

中文題目：輸血前抗體篩檢之 MP 法與單株抗體 Daratumumab 相關的特殊發現

英文題目：An interesting finding about the manual polybrene method during pre-transfusion test in Daratumumab therapy

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Introduction :

Daratumumab, a promising novel agent for multiple myeloma, is an IgG1κ human monoclonal antibody targeting specifically against CD38, which is highly expressed on myeloma cells.^{1,2} Interference with compatibility test for pre-transfusion survey is a concerning issue due to expression of CD38 on erythrocyte membranes, which would reactive with free daratumumab in patients after therapy.³ This results in pan-reactive agglutination in standard indirect antihuman globulin (Coombs') test for antibody screening and cross-matching test in pre-transfusion screen, which results false positive screen test and/or masks clinical relevant red-cell alloantibodies in patients with daratumumab.⁴

Case presentation :

This is a 74 years old male who was diagnosed with multiple myeloma, Internal Staging System (ISS) stage II, IgA/lamda type, in 2013 with initial presentation of pancytopenia and hypercalcemia. He had received multiple courses of treatment from May 2013 to October 2017, but with progression disease later on. Therefore, Daratumumab was used for relapsed and refractory multiple myeloma treatment. Because of documented false-positive pre-transfusion indirect antiglobulin test (IAT) from previous studies, we had performed tests before blood transfusion after starting Daratumumab treatment. Surprisingly, the manual polybrene (MP) method does not effect by Daratumumab. Instead, there is still panagglutination when using traditional IAT method.

Discussion :

Several solutions have been proposed to overcome this issue.^{5,6,7} These include pretreatment of red cells with dithiothreitol (which inhibits daratumumab binding by reduced CD38 disulfide bridges),⁸ the use of antiidiotypic antibodies against daratumumab, supplementation of soluble CD38 to bind daratumumab, the use of red cells from newborns as test cells since they express low CD38 level, and adding F(ab')₂ fragments to block CD38 epitope on red cells.⁹ However, each method has inherent limitations, such as time/labor consuming, destroy red cells antigens, and/or insufficiently standardized for use in routine practice.

Polybrene is a quaternary ammonium polymer which could facilitate detection of red cell antibodies. Manual polybrene (MP) method is a simple and rapid way for detection of red cell antibodies¹⁰ showing comparable results with standard pre-transfusion test¹¹ and has been used in

many clinical laboratories for pre-transfusion screen. Here are reported that, with MP method, there was no interference of indirect antiglobulin test in patients with daratumumab therapy. The patients had negative indirect antiglobulin test by either standard peg-antihuman globulin (peg-AHG) or MP methods before daratumumab treatment, but indirect antiglobulin test by peg-AHG method turned to be positive after first shot of daratumumab, while persistence of negative results were noted by MP method (Figure 1). Even in a patient who had 9 times of daratumumab to now had negative results from MP method and positive results from peg-AHG method. Antibody identification of the samples showed positive of IgG type of antibodies, which consist of daratumumab agent.

As for the efficacy of MP method for pre-transfusion screen, it gives higher sensitivity in the Rh, Kidd and Duffy systems, compared to the antiglobulin reaction.¹⁰ The main shortcoming of the manual Polybrene test is its lack of adequate sensitivity in the Kell system. However, it could overcome by performing a supplementary antiglobulin reaction on the sensitized, Polybrene-treated, red blood cells.¹⁰ As the result, manual polybrene method has been widely used in many hospitals for decades in Taiwan with comparable results. With no interface with daratumumab, MP method showed its advantage in pre-transfusion test.

As the developments of monoclonal antibodies for many kinds of diseases, the possibility of interferences in laboratory tests increases.^{12,13} Since red cells interact with daratumumab resulting in the interference of pre-transfusion test, we report that MP method could be a simple, quick and effective solution for this important issue.

