Extreme Thrombocytosis—An Unusual Presentation of Inflammatory Bowel Disease

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Abstract

Thrombocytosis or a high platelet count (a count greater than 400×10^9/L) is a common observation especially with the increased ordering of routine complete blood counts. When found, it may create a diagnostic challenge as transient elevations in platelet counts can occur for a number of reasons such as inflammation or infection, and these usually resolve spontaneously; but an elevated platelet count may be the only indication of an underlying serious disease to which no other clinical findings pertain. The report details a case of extreme thrombocytosis which masked an underlying diagnosis of inflammatory bowel disease.

Key words: inflammatory bowel disease, platelet, thrombocytosis

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Introduction

A high platelet count is a common finding in hospitals and is often not due to a primary bone marrow problem. A secondary cause can be identified in most of the cases and as such the associated symptoms need to be sought and investigated earnestly in a patient with thrombocytosis. A high platelet count should be considered a diagnostic clue rather than a diagnosis in itself.

Case Report

A 25-year-old woman initially presented to the hospital with abdominal pain associated with several episodes of vomiting and diarrhea one month after the delivery of her son. She was seen in the casualty where the possibility of obstetric complications was ruled out. Stool cultures were negative and she was treated as an outpatient with advice on adequate rehydration. Even after a week of rest and fluid intake, she continued to be extremely fatigued with a bowel frequency of twice a day. A second visit to the family practitioner initiated some blood tests, which demonstrated a mean hemoglobin concentration (Hb) of 11.0 g/dL, mean corpuscular volume (MCV) of 93 fl, white blood cell count (WCC) of 10.5×10^9/L and a platelet count (plt) of 1,963×10^9/L. A repeat blood test was arranged after a week. As the platelet count continued to be high, a hematology referral was made. At presentation, the patient did not report any features of associated vasomotor symptoms like erythromelalgia, or any hemorrhagic or thrombotic complications, which may be observed in patients with very high platelet counts. Common causes of reactive thrombocytosis such as iron deficiency (normal MCV and serum ferritin of 89 ng/mL) and splenic hypofunction (no Howell Jolly bodies or target cells on the blood smear) were also ruled out. The platelet count being persistently high suggested the possibility of essential thrombocythemia (ET) and a bone marrow examination was performed. The test was not conclusive with any evidence of increased fibrosis or megakaryocyte clusters on the trephine biopsy. Cytogenetic analysis was not beneficial, but JAK 2 mutation analysis was negative. [JAK 2 mutation has recently been found to be useful for the diagnosis of myeloproliferative diseases and is positive in about 50% of cases of essential thrombocythemia.] She was started on aspirin and hydroxycarbamide for the extremely high platelet count. A thorough discussion on hydroxycarbamide about the benefit of reducing the platelet count and the rare risks of leg ulcer and very minimal risk of acute leukaemia was discussed with the patient before commencing the drug. However, the hydroxycarbamide medication had to be stopped in a month because the patient developed...
mouth ulcers and an urgent follow-up was arranged for consideration of alternative treatment for the thrombocytosis in the form of anagrelide or interferon.

A further diarrheal illness brought her back to casualty six weeks after her initial presentation when she was found to have blood and mucus in her stools. Direct questioning revealed a history of loose bowels up to 5 times a day for about five months, which raised the suspicion of inflammatory bowel disease (IBD).

Clinical examination demonstrated diffuse abdominal tenderness. There was also evidence of mouth ulcers and patchy hair loss. These were attributed on a previous occasion to hydroxycarbamide and the drug was stopped with no resolution of the symptoms. The repeat Hb was 10.4 g/dL, WCC of 13.2×10^9/L, plt of 1,430×10^9/L. The erythrocyte sedimentation rate (ESR) was elevated at 56 mm/hr and C-reactive protein (CRP) was high at 44 mg/l. Abdominal radiography on this admission showed dilated loops of large bowel with edema (Fig. 1). Computerized tomography scan confirmed these findings (Fig. 2). Gastrointestinal endoscopy and biopsy revealed inflammatory infiltrates of the bowel wall (see Figs. 3, 4). The assessment of gastrointestinal tract demonstrated mucosal ulcers mainly in the distal ileum and the ascending colon and a diagnosis of IBD (Crohn’s disease) was made. The possibility of ischemic colitis was ruled out because of the recurrent episodes of diarrhea, the associated systemic signs of hair loss and mouth ulcers and also the absence of ischemia on the biopsy.

The patient was commenced on mesalazine and steroids for the treatment of the inflammatory bowel disease. The abdominal symptoms soon improved and her platelet count normalized (less than 400×10^9/L) after eight weeks of treatment without any definitive therapy for the thrombocytosis. Surprisingly, with every relapse of the bowel disease, she develops a platelet count of around 1,000×10^9/L, which settles with the active treatment of the IBD.

**Discussion**

A high platelet count or thrombocytosis is most often due to a secondary cause rather than a primary bone marrow disorder. If confirmed by repeat testing, the initial step is to perform a comprehensive history and physical examination. It is also important to determine, using available records when possible, the duration of the patient’s thrombocytosis. The longer, the high platelet count has persisted, the chances
of it being due to a primary cause is more likely though not imperative. At the same time, a high platelet count is more commonly caused by a reactive process in the general population. In a series of 732 medical and surgical patients with platelet counts of 500×10^9/L or higher, 643 (88 percent) had secondary thrombocytosis; the most frequent underlying causes were major surgery, infection, cancer, and chronic inflammation (1). It is also important to stress here that the degree of elevation in the platelet count does not clearly differentiate primary from reactive thrombocytosis. In a series of 280 consecutive hospitalized patients with platelet counts of 1000×10^9/L or higher, 231 (82 percent) had reactive thrombocytosis, 11 (4 percent) had thrombocytosis of uncertain cause, and only 38 (14 percent) had primary cause (2).

Thus, a thorough search for an underlying systemic disease is mandatory before attributing the high count to a bone marrow problem.

The observation that active IBD is associated with thrombocytosis has been noted as early as 1968, where three out of the six patients were given myelosuppressive treatment (busulphan) (3). The incidence of thrombocytosis in IBD has not been thoroughly examined, though the results of an interesting observational analysis by Harries et al of 212 adult patients with infective diarrhea and 27 with IBD is noteworthy (4). The platelet count was greater than 450×10^9/L in 59% patients with IBD while only 1.6% patients with infective diarrhea had a similarly high count. They even concluded that a raised platelet count in a patient admitted to hospital with ‘acute gastro-enteritis’ suggests IBD.

The role of platelets in IBD is now well established in literature (3). Irving et al described the increased frequency of thromboembolic complications occurring in patients with IBD due to the involvement of platelets (5). Increased platelet activation and aggregation have been demonstrated to be the features of IBD and has been proposed to contribute to the pathogenesis of mucosal inflammation seen in the condition (6). Platelet count has also been shown to correlate with disease activity in IBD but has not been widely accepted as a prognostic marker in clinical practice as there are other factors such as hemorrhage from the bowel, and iron deficiency anaemia which can cause an elevation of the platelet count (7).

Reactive thrombocytosis secondary to IBD usually resolves when the bowel disorder is treated successfully. While the systemic condition is being managed, it is only necessary to check the platelet count occasionally (like once a week). The dilemma arises when the platelet count is very high (over 1,000×10^9/L) at presentation as in the present case. Though the chance of thrombosis is extremely rare with reactive thrombocytosis, some hematologists tend to give an anti-platelet agent or low molecular weight heparin in these circumstances especially if there is another coexisting risk factor for thrombosis (8). It is important to bear in mind that IBD itself is a risk factor for thrombosis because of the inflammatory nature of the condition and the associated factors like dehydration and relative immobility. Additional caution with the antiplatelet drugs is also required in these situations as those with very high platelet counts (over 1,500×10^9/L) generally have a bleeding tendency as well (9).

In summary, a high platelet count is not a rare event in the acutely ill patient with inflammatory bowel disease. It usually represents a reactive phenomenon and may be considered as a prognostic marker for the bowel disease in combination with other inflammatory markers.

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References


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