Eosinophilic Pneumonia in a Patient With Ulcerative Colitis Treated With Mesalazine: a Case Report

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Case report

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Abstract

Background: Mesalazine, also known as mesalamine or 5-ASA, is considered a safe drug and thus widely prescribed for Inflammatory bowel disease (IBD) patients. Mesalazine was previously recognized as a drug that can rarely cause pneumonia because lacking a sulfa component. Nevertheless, although still a rare complication, more and more cases have been reported nowadays.

Case presentation: We describe the case of eosinophilic pneumonia (EP) in a 39-year-old woman with ulcerative colitis during treatment with mesalazine. We discontinued mesalazine after drug-induced EP was identified, and she made a prompt recovery.

Conclusions: The diagnosis of EP is readily missed due to the rarity and the pulmonary complications of IBD. Since the treatment of pulmonary complications of IBD and EP varies, it is crucial to differentiate them. A prompt recovery can be expected in patients with EP after discontinuing the causative drug.

Introduction

Mesalazine is an FDA-approved drug that has been widely used on moderate to severe IBD patients. Lung involvement in IBD patients is not uncommon, up to 55% of IBD patients suffer from latent interstitial lung disease¹. However, the rate of mesalazine-induced EP is relatively scarce, and there are only 42 cases reported from 1991 to 2015². Sulfasalazine and mesalazine are the major drugs responsible for EP in IBD patients. The majority(89%) of IBD patients complicated with mesalazine-induced EP develop pulmonary symptoms within one year³.

We report a case of mesalazine-induced EP that was free of pulmonary symptoms for five years, and the cause of EP has not been identified for seven years since symptomatic, during which she intermittently suffered from cough and peripheral eosinophilia.

Case Presentation

A 39-year-old Asian female presented with a history of a dry cough that was on and off since June 2013 and an occasional elevation of eosinophil count. Her medical history is significant for ulcerative colitis (UC) diagnosed in 2003, and she was on mesalazine (4 g/d) since 2008.

In October 2013, she was admitted for a UC flare. Physical examination was unremarkable except for some bilateral crackles. A chest CT scan was ordered because of a mild cough during the hospitalization, which showed multiple bilateral infiltrates (Image A), and bronchoscopy revealed normal airways. Empiric moxifloxacin and ketotifen were started for the presumed bacteria pneumonia but she continued to have a dry cough for two weeks since discharge. As a consequence, she was readmitted. She was febrile(37.7°C), her blood pressure was 101/64 mmHg, her heart rate was 113/min and her respiratory rate was 20/min. Lab tests showed significant eosinophilia ($3.83 \times 10^9/L$), which composed 40% of all WBC. The Erythrocyte sedimentation rate was 55 mm/h (Normal range: <20) and C-protein of 52.8 mg/L

(Normal range: <10). EP was diagnosed. Intravenous methylprednisolone 40 mg/d was administered and the cough subsequently subsided. Several CT scans since discharge showed gradually but not completely resorption of the infiltrates.

In June 2014, while gradually decreasing the methylprednisolone dose to 2 mg/d, she developed a dry cough again. Upon further interview, she admitted a 2.5-kg weight loss. Physical examination showed some bilateral dry crackles. Lab finding was significant for eosinophilia ($1.56 \times 10^9/L$) which composed 17% of all WBC. CT scan showed worsened bilateral infiltrates since the last discharge (Image B). Methylprednisolone was prescribed 32 mg/d as discharge, and the dose was gradually decreased and eventually maintained at four mg/d until June 2020. During this period, she still occasionally developed a mild cough, eosinophilia and pulmonary infiltrates.

In June 2020, when the patient was admitted for the third time due to a UC flare, a suspicion of mesalazine-induced EP was made. Mesalazine was immediately stopped. Methylprednisolone dose was increased to 16 mg/d and gradually decreased in the next two months to control colitis. As a result, the patient had immediate relief, chest CT scan one month later revealed no abnormal finding (Image C). For the next four months since discontinuing methylprednisolone, she had complete relief from coughing. Repeated peripheral eosinophil counts during this period also remained normal.

Discussion And Conclusions

We have described an unusual case of drug-induced EP. There are only 42 cases of mesalazine-induced EP available from 1991 to 2015². According to a summary of mesalazine-induced lung diseases³, among patients who developed EP results from mesalazine, the usual period from initial dose to symptom onset is within one month (4 out of 9), some (4 out of 9) patients developed symptoms from 1 month to 1 year, only one patient developed symptoms longer than one year since initiating mesalazine. Our patient has a period of 5 years between the first dose of mesalazine and the onset of EP, which is quite rare.

EP, also known as pulmonary infiltrates with eosinophilia syndrome, can be either primary and secondary. The etiology of EP remains unknown. Drugs, toxins and parasite infection are all important causes of secondary EP. Daptomycin, sulfasalazine and mesalazine are common culprits⁴.

Although the pathogenesis is not fully understood, lung involvement in IBD patients is not uncommon. Abnormal pulmonary function test is noted in 25% Crohn's disease (CD) patients and 6% UC patients; abnormal chest CT scan is seen in 50% of patients with IBD⁵. 20–55% of patients with IBD suffer from latent interstitial pulmonary involvement, among which drug-induced lung disease is most common¹. EP in IBD patients most commonly occurs in patients taking sulfasalazine. However, although relatively rare, EP also can be caused by mesalazine and methotrexate⁶.

A diagnosis of drug-induced EP should be suspected in a patient with an abnormal chest CT scan and peripheral, bronchoalveolar lavage, or lung tissue eosinophilia, especially in patients using sulfasalazine

or mesalazine. Lung biopsy is rarely required⁷.

Due to the rarity of the complication, mesalazine-induced EP is often misdiagnosed. Marked peripheral, bronchoalveolar lavage eosinophilia and a CT image suggestive of EP are all clues to the diagnosis of EP. A prompt recovery can be expected after discontinuing the causative drug⁸.

List Of Abbreviations

Inflammatory bowel disease (IBD)

eosinophilic pneumonia (EP)

ulcerative colitis (UC)

white blood cells (WBC)

Declarations

Ethics approval and consent to participate

The participant has given her consent to participate

Institution: Second affiliated hospital of Zhejiang University School of Medicine

Consent for publication

The participant has given her consent for publication

Availability of data and material

The datasets generated and/or analysed during the current study are not publicly available due to the privacy of the patient that participated in the study but are available from the corresponding author on reasonable request.

Competing Interest

The authors declare that they have no competing interests

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Author Contributions

YH: literature search, data collecting, and manuscript writing. YC: interpretation and critical revision of the manuscript, final approval of the version to be submitted. Both authors have read and agreed to the

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Figures

Figure 1

Computed tomography of the chest in October 2013 [A], June 2014 [B], and July 2020 (one month after discontinuing mesalazine) [C]