antibody such as anti-Di^a should be considered. In our case, confirmation was achieved using Di^a-positive red blood cells obtained from the local blood center, which showed reactivity with the patient's plasma. Compatibility testing was performed using the manual polybrene method, allowing the identification of suitable leukocyte-reduced PRBCs for transfusion. There was no need to source

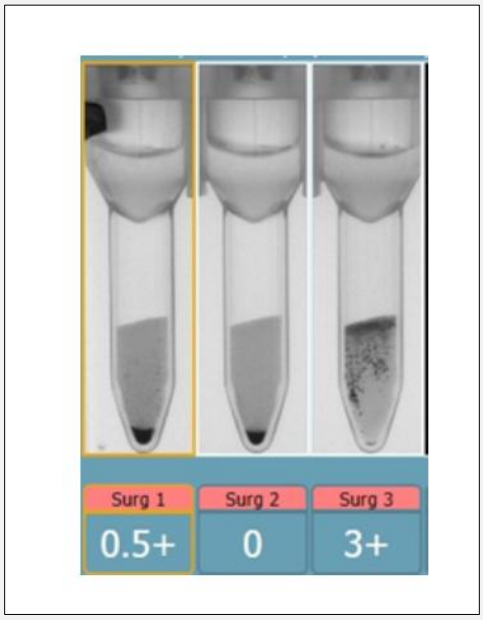

Figure 1. Initial antibody screen results from the ORTHO AutoVue Innova automated analyzer, showing reactivity with Screening Cell I (0.5+), Cell II (0), and Cell III (3+).

These findings were subsequently confirmed by manual polybrene testing.

Di[a] (-) units, and the transfusion was completed without adverse events. All findings, including antibody specificity and transfusion compatibility, were documented in the laboratory information system (LIS). Awareness of the local prevalence of Di[a] and practical serologic workups are critical to ensuring safe and efficient transfusion management.

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Declaration of Generative AI in Scientific Writing:
Generative AI, including ChatGPT (OpenAI), was used only to enhance the grammar and clarity of the manuscript. It was not used for data analysis, scientific interpretation, or the creation of intellectual content. All final content remains the responsibility of and was approved by the authors.

Declaration of Interest:
There are no conflicts of interest associated with this paper.

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