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Case Report

AZITHROMYCIN-INDUCED HYPERSENSITIVITY AND COVID-19: A CASE REPORT

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ABSTRACT

An adverse drug reaction is called drug hypersensitivity syndrome. However, experts regard macrolide allergies to be infrequent. Moreover, this group of antibiotics is considered relatively safe. Although azithromycin is prescribed in COVID-19 patients due to the positive observed effects, hypersensitivity syndrome from this agent has rarely been reported. The case study discusses a 30-year-old man, who was diagnosed with coronavirus disease 2019 and exhibited fever (39.1°C), diffuse maculopapular rash, shortness of breath, wheezing, swelling, itching, pain, subconjunctival hemorrhage, eosinophilia (8.9% of 10.2×10^3/μL leukocytes), and elevated aminotransferase level following treatment with azithromycin. The Naranjo algorithm classified this case in the "definite" category. Therefore, due to the high prevalence of COVID-19 and increased administration of azithromycin, physicians should be made aware of the potential for unusual toxicity associated with azithromycin, which may become more prevalent as its use continues to expand in the future.

Keywords: Drug allergy, Macrolide, Severe acute respiratory syndrome-related coronavirus-2, Case report.

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INTRODUCTION

Drug hypersensitivity syndrome is a form of adverse drug reaction (ADR) with rare mortality and high morbidity [1]. Macrolides have good cell penetrance, bactericidal, and bacteriostatic properties, as well as immunomodulatory and anti-inflammatory effects [2]. Macrolides are commonly used to treat infections of the airways that are acquired within the community [3]. Some macrolides expend anti-inflammatory and immunomodulatory activity [4]. The drug-induced rash is observed in close to 6% of cases [5]. Azithromycin also expands bactericidal and bacteriostatic impacts by binding to the large ribosomal subunit and prevents protein synthesis by inhibiting peptide translocation [6]. Compared to erythromycin and clarithromycin, azithromycin has a lower incidence of drug interactions [7]. Although commonly prescribed, azithromycin has been associated with rare reports of serious cutaneous adverse reactions in clinical practice [8]. One case of drug reaction with eosinophilia and systemic symptoms syndrome (DRESS) connected to azithromycin in an adult was reported [8]. Globally, as of February 20, 2022, a total of 422 million confirmed cases and 5.8 million deaths of coronavirus disease 2019 (COVID-19) have been reported [9]. Humans and other animals can be affected by COVID-19, which is a zoonotic disease [10]. Long-term effects of COVID-19 refer to symptoms that persist for weeks to months after the initial recovery period [11]. There is an urgent need to find and use effective treatment. The positive observed effects of azithromycin in COVID-19 were reported by Gautret *et al*. [12]. In this study, we describe an unusual azithromycin-induced hypersensitivity in COVID-19 patients.

CASE REPORT

A 30-year-old male patient with a history of fever, diffuse maculopapular rash, shortness of breath, wheezing, swelling, itching, pain, and subconjunctival hemorrhage was reported. The patient had no previous history of drug hypersensitivity or atopic diseases. In hospital, he was prescribed a tablet azithromycin for 6 days (500 mg once daily) due to treatment of coronavirus disease. 8 h after complying with the prescription, the patient observed symptoms. Physical examination showed an oxygen saturation of 85% on room air, respiratory rate of 19, febrile patient (39.1°C), pulse of 135, and blood pressure of 103/58. A skin examination showed a maculopapular rash on the shoulder blade, neck, hand, and foot region (Fig. 1). The oral cavity was normal. Abnormal laboratory findings included peripheral blood eosinophilia (8.9% of 10.2×103/μL leukocytes), no atypical lymphocytes, and liver dysfunction with mildly elevated (alkaline phosphatase=185 U/l, reference range 120 U/L) and (aminotransferase level=73 U/L, reference range up to 50 U/L and aspartate aminotransferase =85 U/L, reference range up to 50 U/L) were seen. The infectious disease specialist stopped azithromycin treatment, advised topical 1% hydrocortisone cream to apply to the affected area of the skin 3 times per day, and two ampoules of promethazine 50 mg/2 mL to be taken. On follow-up, the patient reported that her symptoms resolved pending 2 days of terminating treatment.

Using the ADR likelihood scale (Naranjo algorithm) to standardize the assessment of causality for ADRs. The total score range of the reaction was +11, which is considered definite (Table 1).

DISCUSSION

The COVID-19 pandemic is a highly contagious respiratory disease caused by the severe acute respiratory syndrome-related coronavirus-2 [13]. Recent reports have shown that azithromycin is a hopeful candidate for COVID-19 therapy [14,15]. DRESS is a potentially life-threatening condition. Drugs such as antimicrobial agents, anticonvulsants, and antipyretics are frequently responsible for causing an ADR with systemic symptoms syndrome and eosinophilia [8]. Immediate hypersensitivity reactions typically develop within the 1st h after last taking medication and are commonly manifested as angioedema, urticaria, rhinoconjunctivitis, anaphylactic shock, and bronchospasm [16]. Delayed hypersensitivity reactions typically arise between 1 h and 72 h after the last dose [17]. Macrolides are a well-established type of antimicrobial agents that have been in use for a long time [18]. Macrolides are used for the treatment of complicated infections [19]. Studies on the safety of macrolides are rare [20]. However, macrolides' allergy is considered a rare event and occurs in <3% of patients undergoing treatment [17,20,21]. At present, there has been a significant increase in the prevalence of ADR to azithromycin, due to the rapid rise in its usage over the past decade [22]. Azithromycin is one of the best tolerated macrolides and might potentially cause severe adverse reactions [23]. Cases of azithromycin reaction with systemic

symptoms, eosinophilia, contact reactions, dermatitis, skin eruptions, hypersensitivity syndrome, and immunoglobulin E-mediated allergic reactions were reported [18,23-27]. One case of severe aggravation of myasthenia gravis has been reported in a patient receiving 500 mg of azithromycin [28].

CONCLUSION

In clinical practice, physicians have a tendency to prescribe azithromycin to COVID-19 patients. Due to the high prevalence of COVID-19 and increased administration of azithromycin, physicians should be made aware of the potential for unusual toxicity associated with azithromycin, which may become more prevalent as its use continues to expand in the future.

ETHICAL CONSIDERATIONS

Compliance with ethical guidelines

The study protocol was in conformity with the ethical guidelines of the 1975 Declaration of Helsinki, revised in 1983. The author confirms that informed consent was obtained from the legal relatives of the decedent before drafting this report. Private information, including name and surname, was removed from the datasheet to comply with ethical concerns.

INFORMED CONSENT

A written informed consent was obtained from the patient for the publication of this case report.

AUTHOR'S CONTRIBUTION

None.

CONFLICT OF INTEREST

The author declared no conflicts of interest.

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