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Background

Multiple sclerosis treatment with natalizumab is known to be associated with various side effects and it requires regular monitoring that includes brain magnetic resonance imaging and frequent blood work analysis. This case report describes an occurrence of immune thrombocytopenia directly following natalizumab infusions.

Objective

To evaluate the connection between new onset immune thrombocytopenic purpura in a multiple sclerosis patient and administration of natalizumab.

Methods

In this case report all the data was retrospectively acquired at the MS Multiple Sclerosis Comprehensive Care clinic at Baylor College of Medicine in Houston.

Results

A 25-year-old African American woman presented with left optic neuritis, had abnormal brain MRI that fulfilled Barkhof criteria and was diagnosed with relapsing-remitting multiple sclerosis. The initial onset of symptoms was 1 year prior when she had left facial twitching for over 1 month. She started weekly IM beta-interferon 1a. Symptoms in the following years included intermittent left facial twitching, left blepharospasm, right leg numbness, pain, and weakness exacerbated by running and heat. Due to inadequate response to beta interferon and adherence issues, the treatment with natalizumab was considered a year and a half after the initial diagnosis. Baseline bloodwork showed mild anemia that had been present for several years. Thrombocyte levels were normal, as was the remainder of the bloodwork. She received the first dose of natalizumab after she stopped beta interferon two months prior. There were no systemic or allergic reactions during the infusion.

Results cont.

About 3 weeks after the infusion she developed petechial lesions in her oral mucosa and bruises in her right upper extremity and in lower extremities bilaterally. Blood tests showed severely low platelet counts (see figure 1). She stopped the natalizumab. Low platelet counts persisted and she was diagnosed with immune thrombocytopenic purpura (ITP). She started taking 80 mg of oral prednisone daily followed by a taper for 3 months with disappearance of ITP symptoms. The thrombocyte levels returned to normal. In addition, all the tests for other rheumatologic, infectious, or autoimmune etiologies of thrombocytopenia, as well as liver function tests, were normal. The antiplatelet antibodies were negative. Upon stabilization of the thrombocyte values and complete resolution of all skin lesions, she resumed natalizumab since ITP was not believed to be related to the medication.

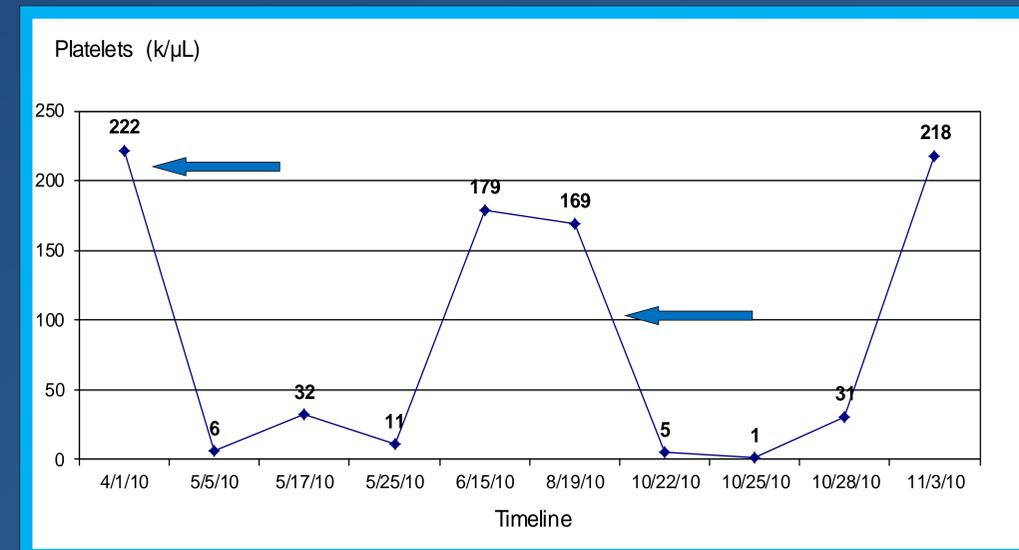


Fig 1. Platelet levels before and after natalizumab infusions

The black arrows point to the time of natalizumab infusions. The thrombocyte counts are on the Y-axis and the dates on the X-axis. The thrombocyte counts correspond to each date on the X-axis

Results cont.

She received the second dose of natalizumab, and two weeks later she developed ecchymoses and petechiae on her lower extremities, had prolonged and more intense menstrual bleeding and had reported an episode of hematochezia. The complete blood count again showed marked thrombocytopenia (see figure 1). She discontinued the natalizumab and started 80 mg of prednisone daily with rapid improvement of thrombocyte levels and complete resolution of the symptoms. There was no other exposure to medications known to cause thrombocytopenia, either during or before natalizumab treatment.

Conclusion

Since immune thrombocytopenic purpura recurred following re-challenge with natalizumab, we concluded that the most likely etiology for the ITP was exposure to this monoclonal antibody. Although ITP has been reported as an adverse side effect of another monoclonal antibody in multiple sclerosis patients, alemtuzumab,¹ it has not previously been seen with natalizumab. Possible pathogenesis involving natalizumab-induced thrombocytopenia is not known at this point. In a recent study, a group of investigators proposed diverse mechanisms by which different drugs can promote platelet destruction² but the etiology of drug-induced immune thrombocytopenia is complex and poorly understood. The recommendation remains unchanged for all the patients treated with natalizumab: regular monitoring of the blood count, among other tests.

References

1. CAMMS223 Trial Investigators, Coles AJ, Compston DA, Selmaj KW et al. Alemtuzumab vs. Interferon Beta-1a in Early Multiple Sclerosis. *N Engl J Med* 2008;359:1786-801.
2. Aster RH, Curtis BR, McFarland JG et al. Drug-induced immune thrombocytopenia: pathogenesis, diagnosis, and management. *J Thromb Haemost* 2009;7:911-8