Case Report

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Daratumumab: The perplexity in immunohematology with emerging horizons in myeloma therapy

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Abstract:

CD38 is a disulfide-linked molecule present on red blood cells (RBCs) and daratumumab; an anti-CD38 monoclonal antibody is a novel agent for treating multiple myeloma patients. It also binds to the RBC along with the plasma cells in concern, creating a menace in the immunohematology workups and requires the use of dithiothreitol-treated cells to rule out its interference. Appropriate and timely communication with the clinicians about the patient history goes a long way in solving complex looking immunohematology workups.

Keywords:

Anti-CD38, daratumumab, immunohematology, multiple myeloma

Introduction

Pretransfusion testing is an essential prerequisite before releasing blood components for transfusion.[1] CD38 is a disulfide-linked molecule present on red blood cells (RBCs) and daratumumab (DARA), an anti-CD38 is a novel agent for treating multiple myeloma patients. It also binds to the RBC along with the plasma cells in concern, creating a menace in the immunohematology workups.[2] We describe a case of multiple myeloma on DARA, which lead to newer learning concepts and expanding our horizon.

Case Report

A 66-year-old female was referred to our department for blood grouping and antibody screening. She was a prospective candidate for peripheral blood stem cell transplant for refractory multiple. There was a history of RBC transfusion 7 months ago elsewhere. The patient was typed as Group O, Rh D positive. Antibody screening was positive on Neo Iris (Immucor, INC., Norcross, GA, USA). Antibody identification (Capture-R Ready-ID, Immucor, INC., Norcross, GA, USA) was then performed which turned out to be pan-positive with varying strengths indicating the presence of multiple alloantibodies. The auto-control and direct antiglobulin test (DAT) were negative.

Extended typing for Rh, Kell, Kidd, Duffy, MNS, and Lewis group done by tube technique using commercially available antisera (Immucor, INC., Norcross, GA, USA) revealed C + c + e + E-K-Jka-Jkb + Fya + Fyb-M-N + S-Leb-. On crossing out and excluding the antigens for which the patient was positive, antibodies against E, K, S antigens were considered. Yet, there was an unidentified antibody whose specificity could not be ascertained. A re-check of all the results was done. We went back to the patient and his treating clinician and elucidated a detailed history. It showed that the patient was on DARA treatment which could have possibly led to the interference in the immunohematology workup.

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For confirmation of the above fact, dithiothreitol (DTT)-treated reagent red cells were tested by the gel card method (IgG + C3d, Bio-Rad Laboratories, Inc.,) in accordance to the method described in technical manual. Autocontrol and DAT were also performed on gel cards.[1]

The patient sample was also tested with ficin-treated reagent red cells (Immucor, INC., Norcross, GA, USA) by tube technique at anti-human globulin phase.

The preexisting pattern of reactivity disappeared in both the scenarios and the antibody identification panel was completely negative indicating the interference of DARA in antibody testing in this case. The presence of anti-K antibody was questionable as "K" antigen is destroyed by DTT. However, "K" remains unaffected by ficin, and so its presence was also ruled out.

Two donor units of Group O Rh "D" positive were treated with DTT similar to the reagent cells. After DTT treatment, they were cross-matched with patients' sera and were found compatible. The course of transfusion was uneventful.

Discussion

DARA is a monoclonal antibody-targeted against CD38 used for treatment in cases of refractory multiple myeloma. The protein CD38 is overexpressed on myeloma cells, therefore, serving as the target for DARA.[3] CD38 is also weakly expressed on red cells, therefore, causing interference in antibody screening and identification work-ups, thereby complicating the pretransfusion compatibility. It is said to interfere with the investigations up to 2–6 months after infusion. However, it does not interfere with routine ABO blood grouping.[4] A proper history of the patient and close coordination with the treating clinician is important to solve the interference of such drugs in the pretransfusion testing.

The use of DTT to cleave the ectodomain of CD38 on RBC has been studied and practiced to overcome the DARA interference in pretransfusion testing. Along with cleaving CD38, it also denatures other red cell antigens such as those of the Kell, Dombrock, Indian, Knops system and the corresponding antibody, if present, will go undetected. These antigens, other than Kell, are very less prevalent. Therefore, it is always suggested to transfuse Kell-negative packed red cell (PRC) unit to such patients.[4,5]

Another approach for removing DARA interference is by neutralizing the anti-CD38 by adding soluble CD38 or an anti-DARA idiotype. Although both the methods are equally efficient, DTT is more cost-effective, readily available, and simple to use.[5]

The use of trypsin-treated reagent red cells to remove the DARA interference has also been studied. It is shown to be effective, though inferior to the use of DTT.[5] Ficin, papain, and other enzymes have not been studied extensively. To add to this, we used ficin-treated cells to check as to what happens to the reactivity in such cases. To notice, the reactivity disappeared with ficin as well. The advantage of using ficin was that we could rule out the presence of anti-K antibodies as the Kell antigens are not destroyed by ficin. The antigens destroyed by ficin like that of the Duffy and MNSs blood group system were ruled out previously by the use of DTT-treated reagent red cells. Therefore, the presence or absence of Kell antibody can be ascertained with confidence after using ficin-treated cells.

Conclusion

Without a proper drug history, it was misinterpreted as a case of unsolved multiple alloantibodies. This emphasizes the importance of detailed communication with the clinicians. It helped in concluding the results by the use of DTT-treated reagent red cells to remove the interference of DARA. Ficin-treated reagent red cells were helpful in ruling out the presence of anti-Kell antibody which is frequently missed by the use of DTT.

Therefore, the clinicians must be educated about such interferences which will lead to close coalition between the transfusing facility and the clinicians for the betterment of patient care.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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