soho2023
ELEVENTH ANNUAL MEETING

MYELOFIBROSIS AND CONCURRENT LYMPHOPROLIFERATIVE DISORDER DURING JAKI THERAPY: COULD FEDRATINIB BE THE TURNING POINT?

A. DUMINUCO [1], A. NARDO [1] and G.A. PALUMBO[1]
1. Hematology Unit with BMT, Policlinico "G.Rodolico-San Marco." Catania, Italy

AZIENDA OSPEDALIERO UNIVERSITARIA POLICLINICO - CATANIA -

INTRODUCTION

The simultaneous presence of myeloproliferative diseases, specifically myelofibrosis (MF) and lymphoproliferative disorders (LPD), has been reported (1). The first-in-class JAKi ruxolitinib (RUX) can control the disease, splenomegaly, and systemic symptoms. The inhibition of the JAK-STAT pathway leads to a state of immunosuppression, with an increased risk of infections or growth of pre-existing lymphoid clones, resulting in LPD. Considering the studies currently available evaluating the correlation between myeloproliferative neoplasms (MPN) and LPD, we note different results. In the cohort of Pemmaraju and colleagues, only 9 (0.56%) MF patients developed an LPD, of which 6 were previously treated with RUX. In the European group, 4 (5.8%) of 69 patients who received JAKi treatment experienced aggressive B-cell non-Hodgkin lymphomas, reporting an increased risk compared with patients treated with other drugs (2–0.36%) (2-3).

AIM

In our experience, we report the cases of 2 patients affected by LPD arising during treatment with RUX for MF and for whom we decided to switch therapy to fedratinib (FED) with subsequent spontaneous disappearance of LPD.

CASES PRESENTATION

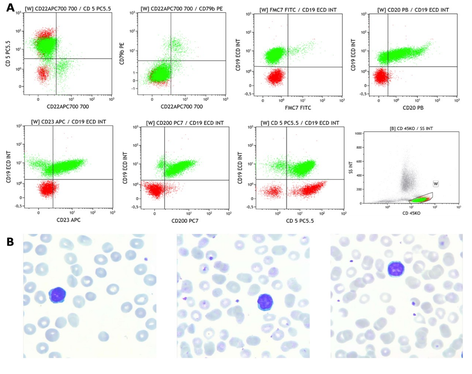
The first is a case of a 65-year-old woman affected by JAK2-mutated PPV-MF. After about 12 months of treatment with RUX, we found 2 new cutaneous lesions in the scapular region, diagnostic for cutaneous marginal zone lymphoma (MZL). Considering the relationship between LPD and RUX treatment, we discontinued RUX administration. We started therapy with FED at the standard dose of 400 mg daily, with the progressive disappearance of the lesions in about 2 months and reasonable control of the underlying MF (Figure 1).

The second patient is a man affected by CALR-mutated PET-MF who began RUX treatment. During the follow-up, after 5 months of RUX, lymphocyte count had increased, with immunophenotype diagnostic for chronic lymphocytic leukemia (CLL) (Figure 2). After the LPD diagnosis, we decided to withdraw RUX and treat the patient with FED without accessory treatment for the indolent CLL. Immediately after the RUX discontinuation, we witnessed a progressive decrease in lymphocyte count, reaching values around the upper threshold limit.

Figure 1. Skin lesions arose during therapy with ruxolitinib (A), with the largest measuring about 2.5 cm (B), and disappeared after withdrawal of ruxolitinib and shift to fedratinib (C - biopsy results were also evidenced)



Figure 2. Immunophenotype evaluated in flow cytometry (A – in green) and peripheral blood smear (B) of clonal lymphocyte population evident during ruxolitinib therapy and diagnostic for CLL



CONCLUSIONS

Our limited series suggests carefully evaluating patients affected by MPN and treated with JAKi, with the key role of FED in these cases instead of RUX.

REFERENCES

1. Rumi E, Passamonti F, Elena C, Pietra D, Arcaini L, Astori C, et al. Increased risk of lymphoid neoplasm in patients with myeloproliferative neoplasm: a study of 1,915 patients. Haematologica [Internet]. 2011 Mar [cited 2023 Apr 28];96(3):454–8. Available from: https://pubmed.ncbi.nlm.nih.gov/21109692/
2. Porpaczy E, Tripolt S, Hoelbl-Kovacic A, Gisslinger B, Bago-Horvath Z, Casanova-Hevia E, et al. Aggressive B-cell lymphomas in patients with myelofibrosis receiving JAK1/2 inhibitor therapy. Blood [Internet]. 2018 Aug 16 [cited 2023 Apr 28];132(7):694–706. Available from: https://pubmed.ncbi.nlm.nih.gov/29907599/
3. Pemmaraju N, Kantarjian H, Nastoupil L, Dupuis M, Zhou L, Pierce S, et al. Characteristics of patients with myeloproliferative neoplasms with lymphoma, with or without JAK inhibitor therapy. Blood [Internet]. 2019 May 23 [cited 2023 Apr 28];133(21):2348–51. Available from: https://ashpublications.org/blood/article/133/21/2348/272729/Characteristics-of-patients-with

CONTACT INFORMATION

Dr. Andrea Duminuco
Hematology Unit with BMT, Policlinico "G.Rodolico-San Marco." Catania, Italy
andrea.duminuco@gmail.com