

Educational & Teaching Material

Case Report



Case report of clindamycin graded challenge in an AIDS patient allergic to clindamycin

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Conflict of Interest

The authors have no financial conflicts of interest.

ABSTRACT

The aim of this study was to report the success of a clindamycin graded challenge. The patient was a 39-year-old human immunodeficiency virus-infected male with toxoplasmic encephalitis (TE) with a history of trimethoprim/sulfamethoxazole (TMP/SMX) and clindamycin allergy. He developed a reaction during TMP/SMX desensitization. Following the reaction, a graded challenge with clindamycin was performed in this study, and he became tolerant to clindamycin. No adverse drug reactions developed during the graded challenge. He successfully continued suppressive therapy with no further reactions or recurrences.

Keywords: Clindamycin; Graded challenge; Toxoplasmic encephalitis; AIDS patient

INTRODUCTION

Toxoplasmic encephalitis (TE) is found in 23.2% of patients with acquired immune deficiency syndrome (AIDS) in Thailand [1]. Recently, there has been a scarcity of TE treatment regimen. Therefore, a graded challenge is one method of safely using suspected medications in patients with a history of minor adverse drug reactions (ADRs) and multiple drug allergies needing medications to treat TE.

A graded challenge is defined as an administration of progressively increasing doses of a medication until a therapeutic dose is reached. The objective of a graded challenge is to verify or exclude the reaction in patients who are unlikely to be allergic to a specific medication. When the reaction is non-immunoglobulin E (IgE) mediated, graded challenges are a recommendable strategy to reintroduce medication. The patient who tolerates a graded challenge without allergic reactions is considered as nonallergy [2, 3]. Herein, we describe the case of an AIDS patient with a history of trimethoprim/sulfamethoxazole (TMP/SMX) and clindamycin allergy who was reintroduced to clindamycin by a graded challenge strategy to treat TE.

Author Contributions

Conceptualization: Thitinun Raknoo, Orawan Sae-lim, Sutthiporn Pattharachayakul, Siripen Kanchanasuwan. Formal analysis: Thitinun Raknoo, Orawan Sae-lim, Sutthiporn Pattharachayakul, Siripen Kanchanasuwan. Investigation: Thitinun Raknoo, Orawan Sae-lim, Siripen Kanchanasuwan. Methodology: Thitinun Raknoo, Orawan Sae-lim, Sutthiporn Pattharachayakul, Siripen Kanchanasuwan. Project administration: Thitinun Raknoo, Orawan Sae-lim, Siripen Kanchanasuwan. Writing - original draft: Thitinun Raknoo, Orawan Sae-lim, Sutthiporn Pattharachayakul, Siripen Kanchanasuwan. Writing - review & editing: Orawan Sae-lim, Sutthiporn Pattharachayakul, Siripen Kanchanasuwan.

CASE REPORT

This is a case report of a 39-year-old male who was diagnosed with AIDS-associated TE in March 2016. At the time of human immunodeficiency virus (HIV) and TE Diagnosis, the patient had an absolute CD4 T lymphocyte cell count of 39.5 cells/ μ L. He had not been started on any antiretroviral agents because the physicians planned to initiate them after the completion of TE treatment. Initially, the patient received TMP/SMX for TE treatment as an inpatient. One week after starting TMP/SMX, he developed a drug reaction with eosinophilia and systemic symptoms (DRESS) with blood eosinophil 7%, aspartate transaminase (AST) 452 U/L and alanine transaminase (ALT) 248 U/L, so the antibiotic was switched from TMP/SMX to clindamycin. His allergic reaction was treated with chlorpheniramine for 10 days. DRESS slowly resolved after TMP/SMX was discontinued. The patient was discharged with clindamycin monotherapy with a plan to start pyrimethamine and leucovorin as an outpatient. Eleven days after clindamycin was started (approximately 1–2 days after chlorpheniramine was discontinued), he developed maculopapular rash on the face, trunk, extremities, and abdomen. There is no relationship between the potential causes of this reaction and the course of other medications. The causal relationship between this reaction and clindamycin was evaluated by using an ADR probability scale, Naranjo Algorithm, and then categorized as “probable.” All reactions disappeared within a week after discontinuation of clindamycin. Eventually, with the patient’s consent, we decided to do TMP/SMX desensitization. Unfortunately, he suffered from conjunctivitis and maculopapular rash during TMP/SMX desensitization.

This patient had a history of minor ADRs to clindamycin and needed medications to treat TE; therefore, we decided to do a graded challenge of clindamycin and planned to use it in combination with pyrimethamine and leucovorin. The risks and benefits of a clindamycin graded challenge were explained to the patient and informed consent was obtained. A clindamycin graded challenge was initiated by using the protocol described in a case report [4]. The 7-day oral clindamycin graded challenge protocol used in our case report is shown in **Table 1**. The starting dose of clindamycin was 20 mg every 8 hours on day 1. The drug dose was then progressively increased until reaching a full dose of 600 mg 4 times per day within 7 days. Our patient did not develop any allergic reactions during the 7 days graded challenge. After completion of the graded challenge, the patient continued to take therapeutic doses of clindamycin with pyrimethamine, azithromycin and leucovorin for 12 weeks. Eventually, the TE was resolved.

The risks and benefits of a clindamycin graded challenge were explained to the patient and informed consent was obtained. The Institution Review Board of institute approved the report (REC.59-225-19-2).

Table 1. Clindamycin graded challenge protocol

Day	Preparation	Dose (mg)	Administration
1	Clindamycin capsule 150 mg dissolved in 50 mL water	20	6.7 mL TID
2		40	13.3 mL TID
3		80	26.7 mL TID
4	Clindamycin capsule 150 mg	150	150 mg, 1 capsule TID
5	Clindamycin capsule 300 mg	300	300 mg, 1 capsule TID
6	Clindamycin capsule 300 mg	600	300 mg, 2 capsule TID
7	Clindamycin capsule 300 mg	600	300 mg, 2 capsule QID

TID, 3 times per day; QID, 4 times per day.

DISCUSSION

The patient developed DRESS, a severe cutaneous adverse reaction, during TMP/SMX desensitization. Therefore, TMP/SMX and other sulfonamides antibiotic were contraindicated in this patient. The report of SMX and sulfadiazine cross allergy was 31.8% [5]. At this case report time period, the preferred alternative regimens are clindamycin or azithromycin plus pyrimethamine plus leucovorin. Based on the Thailand National Guidelines on HIV/AIDS Treatment and Prevention 2014 [6, 7], the regimen containing clindamycin is strongly recommended with level I quality of evidence (“one or more randomized trials with clinical outcomes”) while the regimen containing has an optional recommendation with level II quality of evidence (“one or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes”). There was no statistically significant difference in efficacy between the combination of pyrimethamine plus clindamycin and pyrimethamine plus sulfadiazine regimens. There was a complete or partial response in 68% and 76%, respectively [8]. The complete or partial response of azithromycin in combination with pyrimethamine for treatment of acute TE in patients with AIDS for 4 weeks was achieved in 35.7% of patients [9].

Our patient had a history of non-serious allergic reactions to clindamycin. The data mentioned above shows that this regimen is effective and has been recommended by peer-review guidelines to treat TE. Therefore, we chose to do a clindamycin graded challenge, expecting greater benefits than risks. Generally, the graded challenge has been recommended in non-IgE mediated reactions. Our patient developed a maculopapular rash 11 days after starting clindamycin, suggests that non-IgE mediated hypersensitivity reactions in nature, though the exact mechanism still remains unclear. The incidence of drug hypersensitivity reactions increases in patients with opportunistic infections who have very low CD4 T lymphocyte cell count [10, 11]. A low incidence (0.4% – 3%) in clindamycin hypersensitivity has been reported [12]. The clinical presentation of clindamycin hypersensitivity reported in literature includes angioedema, generalized maculopapular pruritic reaction, DRESS, Stevens-Johnson syndrome and toxic epidermal necrolysis [12, 13]. Moreover, it is possible that the hypersensitivity state remained for 4–6 weeks after the first episode of TMP/SMX allergy because of the increasing function of the immune system [10, 11]. Flare up reaction was reported in 25% of patients with DRESS, skin eruptions were the most prevalent presentation of the recurrences, followed by eosinophilia in about half of the cases and internal organ damage in 13% of the cases [14]. Our patient developed maculopapular rash on the face, trunk, extremities, and abdomen, and blood eosinophil 10%, normal AST and ALT. Therefore, a self-reported history of maculopapular rash from clindamycin might not, actuality, be a clindamycin allergy.

Currently, many drug graded challenge protocols have been reported as successful in multiple research articles. The drugs that the graded challenge protocols have published worldwide include acyclovir, fluconazole, and TMP/SMX [15-17].

There are a few reports of clindamycin graded challenge protocols. Marcos et al. [4]. reported a patient case with HIV infections who developed a cutaneous eruption after 12 days of TE treatment with clindamycin. The authors progressively increased the dose of clindamycin to reach the full dose within 7 days [4]. The recent study showed the success of rapid (240 minute) oral clindamycin desensitization in a pediatric patient who experienced an anaphylactoid reaction from clindamycin. However, the patient tolerated clindamycin

with 3 premedication regimens (cetirizine 10 mg every 8 hours, montelukast 5 mg daily and ranitidine 60 mg every 12 hours the whole time of clindamycin using) [18]. This protocol might not be practical since the patient with HIV infection needed to take high amounts of medication for a long duration of time.

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