ADVERSE DRUG REACTIONS, INCLUDING SJS, TEN

IBRUTINIB AND PYODERMA GANGRENOSUM IN A PATIENT WITH B-CLL

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Background: Ibrutinib is a small molecule inhibitor of Bruton's tyrosine kinase usually well tolerated.

Observation: We present a 55-year-old man with an 11-year history of B-cell Chronic Lymphocytic Leukemia (B-CLL). In Jun 2015, the patient developed an autoimmune thrombocytopenia that was successfully treated with systemic corticosteroids first, and short time after with six Fludarabine-Cyclophosphamide-Rituximab cycles. In May 2018 the patient developed an autoimmune hemolytic anemia; p53 exon 5 mutation, a p17 deletion, and CLL cells with unchanged gene for the immunoglobulin heavy chain variable region were also found. He received again prednisone and Rituximab. In July 2018, because of disease progression with both superior-inferior diaphragmatic adenopathy and bone marrow B-CLL involvement more than 70%, switch to Ibrutinib (420mg/die) was decided. Four weeks after Ibrutinib initiation, B-CLL responded to treatment but the patient developed on the abdomen and the lower limbs multiple, painful erythematous to violaceous nodules and pustules rapidly evolving in painful ulcer with undermined violaceous borders. A biopsy from ulcer margin revealed massive neutrophils infiltration with leukocytoclasia and marked tissue necrosis with surrounding mononuclear cell infiltrates. Thorax and abdomen CT did not reveal pulmonary or gastrointestinal involvement. Pyoderma gangrenosum (PG) was diagnosed and ibrutinib was suspected as causative agent, because the temporal causality; PG has been only rarely associated to B-CLL. Prednisone 75 mg/die was started and then slowly tapered every 3 weeks; Ibrutinib was reduced to 210mg/die, because risk of further disease progression. Improvement of skin lesion was observed, but maintenance of the remission needed a daily low steroid dose and Dapsone 50mg/die was introduced as steroid-sparing. Ibrutinib was switched to Venetoclax.

Key message: In the literature, only few reports of neutrofilic dermatitis related to ibrutinib have been reported.