Case Report

Skin Rash and Mild Bruising: Is Montelukast a Safe Drug?

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Abstract

Montelukast is one of the commonly used drugs in asthma patients. It is prescribed along with inhalational corticosteroids. Although a relatively safe drug, there is a probability of occurrence of skin rashes and skin bruising. Authors present a case report of a 64-year-old chronic asthmatic woman, reporting widespread erythematous eruptions with mild skin bruising and generalized pruritus mostly affecting her lower abdomen and upper extremities. The rash appeared 28 days after introduction of montelukast (10 mg OD). The physician excluded other attributable factors such as trauma, autoimmune disorders such as Churg-Strauss syndrome, and food allergy. Reappearance of rashes after montelukast introduction and complete resolution of the skin rashes after discontinuing it confirms montelukast as offending drug. Naranjo causality assessment score also revealed a "certain/definite" relationship to the montelukast. Long-term safety of montelukast needs to be reviewed by prescribing physicians to prevent adverse reaction.

Keywords: Bruising, hypersensitivity, montelukast, skin rash

Introduction

Montelukast is a leukotriene receptor antagonist. It binds the cysteinyl leukotriene type 1 receptor. It is commonly prescribed to asthma patients along with inhalational corticosteroids. Several clinical trials have concluded montelukast to be a relatively safe drug.[1] However, common adverse effects (AEs) encountered with montelukast include skin rashes and skin bruising and rarely vasculitis [Figure 1].[2]

The present case report questions the safety of montelukast for adult and elderly patients. There is a need to review its long-term safety based on the increasing adverse drug reaction reports.

Case Report

Authors present a case report of a 64-year-old chronic asthmatic female patient with widespread erythematous rashes with mild bruising and generalized pruritus, mostly affecting her lower abdomen and upper extremities after 28 days of introduction of montelukast as add-on therapy to budesonide. The clinical symptoms included shortness of breath, cough, wheeze, and yellowish sputum. Worsening of symptoms was more in the early morning and during winter. Otherwise, symptoms continued throughout the year. On examination, the patient revealed no history of hemoptysis, fever, rigors, or any drug allergy. Earlier, the patient had been on inhalational budesonide 1000 μg/day (two puffs twice a day). The dose of budesonide was reduced to 800 μg/day. Montelukast was introduced 1 month before the onset of skin rashes in a dose of 10 mg once a day.

Chlorpheniramine in a dose of 4 mg was prescribed to alleviate pruritus. De-challenge followed by rechallenge of montelukast confirmed the association between the drug and skin rashes. Inhalational budesonide can be ruled out as it acts mainly locally rather than systemically. The physician excluded other attributable factors, for example, trauma, autoimmune disorder such as Churg-Strauss syndrome (CSS), and food allergy. The skin biopsy revealed nonspecific inflammatory cells. Antineutrophil cytoplasmic antibodies, C-reactive protein, and IgE levels were not elevated. There was no hypereosinophilia (eosinophils >10%), no evidence of vasculitis, or end-organ damage. Therefore, CSS was ruled out. However, erythrocyte sedimentation rate was found to be elevated to 30 mm/h, commonly seen in asthmatic patients.

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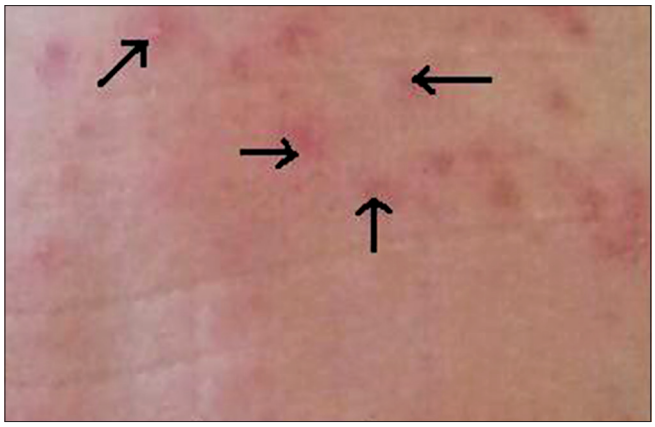

Figure 1: Montelukast induced skin rash on ventral aspect of knee joint

The authors performed a desensitization procedure to the antileukotriene by gradually increasing dose of montelukast starting from low dose 5 mg to reach maximum of 10 mg over a period of 2 weeks. The montelukast was stopped as she relapsed with skin rashes following rechallenge during the procedure. Studies have shown that small incremental dose of offending drug tends to reduce leukotriene production and downregulate cysteinyl leukotriene receptors. This further decreases histamine and tryptase release from mast cells.[3]

Till date, due to lack of any standardized diagnostic test to confirm montelukast hypersensitivity, clinicians rely on the history of duration, frequency, and clinical symptoms after drug intake to confirm the diagnosis of drug-induced AE.

As per Naranjo probability criteria, the temporal association of drug administration and AE was assessed using set questionnaire.[4] Our patient's Naranjo assessment score was 10, which falls into the accepted range for a "certain/definite" relationship to the drug therapy. The appearance of rash after 28 days of introduction of montelukast shows the adverse drug effect to be of delayed hypersensitivity type. Rechallenge with montelukast during desensitization procedure confirmed the certainty of definite association with the above-said drug. Furthermore, the complete resolution of the skin rashes after discontinuing montelukast goes in favor of the montelukast causing AE.

Discussion

Montelukast is generally a well-tolerated drug in adults and elderly patients. AEs are comparable to placebo in several clinical trials. The most common AEs observed in these trials were headache, fatigue, pharyngitis, upper respiratory tract infection, gastrointestinal disorders, and rash.[5,6] Although package insert lists skin bruising as one of the AEs, not much has been mentioned in existing literature. Skin bruising may be related to arachidonic acid metabolites. Montelukast may inhibit platelet aggregation by interfering with platelet-leukocyte interaction, thereby responsible for bruising.[7] Low-dose corticosteroids given along with montelukast unmask an underlying vasculitis leading to bruising.[8] In children, neuropsychiatric AEs have been reported by blocking CysLT1. Blocking of latter leads to vasculitis in the brain.[9] Hepatobiliary and pancreatic dysfunction has been reported in susceptible patients with altered liver/kidney function tests.[10,11]

Conclusion

Through the present case report, we emphasize on the need for monitoring and reporting even the mild AEs of montelukast. This would help clinicians to diagnose the cases effectively. Although leukotriene antagonists are believed to be relatively safe and are widely used in asthma and allergic rhinitis, authors hope that the present case disseminates awareness of potential adverse reactions to montelukast.

Consent

Consent was obtained from the patient on suitably designed informed consent form.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initial will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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