Anticoagulant Induced Pseudothrombocytopenia- An Incidental Finding

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Case Report

Abstract: Thrombocytopenia may be caused either by impaired platelet production or due to accelerated platelet destruction. In some cases, there is an erroneously low reading of platelet counts in the automated analyzers, without any clinical symptoms. In these situations, with an absence of a positive history, anticoagulant-induced pseudothrombocytopenia may be considered. This phenomenon, albeit rare, presents in both healthy individuals as well as patients with various diseases. It is important to be aware of the situation in order to prevent misdiagnosis, and unwarranted treatments and transfusions.

Key words: anticoagulants, automated analyzer, microscopy, pseudothrombocytopenia.

Introduction:

Pseudothrombocytopenia is defined as in vitro clumping of platelets due to naturally occurring antibodies against modified platelet surface antigens [1]. It is a rare finding that is often associated with temperature- independent antibodies that are formed against platelet antigens, modified by anticoagulants. They cause in vitro clumping and falsely reduced platelet values by the automated analyzer. Various studies have reported this phenomenon in around 0.09- 0.21% of the population [2]. We would like to present an incidental finding of pseudothrombocytopenia in our hospital.

Case Report

A 45 year old female (IP- A014245/13) presented with intermittent episodes of loose stools since past 3 months and low grade fever since 1 month back. The patient gives the history of atleast 4 episodes of loose stools per day. She gives no history of blood in the stools, nor episodes of itching or rash. She had no significant past history except a hysterectomy 4 years ago. Blood investigations were sought and her blood was collected in the EDTA vacutainer. Her initial blood investigations on the automated analyzer showed relative lymphocytosis with severe thrombocytopenia (platelet counts on day of presentation were 56,000cells/L according to the analyzer). She was admitted to the medical ward for further evaluation. The patient was started on a course of antibiotics empirically. Blood investigations were done on all days of her admission. The patient's blood was collected in the EDTA vacutainer and stored in the fridge at 12°C, before running it in the automated analyzer. On the days that followed, the patient continued to have low platelet counts on the analyzer (within the range of 20,000- 60,000) even though the white cell returned to normal distribution. Serological tests for HIV and Hepatitis B were negative. In the meanwhile, the patient had received transfusion of a unit of platelets, as well as surgery consultation. A careful examination of the patient's peripheral smear revealed large clumps of platelets, along with giant platelets (Figure 1and 2). Serial smears on the subsequent days also showed the clumping of the platelets. With absolutely no positive history, normal clinical examination and negative test results, we thought of pseudothrombocytopenia, considering the persistently clumped platelets that we saw in the peripheral smear. A finger prick smear was made. The platelets showed no clumping with near normal counts (Figure 4). We repeated smear with blood collected in EDTA and citrate vacutainer, stored at room temperature and within the fridge, and repeated finger prick sample. Platelet clumping was seen in smears made from both sets of vacutainer, stored in room temperature and in the fridge. The finger prick sample again showed no clumping and a near normal count. Hence, we have come to the conclusion of anticoagulant induced pseudothrombocytopenia in our patient. Had we arrived at our diagnosis earlier, we could have spared the patient days of hospital admission and a platelet transfusion.

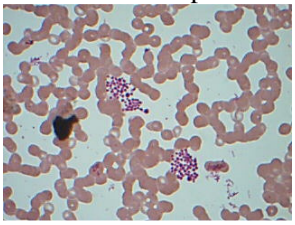

Figure 1: Platelet clumps seen in the EDTA sample (Leishman stain; 40X)

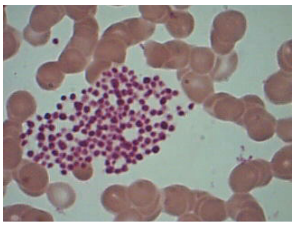

Figure 3: Platelet clumps in citrate sample (Leishman stain; 100X)

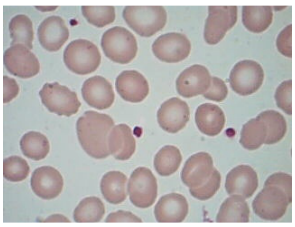

Figure 4: Individual platelets seen with finger prick sample (Leishman stain; 100X)

Discussion

Thrombocytopenia, or reduced platelet counts, may be caused by either impaired platelet production, (due to various factors like infections, drugs, myelofibrosis, etc), or increased destruction of the platelets (due to infections, idiopathic thrombocytopenic purpura, disseminated intravascular coagulation, etc), or sequestration by the spleen. When other inciting factors are all ruled out, the possibility of pseudothrombocytopenia may be considered. Pseudothrombocytopenia is a rare finding, caused by autoantibodies formed against platelet membrane glycoproteins or anionic phospholipids that are modified by the anticoagulants and cold temperature, especially calcium chelating agents [3]. It has been reported that the majority of these antibodies are Ig G, although Ig M and Ig A antibodies have also been described in studies [4, 5]. In the case of EDTA- induced pseudothrombocytopenia, antibodies are found to be most reactive with the GP IIb/IIIa molecule found on the platelet surface after the calcium chelating effect of EDTA exposes the GP IIb molecule, hence causing agglutination [8]. In Bizarro studies, he confirmed that in vitro clumping was a gradual process and was most likely to develop in room temperature than in body temperature. Although healthy individuals also present with this phenomenon, the incidence is higher with patients with viral infections (like hepatitis A, rubella, cytomegalovirus, influenza A, etc), trauma, autoimmune disorders, and neoplasm. With the extensive use of vacutainers, anticoagulants and automated analyzers, the cases of pseudothrombocytopenia may be easily misdiagnosed, and the patients may be subjected to unwarranted days of hospital admissions, unnecessary treatments and surgeries, and possibly hazardous platelet transfusions. Microscopic examination of the peripheral smear is the only way to lead us to consider the possibility of pseudothrombocytopenia, provided that all other causes of low platelet counts are ruled out.

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