

Brief communications

Prophylaxis of AIDS-related *Pneumocystis carinii* pneumonia with aerosolized pentamidine in a patient with hypersensitivity to systemic pentamidine

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More than 1 million subjects in the United States are infected with HIV with PCP often the presenting manifestation of AIDS.¹ Treatment regimens exist with TMP-SMX or pentamidine, but adverse reactions often occur.² Reinfection is common, and prophylaxis is important. We discuss a patient with allergy to TMP-SMX, pentamidine, and dapsone who received aerosolized pentamidine prophylaxis via a rapid test-dose schedule.

Case report

A 32-year-old white male homosexual, seropositive for HIV, received a sulfonamide for pneumonia, but a pruritic macular rash and fevers developed. In May 1989 he was admitted to another hospital in which PCP was diagnosed and systemic pentamidine was begun. On the fifth day of therapy, 20 minutes into infusion, a facial rash, tongue swelling, and laryngeal edema developed. Laryngeal edema resolved with epinephrine and diphenhydramine, but despite stopping the drug, the rash progressed for 5 days before clearing. He successfully received trimetrexate. Dapsone prophylaxis was attempted, but a rash and fever developed requiring that the drug be stopped. TMP-SMX desensitization for PCP prophylaxis was performed by one of the authors (J. A. S.), slowly, on an outpatient basis beginning with 1 teaspoon of suspension (200 mg of SMX), increasing 1 teaspoon every 5 days to 6 teaspoons daily, and thereafter, 1 teaspoon every 3 days to 8 teaspoons daily. After switching to double-strength TMP-SMX (800 mg of SMX) twice daily, a progressive macular rash developed requiring treatment with diphenhydramine, and the drug was stopped. Five days later, low-dose TMP-SMX (400 mg of SMX) caused recurrence of pruritus. Further administration was not attempted.

Abbreviations used

HIV:	Human immunodeficiency virus
AIDS:	Acquired immunodeficiency syndrome
PCP:	<i>Pneumocystis carinii</i> pneumonia
TMP-SMX:	Trimethoprim-sulfamethoxazole
AZT:	Azidothymidine

In November 1989, the patient consulted one of the authors (C. G. B.) who found no skin rash, a clear chest, a normal chest radiograph, white blood cell count of 2600, and CD4 count of 12/mm³. He received azidothymidine (AZT) 300 mg, daily. It was decided to attempt rapid test-dose administration of aerosolized pentamidine that is approved for PCP prophylaxis.²

PROTOCOL AND RESULTS

The patient was admitted to the St. Luke's/Roosevelt Hospital Center on the general medical floor. Since albuterol and cromolyn sodium prevent the bronchoconstrictive response to aerosolized pentamidine, he was pretreated with nebulized albuterol, 2.5 mg, and cromolyn sodium, 20 mg.³ Skin testing was performed intradermally with pentamidine, 0.015 mg/ml and 0.15 mg/ml (Pentam 300; LyphoMed, Inc., Rosemont, Ill.). He displayed a positive wheal-and-flare reaction to both concentrations, as did four normal control subjects. Three hundred milligrams of pentamidine isethionate was diluted in 20 ml of sterile water (15 mg/ml) and delivered via a Respirgard II nebulizer (Marquest Medical Products, Inc., Englewood, Colo.) at 15-minute intervals at 1:10,000, 1:1000, 1:100, and 1:10 dilutions and at full strength in three divided doses with no adverse reaction (Table I). Two weeks later, he received more rapid test-dose administration of pentamidine diluted 1:100, 1:10, and full strength. Albuterol/cromolyn sodium pretreatment was stopped with no adverse effect. He has been maintained with monthly pentamidine for 25 months.

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DISCUSSION

Adverse drug reactions occur in most patients with AIDS with PCP treated with TMP-SMX therapeutically, and in 17% of patients treated prophylactically.² Reactions to pentamidine are also common in patients with AIDS.² Although toxicities associated with these drugs are usually tolerable, there may be difficulty in treating complications. In particular, administration of corticosteroids might increase infections by interfering with host defense. However, corticosteroids have been used as adjunctive therapy in moderate to severe AIDS-related PCP.⁴ Greenberger and Patterson⁵ underscored the difficulty in readministering a drug that caused an adverse reaction by reporting the coincidental deaths of two patients with AIDS who received pentamidine via a test-dose intravenous schedule after previous adverse reactions to pentamidine.

Although AZT reduces the frequency of second episodes, PCP reoccurs in many HIV-infected patients if no prophylaxis is administered.¹ Although an alternative TMP-SMX desensitization procedure might have been more successful, aerosolized pentamidine was a suitable alternative. Successful treatment with aerosolized pentamidine in patients with adverse reactions to systemic pentamidine has been reported, although no patient had severe laryngospasm.⁶ Little aerosolized pentamidine is absorbed, which may account for the success of our procedure.

Pentamidine has been noted to have nonspecific effects on mast cells and terfenadine, an H₁-blocking agent, to abolish or decrease the wheal reaction to pentamidine.⁷ Skin test reactivity to pentamidine at similar concentrations was demonstrated in our patient, as it was demonstrated in control patients consistent with this finding.

Despite the fact that patients with AIDS often have adverse reactions to TMP-SMX, pentamidine, or both, prophylaxis of PCP with one of these drugs may be required. We suggest that cautious administration of aerosolized pentamidine may be a safe and effective

TABLE I. Protocol for aerosolized pentamidine administration

Dilution*	Volume inhaled (ml)	Pentamidine delivered (mg)†
1:10,000	4‡	0.006
1:1,000‡	4	0.06
1:100‡	4	0.6
1:10	4	6
Full strength§	20	300

*Three hundred milligrams of pentamidine isethionate was diluted in 20 ml of sterile water to elicit a concentration of 15 mg/ml. Dilutions were made serially from this full-strength solution.

†Delivered by a Respirgard II nebulizer at 15-minute intervals after pretreatment 30 minutes before with albuterol, 2.5 mg, and cromolyn sodium, 20 mg by nebulization.

‡Dilutions used for intradermal skin testing.

§Delivered in three inhalation treatments of 5, 5, and 10 ml at half-hour intervals.

solution, particularly if attempts at desensitization to TMP-SMX are unsuccessful.

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