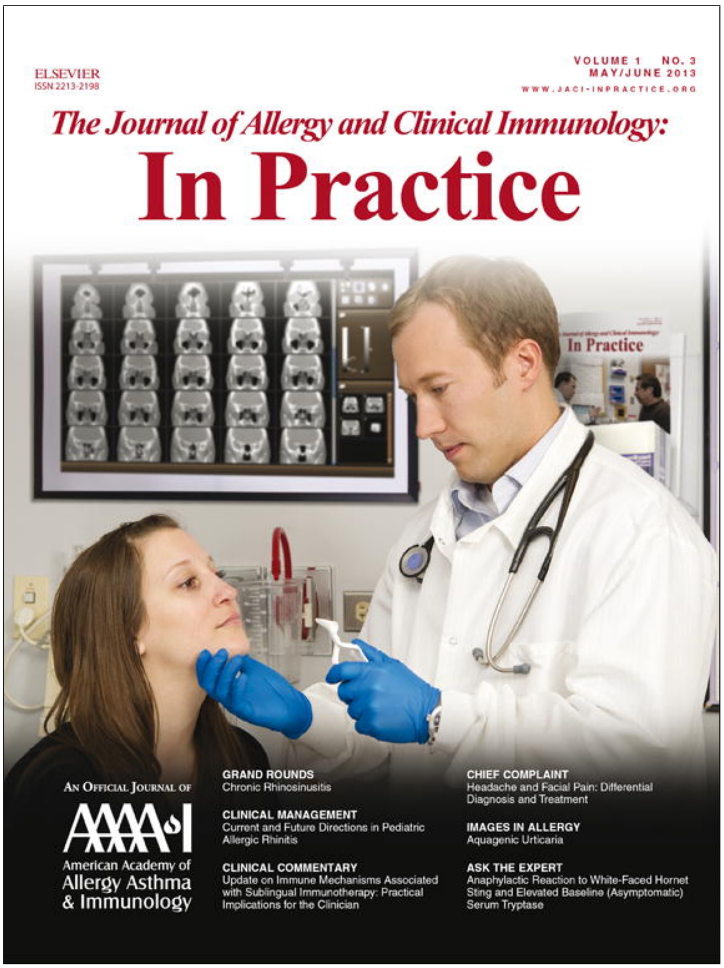

Successful clarithromycin desensitization in a macrolide-sensitive pediatric patient

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Clinical Implication

- Successful desensitization to macrolide antibiotics has been reported in adults but not in pediatric patients. Presented is the successful desensitization to clarithromycin in a macrolide-sensitive, pediatric patient.

TO THE EDITOR:

Hypersensitivity to macrolide antibiotics is estimated to occur in 0.4% to 3% of pediatric patients and poses a serious threat to patients with common infections, including pharyngitis, acne, atypical pneumonia, and infections caused by nontuberculous mycobacterial (NTM) species.[1,2] Patients with macrolide hypersensitivity require alternative medications or treatments that may be suboptimal, especially with NTM infections.[3] Successful desensitization to macrolide antibiotics is reported in adults; however, no reports are published in the pediatric population.[4-7] We report successful desensitization to clarithromycin in a pediatric patient with NTM.

An 11-year-old, previously health, white female without prior drug allergy was admitted with an open fracture of the right ulna, complicated by osteomyelitis with abscess formation. She was initially treated with vancomycin and piperacillin/tazobactam; however, cultures from her wound debridement grew *Mycobacterium fortuitum*, an NTM species, and intravenous clarithromycin and amikacin were initiated. Fifteen to 30 minutes after the second clarithromycin dose began the patient developed a diffuse urticarial rash and abdominal pain. No respiratory or cardiovascular compromise was noted. She was given diphenhydramine, and the symptoms resolved. A similar reaction occurred after initiation of the third dose, this was also successfully treated with diphenhydramine. The allergy/immunology service was consulted for desensitization to clarithromycin, as required for treatment of the NTM infection.

Epicutaneous skin prick testing was performed to both azithromycin (100 mg/mL) and clarithromycin (25 mg/mL); both were negative. Intradermal testing to azithromycin (0.01 mg/mL) and clarithromycin (1 mg/dL) was also negative. The patient showed positive histamine and negative saline controls. Test dosing was not performed despite negative skin testing because of the patient's convincing history of IgE-mediated reaction after 2 successive doses of clarithromycin and concern for induction of further reactions.

In an inpatient setting, oral desensitization with azithromycin was attempted with an adapted protocol (Table I).[5] The patient completed the desensitization protocol without symptom; however, 75 minutes after her next dose of azithromycin, which was approximately 24 hours after she completed the desensitization, she developed a generalized urticarial rash that resolved with diphenhydramine. One week later, oral clarithromycin desensitization, using a similar protocol, was successfully completed (Table II).[4] No premedication was administered before either desensitization or with subsequent doses of macrolide antibiotics. Future doses of clarithromycin were tolerated without reaction.

TABLE I. Azithromycin oral desensitization protocol

Step	Concentration (mg/mL)	Amount (mL)	Dose (mg)	Total dose (mg)
1	0.025	0.6	0.03	0.03
2		1.2	0.06	0.09
3		2.5	0.125	0.22
4	0.25	5	0.25	0.47
5		1	0.5	1
6		2	1	2
7	2.5	4	2	4
8		0.8	4	8
9		1.6	8	16
10		3.2	16	32
11	25	6.4	32	64
12		2.5	64	128
13		2.5	125	253

TABLE II. Clarithromycin oral desensitization protocol

Step	Concentration (mg/mL)	Amount (mL)	Dose (mg)	Total dose (mg)
1	0.05	0.6	0.03	0.03
2		1.2	0.06	0.09
3		2.5	0.125	0.2
4		5	0.25	0.45
5	0.5	1	0.5	1
6		2	1	2
7		4	2	4
8	5	0.8	4	8
9		1.6	8	16
10		3.2	16	32
11		6.4	32	64
12	50	2.5	125	189
13		2.5	125	314

This is the first report of successful desensitization in a pediatric patient with macrolide antibiotic allergy. IgE-mediated reactions to macrolide antibiotics are believed to be infrequent and cross-reactivity among the macrolides are variable.[4] Few studies are published to assist with the management of patients suspected of having an allergy to these antibiotics. Nonirritating concentrations of macrolide antibiotics have been previously published, but the sensitivity and specificity of skin prick and intradermal testing with the use of these concentrations is not well known.[7,8]

Our patient had a convincing history of IgE-mediated reactions to clarithromycin but negative skin testing to clarithromycin and azithromycin, suggesting that the mechanism of her reactions is unknown. Test dosing was not pursued because of her convincing history and concern for induction of future reactions.

Desensitization to azithromycin was initially successful; however, the patient developed urticaria after the next scheduled dose. Although the next scheduled dose of azithromycin was given within 24 hours of completing the desensitization protocol, the half-life of azithromycin is between 68 and 72 hours, making time delay an unlikely cause for the reaction. The subsequent clarithromycin desensitization was successful, and no reactions were seen with future doses. Failed desensitization to a single macrolide does not predict failure to other agents in this drug class, and additional desensitization should be considered.

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