Rituximab-induced acute thrombocytopenia: Report of two cases

Rituximab use in B-cell malignancies has been widely favored by the acceptable toxicity profile of this drug. Episodes of rituximab-induced neutropenia have been reported in some patients, but severe acute thrombocytopenia is very unusual. Here, we report transient severe acute thrombocytopenia after rituximab infusion in two patients with Hairy cell leukemia and mantle cell lymphoma respectively. Interestingly, in both cases, thrombocytopenia was reversible in few days without further therapeutic intervention. The mechanism of this side effect remains unclear. Previous reports suggested the presence of CD20 antigen on the platelets themselves or that soluble CD20 antigen in the circulation may cause an antigen-antibody reaction and immune-mediated cell lysis. It is noteworthy that the two cases reported here as well as the two previously published cases share a massive bone marrow involvement by neoplastic B lymphocytes.

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To the Editor,

Rituximab, a chimeric anti-CD20 monoclonal antibody, is commonly used in treating B-cell malignancies and some autoimmune disorders including immune mediated thrombocytopenia. Rituximab use has been widely favored by the acceptable toxicity profile of this drug. Side effects are restricted to first infusion-related fever, chills, rigors, flushing, nausea and vomiting, which are usually self-limited and generally subside with temporary interruption of rituximab infusion.[1] Episodes of neutropenia have been reported in some patients,[2] but severe acute thrombocytopenia after the administration of rituximab is very unusual. Here, we report transient acute thrombocytopenia after rituximab infusion in two patients with Hairy cell leukemia and mantle cell lymphoma respectively.

Case 1

A 41-year-old man presented with pancytopenia, abdominal pain and mild chest pain of 2 weeks duration. Physical examination showed splenomegaly (4 cm below costal margin). Laboratory tests revealed pancytopenia: leucocytes 2.8×10^9/L, hemoglobin 95 g/l and platelets 85 x 109/l (reference range: 150×10^9/L-400×10^9/L, and high LDH level. Blood smear showed few hairy cell-like lymphocytes. Flow cytometry analysis of peripheral blood was consistent with the diagnosis of hairy cell leukemia with the presence of 5% cells positive for CD20, CD19, CD22, CD11, CD25 and HLA-DR with lambda light chain restriction. CD10 was negative. Tartrate resistant acid phosphatase test was also positive. CT scan of abdomen and pelvis showed splenomegaly and retroperitoneal lymph nodes. Bone marrow biopsy revealed bone marrow infiltration by abnormal lymphoid cells positive for CD20 and DBA44 (a Hairy cell leukemia marker). Patient was pretreated with decadron and benadryl and then received 800 mg of rituximab (375 mg/m2) as part of induction chemotherapy. He developed a minor cytokine release syndrome requiring transient discontinuation of rituximab infusion. On the next day, repeated hemogram showed a drop in platelet count to 7×10^9/L. He was transfused with platelets, and post-transfusion platelet count was 48×10^9/L. His platelet count spontaneously increased to 90×10^9/L after 1 week and 186×10^9/L after 3 weeks. One month later, he received cladribine (8 mg/day) over 7 days and achieved complete remission. His lowest platelet count following cladribine was 68×10^9/L.

Case 2

A 64-year-old man, diagnosed case of mantle cell lymphoma with diffuse lymphadenopathy and bone marrow involvement in 2003, presented to us for further treatment. He previously received 8 cycles of CHOP and achieved a partial response after which he progressed. His laboratory tests were as follows: leucocytes 90.2×10^9/L with 80% lymphocytes, hemoglobin 104 g/L and platelets 90×10^9/L. He was pretreated with decadron and benadryl and then received 700 mg of rituximab (375 mg/m^2). He developed fever and rigors during the infusion and was given acetaminophen. The infusion was stopped for 2 hours and was continued at a slower rate with no complication. Repeated blood count on the next day showed a drop in platelet count to 10×10^9/L. The patient was transfused with platelets, and post-transfusion platelet count was 70×10^9/L Over the next 3 weeks his platelet count ranged from 70×10^9/L to 85×10^9/L.

Rituximab is generally well tolerated. Severe cytokine release syndrome, which occurs during drug infusion, has been reported in patients with massive peripheral blood neoplastic invasion.[3-5] This syndrome is caused by peripheral blood cell lysis and is mainly attributable to increased levels of IL-6 and TNFα.[3-5] Although episodes of neutropenia have been reported after rituximab infusion, isolated acute thrombocytopenia is extremely rare. Our literature search revealed only three cases.[6-8] Also, addition of rituximab to a combination of fludarabine and cyclophosphamide has been associated with significant prolonged thrombocytopenia in patients with relapsed follicular lymphoma.[9] We report here another two cases of acute severe thrombocytopenia requiring platelet transfusion. Interestingly, in both cases, thrombocytopenia was reversible in few days without further therapeutic intervention. The mechanism of this side effect remains unclear. Previous reports suggested the presence of CD20 antigen on the platelets themselves or that soluble CD20 antigen in the circulation may cause an antigen-antibody reaction and immune-mediated cell lysis. It is noteworthy that the two cases reported here as well as three previously published cases share a massive bone marrow involvement by neoplastic B lymphocytes. Finally, we believe that the true incidence of this rare complication may be underestimated since most physicians do not check platelet counts the day after rituximab.

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