A Case Report: Essential Thrombocytosis Jak2 Positive Mutation Initially Refractory to Hydroxyurea

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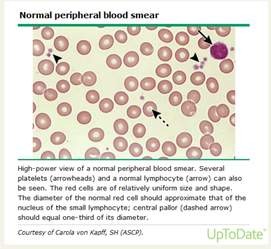
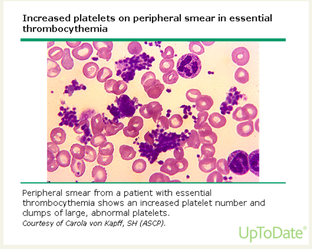
Introduction

- Essential Thrombocytosis (ET) is a rare disorder in which the body produces too many platelets for unknown reasons.
- ET is one of the myeloproliferative neoplasms.
- It can occur at any age, although there is an unexplained predominance for middle age adults particularly females.
- ET occurs from gene mutations such as Janus Kinase 2 (JAK2V617F), myeloproliferative leukemia virus oncogene mutation (MPL) and Calreticulin (CALR) in hematopoietic stem cells. Approximately 55% of patients express the JAK2V617F.
- ET has no specific symptoms or clinical signs; however common clinical presentation is thrombotic or hemorrhagic events such as migraines, TIA, easy bruising, bleeding, and erythromelalgia.
- Physical examination is usually unremarkable however, splenomegaly can occasionally be seen.
- Essential thrombosis is diagnosed when the platelet count is more than 450000 with the presence of JAK2, CALR, or MPL and clinical finding of thrombocytosis.
- In this case presentation, we present an uncommon case of medical refractory ET treated by an unusual treatment.

Case Report

- A 61-year-old male presented to the emergency department with worsening dizziness over the last 48 hours. The episodes of dizziness come in clusters and last for a few minutes and then go away without any modifying factors. He felt that some of the episodes felt like the room was spinning. The dizziness is exacerbated with any sort of exercise or physical activity and occasionally results in bilateral paresthesia to the hands. He had recently seen a hematologist outpatient for a workup of thrombocytosis incidentally found by his primary care physician.
- Laboratory workup initially showed thrombocytosis with a platelet count of 968,000 cells/microliter, hemoglobin of 16 g/d, WBC 17.71x10^3/uL, and HCT 48.7%. He also had an AKI with Cr 1.330 mg/dL, and eGFR 57 along with a mild increase in troponins of 0.063 to 0.102. Lastly, his serum was positive for Jak2 mutation by PCR. Electrolytes, urinalysis and iron studies were all within normal limits.
- Peripheral smear showed thrombocytosis (Plt count 919/uL), neutrophilia (Neutrophil count 10.8/ ul) and monocytosis (Monocyte count 1.5 /uL).
- In the ER EKG showed sinus tachycardia with T wave inversions in V3-V6
- Patient was started on a heparin drip, given IV nitroglycerin and aspirin. Patient was also given meclizine for his dizziness. Cardiology, hematology and neurology were consulted.
- Head CTA showed no intracranial process or abnormality of the arterial vasculature of the head.
- Neck CTA showed no high-grade stenosis or evidence of dissection.
- Abdominal ultrasound showed mild splenomegaly
- Hematologist diagnosed him with Jak2 positive essential thrombocytosis and started him on hydroxyurea with the initial dosage of 500mg daily.
- Neurology evaluated the patient and did not suspect any underlying neuropathy, myelopathy or brain lesions. Recommendations included MRI brain and C-Spine along with outpatient follow-up.
- MRI Brain showed no intracranial process or any pathological enhancement.
- Cardiology ordered a TTE that showed a reduced ejection fraction of 40-45% and a possible thrombus. Heparin was started and a TEE was done showing no thrombus.
- He was then taken for cardiac catheterization and was found to have 95% left proximal LAD thrombotic lesion. A drug eluding stent was placed.
- The patient's presenting symptoms continued, and his course was complicated with platelets reaching 1,036,000. He was not responding to hydroxyurea despite increasing to maximal dosing over several days. Given the the patient was still symptomatic and medically refractory worsening ET, plateletpheresis was done which resulted in a significant reduction of his platelets to 434,000 along with symptomatic improvement.





Discussion

- Our patient presented with dizziness and bilateral paresthesia of the hands. His workup revealed thrombocytosis with a platelet count of 968,000 cells/microliter and PCR positive serum Jak2 mutations
- Other signs and symptoms include various levels of thrombosis including hepatic vein, migraines, headaches, dizziness, transient ischemic attack, erythromelalgia, and bruising. Our patient had thrombosis to his LAD along with dizziness, and mild splenomegaly.
- In our case hydroxyurea was started and platelets did not improve over several days despite increasing hydroxyurea to its maximum dose. The platelets got to be over 1 million and the patient was still symptomatic, resulting in the need of plateletpheresis to acutely decrease his platelets. This resulted in a 58 % reduction of his platelets along with significant symptomatic improvement. The patient's medical course was also complicated with a thrombus to the LAD, which resulted in a drug eluting stent.
- Patients with ET typically respond well to hydroxyurea therapy, however there are cases of ET that do not respond to hydroxyurea. For refractory cases, various treatments such as anagrelide or plateletpheresis can be tried. Overall, the best treatment option for ET depends on many factors including the severity of the condition, signs and symptoms present and each person's response to the therapies.

Conclusion

- Our case presents a patient with positive Jak2 essential thrombocytosis that did not respond to medical therapy and had to be plateletphereis.
- Pt has been following with hematology outpatient and his platelets have been well controlled with hydroxyurea and anagrelide.

References

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