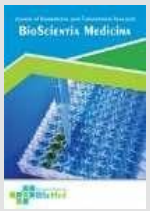
eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Essential Thrombocythemia in Young Women

Anggit Pungkas Wibowo[1*], Eifel Faheri[2]

[1]Internal Medicine Study Program, Specialized Residency Training Program, Faculty of Medicine, Universitas Andalas, Padang, Indonesia

[2]Division of Hematology Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Universitas Andalas/Dr. M. Djamil General Hospital, Padang, Indonesia

ARTICLE INFO

Keywords:
Cytoreductive therapy
Essential thrombocythemia
JAK2 gene

***Corresponding author:**
Anggit Pungkas Wibowo

E-mail address:
anggitpewe@gmail.com

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v7i9.857

A B S T R A C T

Background: Essential thrombocythemia (ET) is a rare disease in which there is an increase in the platelet count of more than 450,000/mm^3. An increase in the number of platelets occurs due to increased proliferation of megakaryocyte series. Although there is an increase in the number of platelets in ET, it has impaired function. ET clinical manifestations in 50% of cases are asymptomatic, but in symptomatic cases can be vascular occlusive events or microvascular thrombosis. **Case presentation:** A 22-year-old woman with complaints of rash on the hands and feet. Physical examination found an enlarged spleen in Schuffner 1 and ecchymosis on the arms and legs, a platelet count of 811,000/mm^3. The peripheral blood smear shows large platelets, the bone marrow picture shows megakaryocytes, which are very easy to find, the size varies with sufficient platelet emission, the JAK2 gene mutation examination shows mutation detection, while the BCR-ABL gene mutation results do not detect gene fusion. Treatment is given cytoreductive therapy in the form of hydroxyurea, while acetylsalicylic acid is not given because there are contraindications for administration. **Conclusion:** Essential thrombocythemia is a neoplastic proliferative disease that occurs in the megakaryocyte series. The diagnosis of ET mostly found mutations in the JAK2 gene. ET management according to risk classification, where acetylsalicylic acid can be given very low and low risk, while intermediate and high risk can be given cytoreductive therapy.

1. Introduction

Essential thrombocythemia is a clonal stem cell disorder hematopoietic multipotential belonging to the myeloproliferative neoplasm group with predominant phenotype expression in the megakaryocyte pathway. Essential thrombocythemia with a prevalence of 24 : 100,000 population in the United States. ET prevalence is higher in women compared to men. Approximately 50% of cases diagnosed with THE were first discovered accidentally during a routine blood test. The most common essential thrombocythemia is found at an average age of 50 years. The cause of essential thrombocythemia is most often caused by mutations in the protein tyrosine kinase JAK2. A study by Accurso et al. found that JAK2 contributed to the reduction of receptor expression of thrombopoietin.[1]

The clinical manifestations of ET can be vascular occlusive events and microvascular thrombosis. Vascular occlusive events include major thrombotic events involving the cerebrovascular, coronary, and peripheral arterial circulation. Clinical manifestations essential thrombocythemia. Most arise from arterial and microvascular thrombotic events. Microvascular thrombosis can cause erythromelalgia, headache, paresthesia, digital ischemia, and necrosis. Erythromelalgia manifestations, including erythema, pain, and warmth.[1,2]

2. Case Presentation

A 22-year-old woman was treated in the internal medicine ward of Dr. M. Djamil General Hospital, Padang, with the main complaint of blueness on the arms and thighs. Complaints accompanied by numbness, tingling in the fingertips, and headaches. Physical examination found a palpable spleen on Schuffner 1's line. Examination of the extremities found ecchymosis in the form of well-defined erythematous macules with a negative diascopy test. On laboratory examination obtained, hemoglobin 13.2 g/dl, leukocytes 8850/mm^3, platelets 811,000/mm^3, PT 10.4 seconds, aPTT 30.6 seconds, and D-dimer 503ng/ml. On examination of the peripheral blood smear, large platelets were found.

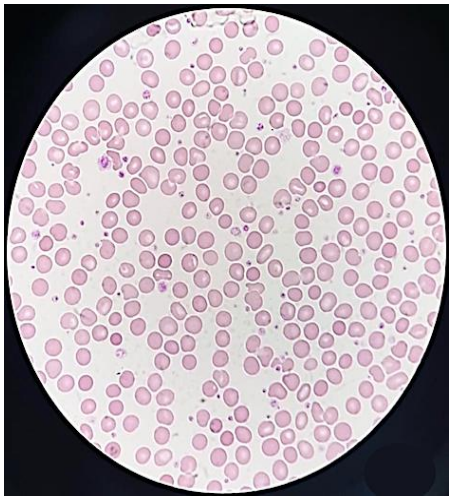
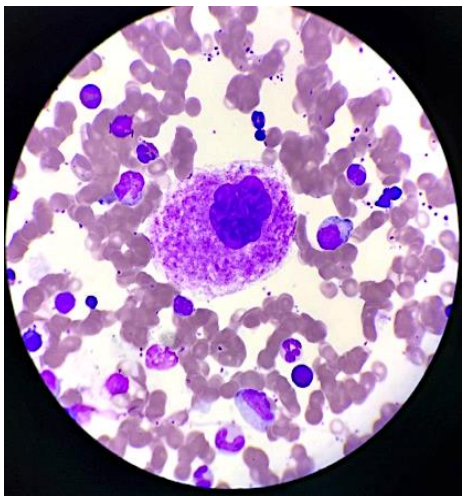
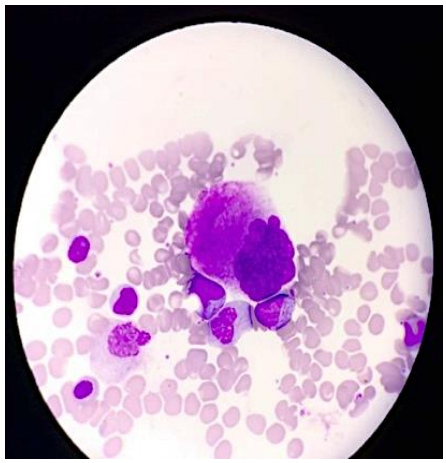


Figure 1. Patient's peripheral blood smear.

The diagnosis of the patient is carried out by examination of bone marrow puncture (BMP), JAK2 gene mutations, and BCR-ABL gene mutations. The results of the bone marrow images obtained megakaryocytes, which are very easy to find, varying in size with sufficient platelet emission. The results of the bone marrow picture are consistent with essential thrombocythemia. In the JAK2 gene mutation examination, the results detected mutations, while the BCR-ABL gene mutation results did not detect gene fusion.





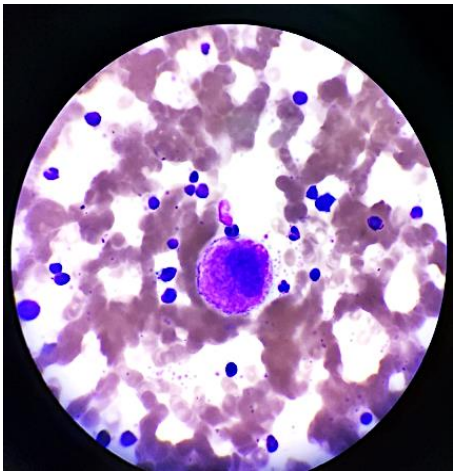


Figure 2. Imaging of the patient's bone marrow.

Management of patients during treatment is given Hydroxyurea 3 x 500 mg as cytoreductive therapy, while treatment during control at the polyclinic according to the low-risk category will be given low doses of acetylsalicylic acid once per day. Relevant patient education on vascular occlusive events and microvascular thrombosis, such as cerebrovascular, coronary, and peripheral arterial symptoms.

3. Discussion

The diagnosis of essential thrombocythemia found in patients such as numbness, tingling at the fingertips, and headache. Physical examination revealed erythematous macules and splenomegaly. Routine blood investigations found thrombocythemia, and the peripheral blood picture showed large platelets. On the results of the bone marrow picture, megakaryocytes were found, which were very easy to find and varied in size with sufficient platelet emission. A genetic examination revealed a JAK2 gene mutation.[1] A study by Babakhanlou et al. demonstrated that the manifestations of bleeding or thrombosis in ET occur mainly in cases of platelet counts exceeding 1,000,000/mm^3. Bleeding is most often in the skin with the manifestation of bruising, subcutaneous hematoma, or ecchymosis. In addition, epistaxis, gum bleeding, or gastrointestinal manifestations may occur but not in severe conditions, except in patients who received aspirin or anticoagulants previously.[2] Bleeding manifestations can be through several mechanisms such as abnormal platelet function, thrombosis with ulcerated infarction, coagulation consumption overproduction, and overproduction of prostacyclin (PGI_2) as a result of

an increase in the number of platelets resulting in suppression of release granule on platelets, as well as decreased ability of platelet aggregation.[2,3]

Another study by Tefferi et al. shows that vascular occlusive events may occur in the microvascular, which can be a clinical symptom of ET. thrombus microvessels can cause erythromelalgia, headache, paraesthesia, finger ischemia, and necrosis. In addition, extramedullary hematopoiesis may occur in the liver or spleen. Splenomegaly is present in up to 20% to 50% of patients. Enlargement of the spleen occurs in ET patients with mild to moderate degrees and tends not to be progressive, whereas hepatomegaly can occur in 15% to 20% of cases.[4-6] The increase in the number of platelets that occurs in ET varies from an increase slightly above normal to a number of million/mm^3. In some cases, anemia and leukocytosis can be found. Other signs of ET on laboratory examination pictures of peripheral blood smears, namely platelets that are clumpy and abnormalities in shape, size, and structure, can be found in giant thrombocytes. Occasionally, fragments of megakaryocytes are found.[5,6] The diagnosis of ET can be made using the Campbell and Green criteria or other criteria of the World Health Organization (WHO). Criteria Campbell and Green include a platelet count of more than 600,000/mm^3 present for at least 2 months, JAK2 mutation is present, no cause of reactive thrombocythemia is found, no evidence of iron deficiency, no evidence of polycythemia vera, no evidence of chronic myeloid leukemia, no evidence of myelofibrosis, there was no evidence of myelodysplastic syndromes. WHO criteria, the diagnosis of ET can be made if all of the major criteria are met or 3 major criteria plus minor criteria. Major criteria include platelet count ≥ 450,000/mm^3, bone marrow picture showed increased proliferative activity of megakaryocytes with hyper lobulated nuclei, no mutations in the BCR-ABL gene were found, no criteria for polycythemia vera, primary myelofibrosis, or other myeloid neoplasms were found. There are mutations in the JAK2, CALR, or MPL genes. While minor criteria include no evidence of reactive thrombocythemia.[5-7]

Management in this case study was given according to the low-risk category because the patient did not have a cardiovascular risk, was under 60 years of age, and had a JAK2 gene mutation. Management of these patients are given antiplatelet aggregators such as low doses of acetylsalicylic acid (80-100 mg/day) to control thrombotic manifestations. However, in patients, there are contraindications for administering acetylsalicylic acid, namely bleeding under the skin (ecchymosis), so patients are given hydroxyurea as the first choice cytoreductive therapy in ET.[5,7,8] Hydroxyurea works to inhibit cell synthesis by inhibiting the activity of ribonucleoside diphosphate enzyme reductase. This enzyme reduces ribonucleotide catalysis, thereby inhibiting cell synthesis. The side effects of hydroxyurea are suppression of the bone marrow, gastrointestinal disturbances such as nausea, vomiting, and diarrhea, and can cause skin changes in the form of rashes and ulcerations on the legs and feet. alopecia. The dose of hydroxyurea given is 15 mg/kg BW, provided that the hemoglobin is ≥ 10 g/dl.[9,10] JAK2 gene mutation is a key diagnostic criterion for ET that has the potential to be given targeted therapy. Targeted therapy for JAK2 inhibitors (ruxolitinib) works by suppressing signals stimulated by JAK2 receptors, which will reduce the number of platelets. Studies by Gunawan et al. showed that the administration of ruxolitinib was more effective in reducing the number of platelets than hydroxyurea. Furthermore, administration of ruxolitinib can avoid transformation into other myeloproliferative, which can occur when hydroxyurea is administered.[11,12]

4. Conclusion

Essential thrombocythemia is a neoplastic proliferative disease that occurs in the megakaryocyte series. The diagnosis of ET mostly found mutations in the JAK2 gene. ET management according to risk classification, where acetylsalicylic acid can be given very low and low risk, while intermediate and high risk can be given cytoreductive therapy.

5. References

1. Accurso V, Santoro M, Mancuso S, Napolitano M, Carlisi M, Mattana M et al. The essential thrombocythemia in 2020: What we know and where we still have to dig deep. Clin Med Insights: Blood Disord. 2020; 13: 1-8.
2. Babakhanlou R, Masarova L, Verstovsek S. A review of essential thrombocythemia and its complications. Clin Adv Hematol Oncol. 2023; 21: 76-84.
3. Brière JB. Essential thrombocythemia. Orphanet J Rare Dis. 2007; 2(1): 1-7.
4. Tefferi A, Barbui T. Polycythemia vera and essential thrombocythemia: 2021 update on diagnosis, risk-stratification and management. Am J Hematol. 2020; 95(12): 1599-613.
5. Bleeker JS, Hogan WJ. Thrombocythemia: diagnostic evaluation, thrombotic risk stratification, and risk-based management strategies. Thrombosis. 2011: 1-16.
6. Tefferi A, Vannucchi AM, Barbui T. Essential thrombocythemia treatment algorithm 2018. Blood Cancer J. 2018; 8(1):2.
7. Wahid, I. Trombositosis Esensial. In: Setiati S, Alwi I, Sudoyo AW, Sinadibrata M, Setiyohadi B, Syam AF, editor. Textbook of disease. In. Jakarta: Interna Publishing. 2014; 2767–71.
8. Tefferi A, Pardanani A. Essential thrombocythemia. N Engl J Med. 2019; 381(22): 2135-44.
9. Keohane C, Harrison C. Essential thrombocythemia: new advances in an old disease. Clin Invest. 2012; 2(6): 603-14.
10. Harrison CN, Campbell PJ, Buck G, Wheatley K, East CL, Bareford D, et al. Hydroxyurea compared with anagrelide in high-risk essential thrombocythemia. N Engl J Med. 2005; 353(1): 33-45.
11. Gunawan A, Harrington P, Garcia-Curto N, McLornan D, Radia D, Harrison C. Ruxolitinib for the treatment of essential thrombocythemia. HemaSphere. 2018; 2(4): 1-7.
12. Jiang JJ, Wang XY, Zhang Y, Jin Y, Lin J. Advances in the inhibitors of Janus kinase. Med Chem. 2014; 4(8): 540-8.