

Case Study

Ruxolitinib as a therapy choice for refractory pruritus in a patient with essential thrombocythemia with CALR mutation

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Abstract

Refractory pruritus associated with Essential Thrombocythemia (ET) is rare. Herein, we present the first report of resistant pruritus responsive to ruxolitinib in an ET patient with a calreticulin mutation.

Introduction

Essential Thrombocythemia (ET) is a Chronic Myeloproliferative Neoplasm (CMPN) that leads to excessive platelet production. Cutaneous symptoms associated with ET include erythromelalgia, acrocyanosis, hematoma, ecchymosis, petechia, purpura, superficial thrombophlebitis, Raynaud's phenomenon, livedo reticularis, microcirculatory abnormalities such as ulceration and ischemic gangrene. Other dermatologic involvements include pruritus, urticaria, and xerosis. The reported incidence of pruritus in patients with ET has varied between 3% and 46% in different studies [1,2]. Ruxolitinib decreased the expression of cytokines and growth factors required for hematopoiesis by inhibiting JAK1/2- STAT pathways, which explains the improvement in polycythemia vera-associated pruritus [3]. We report a case of calreticulin (CALR) mutated ET with refractory pruritus.

Case

A 64-year-old man with a medical history of hypertension and hyperlipidemia presented with itching and burning in

both arms and legs. On admission; hemoglobin was 17.2 g/dL, leukocytes were 15900/mm³ and platelets were 578x10⁹/L. An increased number of platelets in large and several giant forms were seen in the peripheral blood smear. Abdominal ultrasonography showed the normal size of the liver and spleen. Molecular studies were negative for BCR/ABL1 t(9;22) (q34;q11.2), JAK2 and MPL515 mutations; CALR (type 2) mutation was positive. Bone marrow biopsy was hypercellular with no reticulin and fiber increase. After the diagnosis of ET, the patient who was using acetylsalicylic acid 81 mg/day and desloratadine 5 mg/day underwent regular phlebotomy, but hydroxyurea 500 mg twice daily was started because of persistent pruritus. Six months after using hydroxyurea; hemoglobin was 12.6 g/dL, leukocytes were 11400/mm³, platelets were 586x10⁹/L and despite taking hydroxyurea, the patient reapplied with refractory pruritus, which significantly affected the quality of life. Thereupon, ruxolitinib (5 mg twice daily) was initiated. At the next 2-month follow-up, hemoglobin was 15.4 g/dL, leukocytes were 14500/mm³, and platelets were 583x10⁹/L. Therewithal the patient reported complete resolution of pruritus and was very satisfied with the current treatment.



Discussion

Pruritus is a common symptom in CMPN patients and different treatment modalities have been shown to be beneficial, but clinical outcomes are highly variable. Histamine, leukotrienes and interleukin-31 release from mast cells in higher amounts than normal plays a role in the pathogenesis of pruritus in CMPN [4]. Pruritus often has a major impact on the quality of life of patients with ET [5]. Treatment of ET-associated pruritus is primarily empirical. Low-dose aspirin therapy has been shown to be effective in alleviating vasomotor (microvascular) disturbances associated with ET or PV [6]. Antihistamines are often prescribed to treat this condition, but they are usually not effective.

Although both phlebotomy and hydroxyurea treatment was applied to our patient, there was no improvement in pruritus and this pruritus seriously affected the quality of life. Hence, the patient was started on low-dose ruxolitinib (5 mg twice daily). Thus, it was observed that ruxolitinib treatment was effective regardless of platelet count and can be used safely in our patients diagnosed with ET having CALR mutation and refractory pruritus.

In conclusion, we suggest that ruxolitinib, which has proven its efficacy in the treatment of PV-associated refractory pruritus, can be used as an option in the treatment of ET-associated refractory pruritus.

Informed consent

Written informed consent was obtained from the patient.

Author contributions

Concept- KC, PP; Design- KC, PP; Data Collection or Processing- KC, PP; Analysis or Interpretation- KC, PP; Literature Search- KC, PP; Writing- KC, PP.

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