Successful treatment with Rituximab in a patient with life-threatening resistant Thrombotic Thrombocytopenic Purpura

Dear Editor

Acquired thrombotic thrombocytopenic purpura (TTP) is an acute, often life-threatening disease difficult to treat. A 32 year-old female was admitted to our Department with a three-day history of headache, weakness, macroscopic hematuria, and purpura. She had no history of diarrhea and she was pale and icteric with a faded maculopapular eruption on arms and palms. Laboratory results revealed severe anaemia with schistocytes and reticulocytes, thrombocytopenia, hyperbilirubinemia, high blood levels of lactate dehydrogenase (LDH), a high titer of anti-ADAMTS-13 antibodies and low activity of ADAMTS-13. Urinalysis showed macroscopic hematuria and proteinuria.

Diagnosis of TTP was established and the patient was treated with prednisone, intravenous immunoglobulin, plasma exchanges (PE) with fresh frozen plasma and red packed cells. She had no improvement and became resistant to PE. Due to high operative risk, splenectomy was not performed. Plasmapheresis with cryosupernatant on a daily basis was decided. After eight sessions the patient’s clinical condition deteriorated. Treatment with 4 weekly doses of rituximab, in combination with daily plasma exchange and steroids was initiated. The patient responded to rituximab from the first dose and a complete clinical and laboratory remission was achieved. The patient is in complete remission ever since, lasting over 20 months.

An autoimmune process, antibody mediated, is implicated in the pathophysiology of the majority of acute acquired TTP1. Arterial thrombi, the hallmark of TTP, consist of unusually large multimers of von Willebrand factor (vWF). These multimers are cleaved by a serum metalloproteinase (ADAMTS-13)2. In patients with acquired TTP, the presence of an autoantibody results in decreased levels of this metalloproteinase1.

In antibody-mediated disease, there is evidence of increased relapse rates and requirement for more therapy to induce remission. This suggests that PE treatment and steroids alone, are not sufficient to switch off the autoimmune process and prevent relapses. Remission can be achieved with anti-CD20 therapy. Rituximab3 is a chimeric antibody initially used for treatment of malignant lymphoma and autoantibody-mediated disorders that attaches to the CD20 antigen presented on B lymphocytes, apparently triggering an immunological response, which eliminates B cells, including the clone that produces the anti-ADAMTS-13 antibodies.

Our experience substantiates a role for rituximab in resistant and potentially fatal TTP, along with prolonged relapse-free period of the disease, suggesting its strong efficacy.

References

Arampatzi S1, Diamantidis MD2, Perifanis V2, Diza E1, Kaiafa G2

1 Department of Microbiology, AHEPA University Hospital, Aristotle University of Thessaloniki, Greece
2 Department of Haematology, First Propedeutic Department of Internal Medicine, AHEPA University Hospital, Aristotle University of Thessaloniki, Greece

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Corresponding author: Stergiani Arampatzi, MD, MSc, Laboratory of Microbiology Aristotle University of Thessaloniki, Greece, tel +30 6948948011, e-mail: s.arampatzi@yahoo.gr