Ibrutinib-associated Serositis in Mantle Cell Lymphoma

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Figure 1. (A) Chest radiograph demonstrated enlarged cardiomeastinal silhouette, pulmonary edema, and bilateral pleural effusions. (B) Computed tomography of the chest with angiogram revealed no pulmonary embolism, large pericardial effusion (white arrows), and bilateral moderate pleural effusions (asterisks) with compressive atelectasis.

A 65-year-old man with recurrent mantle cell lymphoma presented complaining of dyspnea, fatigue, and orthopnea. He had been diagnosed with mantle cell lymphoma 4 years before, was treated with bortezomib and hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone), and had been in remission. Ibrutinib was initiated 10 weeks before, after retroperitoneal lymphadenopathy was detected on serial imaging, with biopsy confirming recurrent disease with p53 expression. Physical examination was significant for irregular rhythm, decreased breath sounds in the lung bases bilaterally, and trace pretibial edema. Imaging (Figure 1)

revealed bilateral moderate pleural effusion and large pericardial effusion. ECG confirmed atrial fibrillation, and ibrutinib was held. Large pericardial effusion without tamponade physiology and preserved systolic function was found on transthoracic echocardiogram (Figure 2). Left-sided thoracentesis was performed, removing 1 L fluid, followed by right-sided thoracentesis removing 1.25 L fluid. Pleural studies were consistent with an exudate on the left and transudate on the right, and both had negative cytology. There was a lymphocytic predominance in both effusions. Pleuroscopy with pleural biopsies and placement of an indwelling pleural catheter were performed on the left hemothorax (Figure 3). Pleural biopsies on the left hemithorax revealed mesothelial hyperplasia with eosinophils on the biopsy (Figure 3), and pleural catheter was placed. Ibrutinib was not restarted, and pleural and pericardial effusions resolved.

Ibrutinib is a novel, orally active inhibitor of Bruton's tyrosine kinase, and it is an effective and well-tolerated treatment for a variety of B-cell malignancies (1). Toxicities are primarily nonhematologic, including gastrointestinal symptoms, fatigue, hypertension, peripheral edema, and dyspnea, but atrial fibrillation has been described in up to 6% (2). Although serositis has been described with tyrosine kinase inhibitors that target BCR-ABL (breakpoint cluster region protein-Abelson murine leukemia viral oncogene), pleural and pericardial effusions have only rarely been attributed to ibrutinib (3–5). In our patient, the development and resolution of serositis follows the initiation and cessation of ibrutinib. The diagnosis was confirmed after exclusion of other etiologies including malignancy, thromboembolic disease, and infection. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

This research is supported in part by the NIH through MD Anderson's Cancer Center Support Grant (CA016672).

Author Contributions: All authors provided conception and design, acquisition of radiological and pathological data, drafting of the article, critical revision of intellectual content, and final approval of the version to be published.

Am J Respir Crit Care Med Vol 199, Iss 12, pp e43–e44, Jun 15, 2019

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Originally Published in Press as DOI: 10.1164/rccm.201809-1738IM on February 25, 2019

Internet address: www.atsjournals.org

Figure 2. Echocardiogram with pericardial effusion (A) at the time of admission, (B) 1 week after cessation of ibrutinib, and (C) 8 weeks after cessation of ibrutinib. LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

Figure 3. (A) Pleuroscopy revealed a normal-appearing visceral pleura, but parietal pleural was slightly edematous in some portions of the posterior and mediastinal aspects. (B and C) Pleural biopsy reveals a thin zone of mixed inflammatory cells beneath the pleura (B, hematoxylin and eosin stain) and at higher magnification (C, hematoxylin and eosin stain) shows a significant increase in eosinophils (bright red granular cells) in addition to lymphocytes, plasma cells, neutrophils, and monocytes.

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