

Reactive and Extreme Thrombocytosis After the First Infusion of Vedolizumab in an Ibd Patient

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1. Abstract

We report a case of reactive and extreme thrombocytosis in an inflammatory bowel disease patient after receiving the first infusion of Vedolizumab (VDZ). To the best of our knowledge, VDZ does not have this adverse reaction, and this possible association has not been described in the literature.

2. Introduction

Vedolizumab (VDZ), a humanized monoclonal antibody directed against the $\alpha 4\beta 7$ integrin heterodimer, prevents leukocytes from binding to the endothelium of venules within the gastrointestinal (GI) tissues as well as its subsequent extravasation into affected GI mucosa, resulting in gut-selective anti-inflammatory activity [1]. It was approved for the treatment of moderate to severe inflammatory bowel disease (IBD) by the Federal Drug Administration (FDA), the European Medicines Agency (EMA) as well as the National Administration of Drugs, Foods and Medical Devices (ANMAT) in our country for the same indications, in addition to other regions and countries [2-4]. The most common adverse reactions of VDZ are nasopharyngitis, headache, cough, bronchitis, influenza, back pain, rash, pruritus, sinusitis, oropharyngeal pain, and pain in extremities, although these reactions occur at a similar rate in patients receiving placebo [5]. Since no hematologic reactions were reported, we would present our experience on a reactive and extreme thrombocytosis in an IBD patient after receiving his first infusion of VDZ.

3. Case Presentation

A 35 years old gentleman diagnosed in 2013 with mild-moderate Ulcerative Colitis (UC) that involved his left colon. He had a good response to mesalamine in the beginning but 2 years later he started again with symptoms that didn't respond to this strategy. He went to other medical center where systemic corticosteroid was indicated, which was well tolerated, and then immunosuppressants vs. anti-TNF therapy was proposed as a next step therapy; it was decided together with the patient to start with infliximab, which was administered for two years but without a good response. His past medical history includes mood disorder in 2015 treated with escitalopram and clonazepam for one year and now he takes clonazepam 0.5mg as needed; no other remarkable medical history. In 2017 he decided to stop with this treatment and just keep taking steroids by himself without medical control. In September 2019 the patient came back to us with symptoms, his colonoscopy did show pancolitis with a stenotic area in the sigmoid colon. All randomized biopsies (including terminal ileum) didn't show granuloma, just ulcerations, cryptitis and abscesses. Biopsies from the stenosis showed the same histologic pattern. Dysplasia was ruled out in all the biopsies as well as citomegalovirus (CMV). Because of this stenosis, a MR-enterography with pelvis MRI scan was performed which didn't show any alteration in the small bowel nor signs of Crohn disease.

The patient agreed with our suggestion to start with VDZ and he

tolerated the first infusion. The blood control test before the second infusion did show $1083 \times 109/L$ platelets and an Iron Deficiency Anemia (IDA). The result of platelet count was confirmed in another blood sample. The previous blood control test (2 days before receiving the first infusion) did show $136 \times 109/L$ platelets and IDA; since the presentation of his symptoms in 2013, thrombocytosis has never manifested. Also, to the best of our knowledge, VDZ does not have this adverse reaction, and we didn't find that this possible association has been described in the literature.

We decided to stop the treatment with VDZ and a hematology referral was made. After 2 weeks of treatment with iron infusion, platelet count dropped to its normal value ($223 \times 109/L$) and one week later, we went ahead and continued with the induction therapy protocol of VDZ which was well tolerated with a good response to treatment. The patient is doing well now, no IBD symptoms, regular blood tests are normal and he is about to receive the third maintenance infusion at home and planning a control colonoscopy which is a bit delayed because of COVID-19 pandemic.

4. Discussion

The majority of reactive thrombocytosis are less than $1000 \times 109/L$. Extreme thrombocytosis, defined as a platelet count $>1,000 \times 109/L$, is quite rare as only 2 – 5.8% of patients demonstrate this degree of thrombocytosis upon presentation [6]. In IDA, the thrombocytosis is usually mild to moderate degree, where averaging platelets counts around $499 \times 109/L$, and extreme thrombocytosis was reported in only 7% [7]. Platelet count has also been shown to correlate with disease activity in IBD, and thrombocytosis is so far considered a marker of active disease, where both IDA and inflammation may be playing contributory roles in the pathogenesis of thrombotic events in this population [8, 9].

In our case, throughout the years of diagnosis with IBD, the patient has never manifested with thrombocytosis, although the patient has IDA, platelet count was normal, but after the first infusion of VDZ, extreme thrombocytosis appeared. We would think that perhaps it is unlikely that the chronic inflammation and/or IDA per se were the cause of this extreme thrombocytosis. Further research is required for a better understanding of this phenomenon.

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