INTRODUCTION

- Fever is a common symptom with a broad differential diagnosis.
- Ibrutinib withdrawal syndrome is a rare clinical entity presenting with influenza-like symptoms.

CASE DISCRIPTION

A 79-year-old male with a history of chronic lymphocytic leukemia (CLL) on ibrutinib therapy presented with fever, non-productive cough, dyspnea, and altered mental status for 2 days. Initial investigations were positive for leukocytosis and influenza A. A chest x-ray demonstrated bibasilar densities. The patient was admitted for acute hypoxic respiratory failure secondary to influenza A pneumonia and possible bacterial superinfection in the background of immunosuppression.

Hospital course:

- Ibrutinib was withheld due to the presence of an active infection.
- Appropriate antiviral and antibiotic course was completed resulting in improved respiratory symptoms; however, fever persisted.
- Additional infectious work-up was negative and computed tomography scan of the chest, abdomen and pelvis was unrevealing.
- After thorough diagnostic evaluation, and in the absence of any etiology for the febrile episodes, ibrutinib withdrawal syndrome was considered, and the drug was resumed.
- The fever subsided subsequently.

DISCUSSION

- Ibrutinib is a Bruton's tyrosine kinase inhibitor used for the treatment of refractory CLL, Waldenstrom's macroglobulinemia and mantle cell lymphoma.
- Pathogenesis of ibrutinib withdrawal syndrome is unclear.
- Hypothesis: Reactivation of tumor cells during interruption of ibrutinib therapy could lead to cytokine release causing symptoms, such as fever, chills, night sweats, myalgias, arthralgias and headaches.
- ibrutinib therapy is temporarily withheld in the setting of toxicities caused by the drug, to minimize post-surgical bleeding, or in the setting of an active infection which was the case in our patient.
- Reinitiation of ibrutinib often results in resolution of symptoms.