

Rituximab Induced Thrombocytopenia: A Case Report

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Abstract

Rituximab, an anti-CD20 monoclonal antibody, is a generally safe and well-tolerated drug. In recent years, Rituximab has been widely used off-label as the second line treatment in both adults and children with Idiopathic thrombocytopenic purpura (ITP) refractory to first line treatment. Episodes of Rituximab-induced neutropenia have been reported in some patients, but severe acute thrombocytopenia is very unusual. A 43-year-old woman, with diagnosis of Idiopathic thrombocytopenic purpura refractory to first line therapy was treated with Inj. Rituximab 500mg/week for four doses. After the 3rd dose, her platelet count had fallen from pre-infusion level of 1, 17, 000/mm³ to 79,000/mm³ but no signs of hemorrhage. So, it is diagnosed as Rituximab induced thrombocytopenia and clinician decided to delay the 4th dose by a week. After 15 days of 3rd dose, platelet count increased to 88,000/mm³. Then the 4th dose was given. Over the course of time, platelet count showed further increase. Few cases of acute thrombocytopenia with Rituximab infusion have been reported. In our case fall in platelet count was not sudden but was gradual occurring after 1st week. Rituximab-induced thrombocytopenia is likely under diagnosed because most patients do not have blood counts performed the day after treatment. Rituximab should therefore be used with caution; routine blood count should be done frequently to document this potential adverse effect. This case is reported to emphasize a rare and unusual adverse reaction to Rituximab. Early recognition of Rituximab induced thrombocytopenia is critical to prevent serious sequelae.

Keywords: Rituximab, Idiopathic thrombocytopenic Purpura, Thrombocytopenia

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Introduction:

Rituximab is a chimeric monoclonal antibody to CD20 antigen. [1] It

is commonly used in treatment of non-Hodgkin's lymphoma and Rheumatoid arthritis. Rituximab is also under

investigation for the treatment of other conditions including chronic lymphocytic leukemia, Multiple sclerosis, ANA-associated vasculitis and SLE including lupus nephritis. Rituximab has been reported to be effective in patients, including children and infants, with Idiopathic thrombocytopenic purpura refractory to standard treatments. The most common side effects of Rituximab are infusion related symptoms such as fever, chills, rigors and flushing. [2] Pulmonary reactions have been reported including reversible interstitial pneumonia and interstitial fibrosis. Gastrointestinal disturbances may occur, which includes abdominal pain, bowel obstruction and perforation. Severe reactions like tumor lysis syndrome, acute renal failure, respiratory failure, reactivation of hepatitis B virus and progressive multifocal leukoencephalopathy may occur. [1] Episodes of Rituximab-induced Neutropenia

have been reported in some patients, but severe acute thrombocytopenia is very unusual. [3] Here we report a case of thrombocytopenia that occurs after Rituximab infusion in idiopathic thrombocytopenic purpura.

Case report:

A 43- year old female patient with refractory and unresponsive Idiopathic thrombocytopenic purpura was treated with Rituximab. She was initially treated with Corticosteroids, Dapsone, Pantoprazole, Domperidone(Pan-D), Dexamethasone (Decmax), Azathioprine (Azoran) and Multivitamins (Alcolife). There was no improvement in platelet count, hence, clinician advised second line ITP treatment. Inj. Rituximab was administered at a dose of 500mg/week intravenously, once a week for 4 infusions on an outpatient basis. Before starting with Rituximab platelet count was 1,17,000/microlts.

Table1: Rituximab dose schedule and its effect on platelet count

Drug	Dose	Platelet count (/micro lts)	Days of therapy
Rituximab	1 st	1,62,000	7 th day
	2 nd	1,14,000	7 th day
	3 rd	79,000	7 th day
		88,000	14 th day
	4 th	90,000	21 st day
		1,04,000	40 th day
		1,50,000	62 nd day

It was observed that after the 3rd dose, there was a fall in platelet count from pre-infusion level of 1,17,000/mm³ to 79000/mm³, with no signs of hemorrhage. Hemoglobin and leukocyte counts were within normal range. Therefore, clinician decided to delay the 4th dose by a week. After 15 days of the 3rd dose, when platelet count was increased to 88,000/mm³, the 4th dose was given. Over the course of time, platelet count showed further increase. A diagnosis of Thrombocytopenia induced by rituximab was made.

Discussion:

The patient had no history of constraining factor or drug that increase the risk of thrombocytopenia. Causality of thrombocytopenia by rituximab was assessed by Naranjo criteria and this ADR was 'probable'. WHO Uppsala monitoring center causality assessment criteria also indicated 'probable' association with rituximab. Rituximab is generally well tolerated. [3] In recent years, Rituximab has been widely used off-label as the second line treatment in both adults and children with Idiopathic thrombocytopenic purpura refractory to first line treatment. [4] S.Dhand et.al reported a case of rituximab induced acute thrombocytopenia, massive bone

marrow involvement with marked decrease in white blood count and lymphadenopathy. [5] Jun Ho Yi et.al also reported a case of acute thrombocytopenia, leukocytosis and mild anemia occurring immediately after Rituximab infusion. [2] Interestingly, in our case there was only thrombocytopenia with normal hemoglobin and WBC count. Z.K.Otrock et.al reports two cases of ITP with hair-cell leukemia and mantle cell lymphoma. Interestingly in both the cases, thrombocytopenia was reversible in few days without further intervention. [3] In our case, fall in platelet count was observed which was reversible without further intervention after few weeks of completion of 4th dose. Thus, rituximab is often referred to as a double edged sword. [6] Thrombocytopenia is a less common possible unwanted adverse effect of Rituximab therapy. Rituximab-induced thrombocytopenia is likely underdiagnosed because most patients do not have blood counts performed the day after treatment. [5] Proposed theories of rituximab induced thrombocytopenia include; (i) CD20 antigen causing antigen-antibody immune-mediated cell lysis by compliment activation, (ii) CD20 antigen on the platelet surface, (iii) platelet binding of a soluble anti-CD20/rituximab complex, and (iv)

intravascular fibrinolysis. Though, Rituximab use has been widely favoured by the acceptable toxicity profile, it should be used with caution. [3] Routine blood counts should be considered soon after therapy to document this potential adverse effect.

Conclusion: This case is reported to emphasize a rare and unusual adverse reaction thrombocytopenia to Rituximab. Even though it is a rare adverse reaction, the frequent use of this drug makes it important to exercise caution for this potential adverse event. Early recognition of Rituximab induced thrombocytopenia is critical to prevent serious sequelae.

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