Case Report

Post Hemorrhoidectomy Bleeding Caused by Thrombocytosis Induced Coagulopathy

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Thrombocytosis sometimes results in complications of thrombosis or bleeding. It is classified to two types. Primary thrombocytosis is myeloproliferative disorder (autonomous). Secondary thrombocytosis can be traced to another cause, such as inflammation, severe bleeding, iron deficiency, or malignancies. We report a patient with primary thromobocytosis with both postoperative bleeding and thrombotic complications.
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Key Words
Thrombocytosis;
Bleeding;
Thrombosis

It is well known that low platelet counts increase bleeding risks. However, high platelet counts sometimes may also lead to bleeding or thrombosis.

We report a case of post hemorrhoidectomy bleeding caused by thrombocytosis induced coagulopathy.

Case Report

A 54 year-old man presented with rectal bleeding and anal pain with bowel movement for a few days. He received bilateral vasectomy 10 years ago and had history of gout for 7 years. Grade IV Hemorrhoids was diagnosed. Laboratory data showed hemoglobin was 18.4 mg/dl, hematocrit was 54.9%, WBC was 13200/uL. Platelet was 865,000/uL. PT and APTT were normal. He underwent closed Ferguson hemorrohoidectomy and was discharged 2 days later. He presented to ER with massive anal bleeding on the third postoperative day. Fever was up to 38 °C and leukocytosis (WBC 16100/uL) was found in ER. Thrombocytosis may be resulted from wound infection and postoperative status. Antibiotics were administered and a Foley balloon tamponade of the rectum was performed. The bleeding was stopped. Twelve days later, he complained of passage of fresh red bloody stool again. Laboratory data showed hemoglobin was 13.0 mg/dl, hematocrit was 37.4%, WBC was 21000/μL, platelet was 1476000/μL, PT was 12.9 with control of 11.0 sec, APTT was 31.0 with control of 30.0 sec, bleeding time was 2'30''. Bleeding was stopped after Foley balloon tamponade. Abdominal sonography revealed fatty liver. Hematologist was consulted and bone marrow biopsy was performed. Essential thrombocythemia was diagnosed. Hydroxyurea was administered for treatment of essential thrombocythemia. Then, it was shifted to anagrelide due to nausea and malaise. He suffered from small in-

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farction of left temporal lobe 15 months later and chest wall subcutaneous hematoma 3 years later.

Discussion

A normal platelet count in a healthy adult is between 150,000 and 450,000/μl (microliter) (150-450 $\times 10^9$/L) of blood. Thrombocytosis is defined as a platelet count exceeding the top of the normal range.

Thrombocytosis is classified to two types. Primary thrombocytosis is the result of myeloproliferative disorder (autonomous), including polycythemia vera, essential thrombocythemia, chronic myeloid leukemia, myelofibrosis, myelodysplastic syndromes.[1] Secondary thrombocytosis (reactive thrombocytosis) may be caused by increased release of a number of cytokines in response to infections, inflammation, vasculitis, tissue trauma, and other factors.[2] It is often a transient reaction which resolved when the underlying cause is subsided. It is also known as reactive thrombocytosis (RT).

Secondary thrombocytosis (RT) is much more frequent than primary thrombocytosis in both children[3,4] and adults.[5,6] Buss reported a study of 280 consecutive patients with extreme thrombocytosis (platelet count > 1,000,000/μL), RT was diagnosed in 82% and myeloproliferative disorder in 14%, cases of uncertain etiology in 4%. The causes of secondary thrombocytosis included infection (31%), postsplenectomy (19%), malignancy (14%), trauma (14%), noninfectious inflammation (9%), postsurgical status with infection, postsurgical status, and acute blood loss or iron deficiency (6%).[7] (Table 1) High platelet count does not necessarily present any clinical problems, and are discovered by routine complete blood count. High platelet count has the potential to develop thrombosis or bleeding.[8] Thrombosis in the brain causes symptoms with headache, transient ischemic episodes and symptoms (including dizziness, dysarthria, syncope, migraine, seizures).[9] Thrombosis in the tiny blood vessels of the hands and feet leave them numb and red. This may lead to an intense burning and throbbing pain felt mainly on the palms of the hands and the soles of the feet.[10] Bleeding complications involve the skin and mucous membranes primarily and may also involve eyes, gums, skin and brain. The rates of significant thrombosis and hemorrhage for patients with primary thrombocytosis were both 24%, while they were 1% and 3% for patients with reactive thrombocytosis respectively.[7] The degree of thrombocytosis cannot predict the possibility of primary thrombocytosis.[7,11]

Table 1. Causes of secondary (reactive) thrombocytosis

Acute blood loss
Iron deficiency anemia
Hemolytic anemia
Postsplenectomy
Malignancy
Infection
Chronic inflammations and vasculitis (e.g., rheumatoid arthritis, inflammatory bowel disease)
Tissue damage (postsurgical, burns, trauma, fracture, acute pancreatitis)
Recovery from thrombocytopenia (e.g., bleeding, cancer chemotherapy)
Drug reactions (Vincristine, All-trans-retinoic acid, cytokines, growth factors)

There are presently no diagnostic tests that can definitively distinguish between primary and secondary (reactive) thrombocytosis. Once thrombocytosis was found, repeat testing, peripheral blood smear and serum ferritin level should be performed. The risks for developing polycythemia vera, essential thrombocythemia, or associated vascular complications in persons with thrombocytosis were low. The patients with thrombocytosis were only 8 of the 99 patients (8%) on repeat testing at a median interval of eight months (range from 6 to 14 months).[12] (Table 2)[18]

If thrombocytosis is confirmed by repeat testing, further examinations should be undertaken to differentiate whether the high platelet count is secondary or primary. The first step is to take complete history and physical examination. The initial evaluations should exclude many of the common causes of reactive thrombocytosis. Special attention should include recent trauma or surgery, prior splenectomy, local or systemic complaints suggesting infection or inflammation, present and past history of bleeding, thrombosis, iron deficiency, or malignancy.

For the differentiation of secondary from primary thrombocytosis, Messinezy et al found determination of acute-phase reactants (for example, erythrocyte

Table 2. The World Health Organization criteria for the diagnosis of ET

- Sustained platelet count ≥ 450 × 10(9)/L[a]
- Bone marrow biopsy specimen showing proliferation mainly of the megakaryocytic lineage with increased numbers of enlarged, mature megakaryocytes; no significant increase or left-shift of neutrophil granulopoiesis or erythropoiesis
- Not meeting WHO criteria for PV[b], PMF[c], CML[d], MDS[e] or other myeloid neoplasm
- Demonstration of JAK2 617 V > F or other clonal marker, or in the absence of a clonal marker, no evidence for reactive thrombocytosis[f]

Diagnosis requires meeting all 4 criteria.

[a] During the work-up period.

[b] Requires the failure of iron replacement therapy to increase hemoglobin level to the PV range in the presence of decreased serum ferritin. Exclusion of PV is based on hemoglobin and hematocrit levels, and red cell mass measurement is not required.

[c] Requires the absence of relevant reticulin fibrosis, collagen fibrosis, peripheral blood leukoerythroblastosis, or markedly hypercellular marrow for age accompanied by megakaryocyte morphology that is typical for PMF-small to large with an aberrant nuclear/cytoplasmic ratio and hyperchromatic, bulbous or irregularly folded nuclei and dense clustering.

[d] Requires the absence of BCR-ABL.

[e] Requires absence of dyserythropoiesis and dysgranulopoiesis.

[f] Causes of reactive thrombocytosis include iron deficiency, splenectomy, surgery, infection, inflammation, connective tissue disease, metastatic cancer, and lymphoproliferative disorders. However, the presence of a condition associated with reactive thrombocytosis does not exclude the possibility of ET if the first three criteria are met.

sedimentation rate [ESR]) is most useful.[13] Blood ESR, C-reactive protein (CRP) level, fibrinogen level, factor VIII procoagulant activities, and von Willebrand antigen values are significantly elevated in patients with secondary thrombocytosis, whereas they were normal in patients with primary thrombocytosis.[14,15]

When persistent thrombocytosis of undetermined cause presents, searching for occult cancer should be performed thorough physical examination, including examination of stool occult blood, chest radiography and the abdominal sonography to find undetected sources of infection, inflammation or malignancy.

When the clinician is confronted with treatment decisions, determining the cause of thrombocytosis becomes especially critical. Patients with RT do not require treatment because their abnormal platelet count does not have risk for bleeding or thrombotic events. Treatment should be directed to the underlying disease.

In primary thrombocytosis with hemorrhage complications, the first step is to discontinue the use of any platelet antiaggregating agent (such as nonsteroidal antiinflammatory drugs). Initial laboratory evaluation should include a workup for disseminated intravascular coagulation and coagulation factor deficiency. Acquired factor V deficiency is sometimes seen in association with primary thrombocytosis and is treated with fresh frozen plasma infusion or platelet concentrates.[16]

In the case of thrombosis with platelet count greater than 800,000/μL, immediate platelet apheresis is recommended. Therapy with a platelet-lowering agent should be started with the goal of keeping the platelet count below 400,000/μL.[17]

Conclusions

When thrombocytosis was found in a patient prior to surgery, differentiating between primary and secondary thrombocytosis is important and difficult. Secondary thrombocytosis does not result in hemorrhage or thrombotic complications, but the underlying problems must be identified and treated. In contrast, primary thrombocytosis is associated with thrombotic and bleeding complications. Patients with high risk of complications should receive prophylactic platelet-lowering therapy.

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病例報告

因血小板過高引發的痔術後出血

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血小板過高可能發生血栓或出血的併發症。它可分爲原發性和繼發性兩種。原發性血小板增多症 (Essential thrombocytosis) 屬骨髓增生性疾病，次發性血小板增多症 (Secondary thrombocytosis) 則是因其他疾病所引起的，包括慢性炎症、出血、鐵質缺乏或是惡性腫瘤等因素。我們經歷一個痔瘡手術前發現有血小板過高的病患，術後發生兩次肛門出血，後來診斷爲原發性血小板過多症 (Essential thrombocythemia) 的病例。

關鍵詞　血小板增多、出血、血栓。