

Balsalazide-Induced Pneumonitis Causing Dyspnea in a Patient With Inflammatory Bowel Disease

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ABSTRACT

Inflammatory bowel disease complications can be related to inflammatory bowel disease-related pulmonary diseases or a form of hypersensitivity pneumonitis secondary to the immunosuppressive medications. We present a patient with intermittent chest pain and hypoxic respiratory failure who was found to have balsalazide-induced pneumonitis. We discuss the treatment and long-term outlook.

INTRODUCTION

The current recommended treatment of mild-to-moderate ulcerative colitis (UC) is 5-aminosalicylic acid (5-ASA) and its derivatives. Although there have been documented reports of pulmonary toxicity with sulfasalazine, there have been few reported lung toxicities seen with 5-ASA components alone, such as mesalamine.¹ We present a case of a patient with mild-to-moderate UC treated with balsalazide who developed balsalazide-induced pneumonitis.

CASE REPORT

A 68-year-old woman with a medical history of UC on balsalazide presented with several months of intermittent, nonradiating chest pain, orthopnea, and dyspnea on exertion which had acutely worsened over 4 days. The patient was afebrile with an elevated heart rate of 115 beats/min, higher than normal blood pressure of 153/84 mm Hg, respiratory rate of 22 breaths/min, SpO₂ 88% on room air, which improved to 93% with 3 L via nasal cannula. Physical examination revealed bibasilar crackles. An electrocardiogram revealed normal sinus rhythm and no acute changes. A thoracic x-ray also showed no acute process. Computed tomography angiogram was negative for pulmonary embolism but demonstrated nonspecific bilateral ground-glass opacities within both lungs. The patient was admitted for further evaluation. Complete blood count, comprehensive metabolic panel, troponins, thyroid-stimulating hormone, pro-B-type natriuretic peptide were all within normal limits.

She underwent cardiac evaluation with nuclear medicine multigated acquisition scan that revealed a low-normal left ventricular ejection fraction of 50%, small pericardial effusion, and left ventricular septal wall hypokinesis. A transthoracic echocardiogram revealed an ejection fraction of 40%–45% with global hypokinesis and left atrial dilation. The left heart catheterization revealed nonobstructive coronary disease. The patient was started on guideline-directed medical therapy including intravenous diuretics, lisinopril 20 mg, metoprolol succinate 75 mg, and aspirin 81 mg. Despite medical therapy, the patient continued to complain of intermittent chest pain and dyspnea on exertion.

A pulmonary function test showed no obstructive or restrictive process, but a decreased diffusing capacity for carbon monoxide at 51%. Bronchoscopy with bronchial alveolar lavage demonstrated lymphocytosis, moderate eosinophilia with plasma cells. Right heart catheterization showed normal filling pressures without pulmonary hypertension. Infectious workup including respiratory polymerase chain reaction, parvovirus B19 antibody, coxsackie A and B antibody panel, adenovirus, and human herpesviruses were

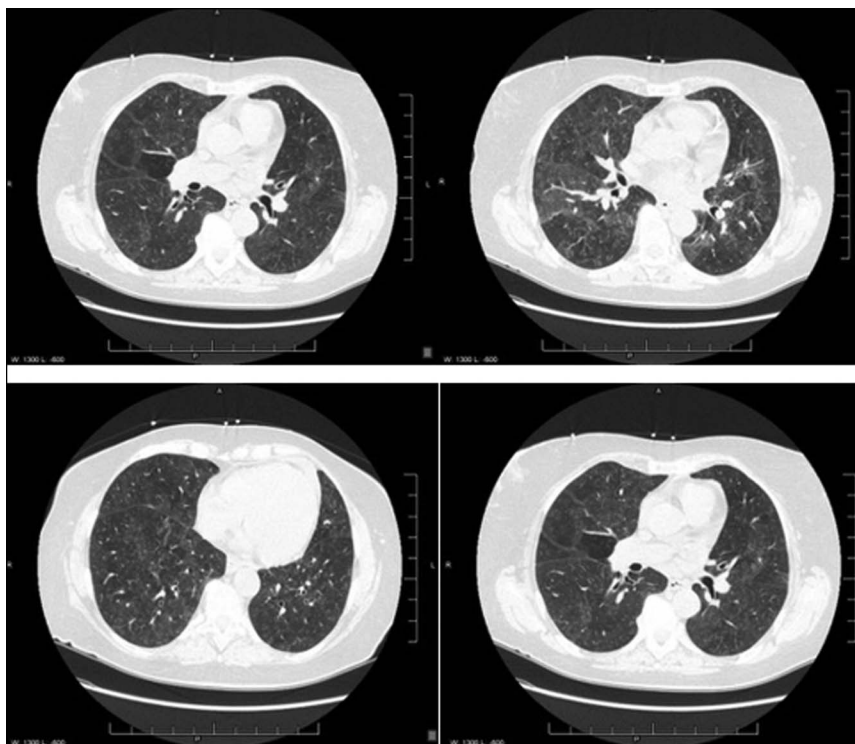


Figure 1. Thoracic high resolution computed tomography without contrast showed upper lung predominant ill-defined nodular ground-glass opacities, mild bronchial wall thickening, and mosaicism with moderate air trapping on expiratory phase.

all negative. Thoracic high resolution computed tomography (HRCT) without contrast showed upper lung predominant ill-defined nodular ground-glass opacities, mild bronchial wall thickening, and mosaicism with moderate air trapping on expiratory phase (Figure 1).

Further laboratory workup revealed an antinuclear antibody titer of 1:80 with a homogenous pattern, Rheumatoid factor of < 10 IU/mL, negative anti-Sjogren syndrome type A, positive anti-Sjogren syndrome type B, negative Scleroderma-70, negative anti-Jo-1 antibody for myositis, negative cyclic citrullinated peptide for rheumatoid arthritis, negative antismith and antidouble-stranded DNA for systemic lupus erythematosus, negative antiribonucleoprotein antibody for mixed connective tissue disease. Hypersensitivity pneumonitis fluorescence enzyme immunoassay panel inclusive of *Aspergillus fumigatus* immunoglobulin G, *Micropolyspora faeni* immunoglobulin G, and *Thermoactinomyces vulgaris* were all within the normal range. The patient denied any exposure to asbestos, toxic chemicals, or cigarette use. During this time, she did not have a worsening of her UC symptoms. Inflammatory markers such as a C-reactive protein level of 7.86 mg/L and a fecal calprotectin level of 153 μ g/g were noted during the time of admission.

Interestingly, balsalazide was started approximately 8 weeks before the onset of the patient's presenting symptoms. With the above findings on the HRCT and negative laboratory workup, balsalazide-induced hypersensitivity pneumonitis was suspected. Balsalazide was discontinued, and the patient was

started on prednisone 60 mg for 2 weeks followed by steroid dose tapering. On follow-up for her UC, she was initiated on vedolizumab with adequate maintenance of her UC. The patient followed up with pulmonary, cardiology, and gastroenterology and was noted to have significant improvement without any recurrence of her symptoms.

DISCUSSION

Drug-induced pneumonitis and lung toxicities from sulfasalazine are well documented, although very few cases of 5-ASA derivatives have been found in the literature. Only 4 case reports of drug-induced pneumonitis secondary to mesalamine have been reported with none of balsalazide. A meta-analysis by Rahimi et al looked at the effectiveness of balsalazide versus mesalamine in the induction, maintenance, relapse, and medication side effects. Balsalazide was noted to be more effective in induction but had similar rates for maintenance, relapse, and drug side effects. Owing to these results, patients are commonly started on balsalazide for induction and maintenance therapy.¹

The diagnosis of pneumonitis is difficult in the setting of inflammatory bowel disease (IBD) with a concern of pulmonary manifestations such as, bronchiectasis, bronchitis, tracheobronchitis, bronchiolitis, obstructive lung disease, interstitial lung disease, organizing pneumonia, granulomatous disease, eosinophilic pneumonia, vasculitis, amyloid nodules, diffuse alveolar hemorrhage, usual interstitial pneumonia-like pattern,

desquamative and nonspecific interstitial pneumonitis, and colobronchial and esophagopulmonary fistulas.²

As mentioned above, there are numerous IBD-related pulmonary manifestations, which can present as productive or non-productive cough, wheezing, shortness of breath, dyspnea on exertion, hemoptysis, and chest pain. IBD-related pulmonary disease is very difficult to distinguish from other etiologies, in part, because pulmonary complaints can present when IBD activity is quiescent. Pulmonary complications from IBD typically respond well to steroids, whereas drug-induced pneumonitis responds well to the removal of the inciting agent.³ HRCT is used for defining radiographic abnormalities, although it is rarely specific for drug etiology.

Our patient had an extensive workup that was negative for cardiovascular, infectious, rheumatologic, or IBD-related etiologies. The combination of HRCT demonstrating ground-glass opacities, and lymphocytosis and plasma cells found on bronchial alveolar lavage made balsalazide-induced pneumonitis the leading diagnosis because it met the diagnostic criteria per American Thoracic Society Clinical Practice Guidelines.⁴ The time frame of the patient's symptoms in relation to starting balsalazide supported the diagnosis of drug-induced pneumonitis and was strengthened when balsalazide was discontinued with the initiation of prednisone leading to improvement in patient's symptoms.

There are limited documented cases of mesalamine-induced hypersensitivity pneumonitis and no documented cases with balsalazide. A broad differential, including IBD and IBD-related medications, should be considered in a patient presenting with pulmonary symptoms without a definitive etiology. Discontinuation of the drug and transition to an alternative drug class for IBD therapy is imperative in management.

DISCLOSURES

Author contributions: J. Sobecki and M. Minaudo wrote the manuscript. K. Patel and R. Kahl edited the manuscript. J. Sobecki is the article guarantor.

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