Complete Hematologic Remission of Essential Thrombocythemia and Associated Myelofibrosis After Treatment with Anagrelide. A 12-year Follow Up

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Introduction

Essential Thrombocythemia (ET) is a myeloproliferative disorder characterized by proliferation of megakaryocytes, resulting in thrombocytosis. Treatment with anagrelide results in a significant reduction in platelet count by reducing megakaryocyte hypermaturation; however, it has been associated with increased risk of fibrotic progression. Scarce literature exists about anagrelide-induced complete remission of the disease on long-term treatment.

Clinical Case

We present a case of a 46 year-old female with no past medical history, who was diagnosed with ET in 2004 after the incidental discovery of thrombocytosis. At the time of the diagnosis, physical exam was unremarkable. Lab work was significant for thrombocytosis (993 K/µL), leukocytosis (13.3 K/µL), and normal hemoglobin level (13.9 g/dl). Comprehensive metabolic panel, coagulation profile, iron studies, vitamin B12 and folic acid levels were within normal limits. Peripheral smear showed increased platelet count with some large platelets; no blasts were identified. Consequently, bone marrow aspiration/biopsy was performed and showed hypercellular marrow, with moderate increase in number of megakaryocytes. Findings were consistent with myeloproliferative disorder, favoring ET. Cytogenetic testing, BCR/ABL gene rearrangement analysis, JAK-2 mutation and Philadelphia translocation were negative. Peripheral blood flow cytometry failed to detect any immunophenotypic evidence of B-cell or T-cell lymphoid neoplasm or acute leukemia. Patient was started on anagrelide 1 mg twice daily and aspirin 81 mg daily. Few months later, on a follow up visit, patient complained of fatigue and night sweats; physical exam was unremarkable. Lab testing revealed normalization of platelet count (176 K/µL), and drop in hemoglobin level (9.7 g/dl). Workup for hemolysis was negative. Peripheral smear showed giant platelets and tear drop cells. Bone marrow aspiration was attempted and failed due to dry tap. Biopsy demonstrated hypercellular marrow with marked reticulin fibrosis, and no blasts were identified. Findings were consistent with myelofibrosis. Treatment regimen was continued with reduced dose of anagrelide. Subsequently, the patient started showing gradual improvement of symptoms and lab work results, in which platelet count remained <400 K/µL and hemoglobin level approached the baseline. Given the clinical and lab work stability, anagrelide was discontinued in 2014. Bone marrow examination repeated in 2015 and showed normocellular marrow with no morphologic evidence of involvement by myeloproliferative neoplasia; adequate number of megakaryocytes was identified without significant clustering. Reticulin stain showed minimal reticulin fibrosis. Two years after discontinuing anagrelide, the patient remained asymptomatic with normal blood counts. No thrombotic or bleeding events were observed.

Discussion

As to our knowledge, complete remission of ET has been described in few case reports after treatment with interferon alpha and ruxolitinib, but not after anagrelide. In the above case that we followed over 12 years, treatment with anagrelide was associated with persistent complete hematologic response and bone marrow remission. More studies are needed to assess the long-term effects of anagrelide.

References:

1) Tefferi A1, Barbui T. Polycythemia vera and essential thrombocythemia: 2015 update on diagnosis, risk-stratification and management. Am J Hematol. 2015 Feb;90(2):162-73. doi: 10.1002/ajh.23895.
2) Harrison CN, Campbell PJ, Buck G, et al. Hydroxyurea compared with anagrelide in high-risk essential thrombocythemia. N Engl J Med 2005;353(1):33-45.
3) Quintas-Cardama A, Kantarjian H, Manshouri T, et al. Pegylated interferon alfa-2a yields high rates of hematologic and molecular response in patients with advanced essential thrombocythemia and polycythemia vera. J Clin Oncol
4) Cervantes F, Alvarez-Larran A, Talarn C, Gomez M, Montserrat E. Myelofibrosis with myeloid metaplasia following essential thrombocythaemia: actuarial probability, presenting characteristics and evolution in a series of 195 patients. Br J Haematol. 2002;118:786–90.
5) Juergen Thiele and Hans Michael Kvasnicka. Myelofibrotic transformation in essential thrombocythemia. Haematologica. 2009 Mar; 94(3): 431–433.
6) Yoon SY1, Li CY, Mesa RA, Tefferi A. Bone marrow effects of anagrelide therapy in patients with myelofibrosis with myeloid metaplasia. Br J Haematol. 1999 Sep;106(3):682-8.

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