Immunoglobulin-resistant delayed hemolytic transfusion reaction treated with rituximab in an adult sickle cell patient

Sickle cell disease (SCD) is a worldwide distributed hemoglobinopathy and transfusion strategies are required for treatment of acute and chronic SCD-related clinical manifestations.[1,2] The delayed hemolytic transfusion reaction (DHTR) is a life-threatening transfusion complication of SCD.[3-6] The DHTR is defined by the acute decrease of hemoglobin (Hb) levels with hemolysis and hemoglobinuria after 2 or 3 to 15 days after the blood transfusion. The hemolytic phenotype of DHTR is associated with symptoms of severe sickle cell–related vasoocclusive crisis such as pain.[3-6] Although alloantibodies and autoantibodies have been identified in few DHTR patients, the mechanism(s) responsible for red blood cell (RBC) destruction in DHTR is largely unknown.[3-6] Recently intravenous immunoglobulin (IVIG) has been proposed for treatment of DHTR in children with SCD,[6] although previous case reports described the use of the monoclonal chimeric anti-CD20 antibody (rituximab) for treating or preventing DHTR in children or in adult patients with SCD.[3-5] A 26-year-old man with SCD (SS, HbS: 79%) was referred in June 2012 to our department for severe vasoocclusive crisis with bone pain and fever (Fig. 1). He was treated with fluids, analgesics, and erythrocytapheresis using antigen-matched RBCs.[1] The patient was negative for direct antiglobulin test (DAT). On Day 3 after erythrocytapheresis Hb levels decreased (10.4-6.7 g/dL), the lactate dehydrogenase (LDH) values increased (700–2200 U/L) with hemoglobinuria and worsening of bone pain (Fig. 1). The DAT was still negative and the diagnosis of DHTR was made. The patient was treated with IVIG at the dosage of 0.5 g/kg/day for 5 days (Fig 1). Steroids were avoided, since the patient was admitted to the hospital for severe acute vasoocclusive crisis and steroids can worsen the acute clinical manifestation related to SCD. We observed a gradual amelioration of the patient's pain, whereas Hb levels were still low, associated with hemoglobinuria and persistence of high LDH levels despite the increased reticulocyte count, suggesting a DHTR resistant to immunoglobulin treatment (Fig. 1). On Day 11 after erythrocytapheresis and on Day 4 after the end of the immunoglobulin treatment, the patient again experienced severe pain with abdominal localization and further reduction of Hb level. The abdominal ultrasonography showed splenic sequestration. Since we hypothesized a DHTR resistant to immunoglobulin treatment

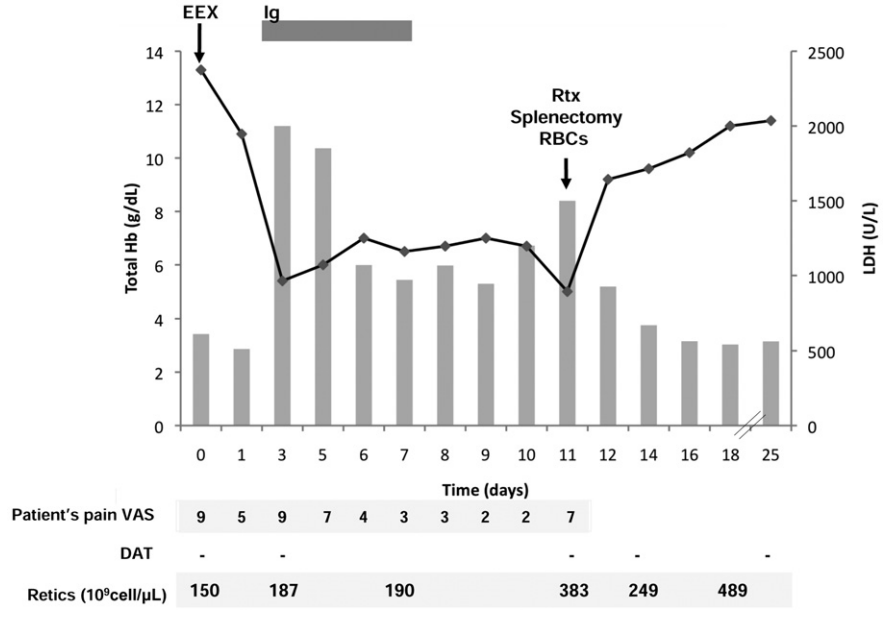

Fig 1. Clinical presentation of the immunoglobulin (Ig)-resistant DHTR episode in a adult patient with SCD. The arrows indicate: erythrocytapheresis treatment (EEX) and the administration of rituximab (Rtx) followed by transfusion of RBCs. (▬) LDH (U/L); (–◆–) Hb (g/dL).

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and we needed to transfuse the patient before and/or during splenectomy, we used rituximab (375 mg/m^2) before transfusion of RBCs.[5] The serology for hepatitis B was compatible with past infection. The patient underwent a splenectomy. In the following days the Hb levels rapidly increased, the LDH levels reduced, and the hemoglobinuria disappeared with amelioration of the patient's clinical condition. The Hb levels were stable (11.8 g/dL) 15 and 40 days after rituximab. The DAT was still negative 30 days after the patient's discharge. The patient was then placed under hydroxyurea treatment to reduce the transfusion requirement. Although rituximab treatment was effective in DHTR, it must be pointed out that SCD patients treated with rituximab should be closely followed up due to the fact that rituximab can induce prolonged immunosuppression, which might expose SCD to the risk of severe infections. This case suggests that a portion of SCD patients with DHTR might be resistant to immunoglobulin treatment.[6] Thus, in these patients rituximab should be considered as a therapeutic option.

CONFLICT OF INTEREST

There are no conflicts of interest.

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REFERENCES

1. de Franceschi L, Finco G, Vassanelli A, Zaia B, Ischia S, Corrocher R. A pilot study on the efficacy of ketorolac plus tramadol infusion combined with erythrocytapheresis in the management of acute severe vaso-occlusive crises and sickle cell pain. Haematologica 2004;89:1389-91.
2. De Franceschi L, Cappellini MD, Olivieri O. Thrombosis and sickle cell disease. Semin Thromb Hemost 2011;37: 226-36.
3. Bachmeyer C, Maury J, Parrot A, Bachir D, Stankovic K, Girot R, Lionnet F. Rituximab as an effective treatment of hyperhemolysis syndrome in sickle cell anemia. Am J Hematol 2010;85:91-2.
4. Chadebech P, Habibi A, Nzouakou R, Bachir D, Meunier-Costes N, Bonin P, Rodet M, Chami B, Galacteros F, Bierling P, Noizat-Pirenne F. Delayed hemolytic transfusion reaction in sickle cell disease patients: evidence of an emerging syndrome with suicidal red blood cell death. Transfusion 2009;49:1785-92.
5. Noizat-Pirenne F, Bachir D, Chadebech P, Michel M, Plonquet A, Lecron JC, Galacteros F, Bierling P. Rituximab for prevention of delayed hemolytic transfusion reaction in sickle cell disease. Haematologica 2007;92:e132-5.
6. de Montalembert M, Dumont MD, Heilbronner C, Brousse V, Charrara O, Pellegrino B, Piguet C, Soussan V, Noizat-Pirenne F. Delayed hemolytic transfusion reaction in children with sickle cell disease. Haematologica 2011;96:801-7.