Erythroderma due to Aztreonam and Clindamycin

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Abstract. A 73-year-old woman developed erythroderma with intense pruritus, malaise, and chills 7 days after treatment with intravenous clindamycin. Two years later she experienced a similar reaction with more rapid onset (48 hours) after treatment with aztreonam. Resolution followed withdrawal of treatment in both instances, and intradermal tests proved positive at delayed reading for both drugs.

Key words: Adverse effects. Aztreonam. Clindamycin. Erythroderma. Skin tests. Hypersensitivity, delayed

Resumen. Una paciente de 73 años de edad desarrolló eritema generalizado acompañado de prurito intenso, malestar general y sensación de escalofríos siete días después de haber iniciado el tratamiento con clindamicina intravenosa. Al cabo de dos años, la paciente fue tratada con aztreonam y experimentó una reacción similar, si bien el inicio de los síntomas se produjo con mayor rapidez (48 horas). En ambas ocasiones, el cuadro se resolvió una vez retirado el fármaco. Las pruebas intradérmicas fueron positivas para ambos fármacos en la lectura retardada.

Palabras clave: Reacciones adversas. Aztreonam. Clindamicina. Eritrodermia. Pruebas cutáneas. Hipersensibilidad tardía

Introduction

The term erythroderma or generalized exfoliative dermatitis is applied to any inflammatory skin disease involving the whole or most of the skin surface [1].

The adverse-effect profile of aztreonam and clindamycin has been extensively reviewed in the MEDLINE database, but we retrieved only a single article about erythroderma due to clindamycin [2] and none for erythroderma due to aztreonam.

We describe a patient who developed an erythrodermic reaction following the administration of both drugs on different occasions.

Case Description

A 73-year-old woman was treated with intravenous clindamycin (600 mg/6 h) after abdominal trauma with hemoperitoneum. Seven days after start of treatment, she developed generalized erythema with intense pruritus, malaise, and chills. The eruption started on her trunk and spread over her entire cutaneous surface, including her palms and soles. Clindamycin treatment was stopped and

dexchlorpheniramine and methylprednisolone were started. The patient improved slowly, and slight, superficial desquamation was observed 72 hours later. The complete resolution of the symptoms occurred in 12 days. The patient had not presented adverse reactions to drugs previously. She had neither a personal nor a family history of skin disorders. She did not remember if she had taken clindamycin before. Clindamycin was changed to aztreonam and ceftriaxone, which were well tolerated. Two years later, she was treated with aztreonam (500 mg/8 h) for a urinary tract infection. She experienced a similar effect, but the onset was more rapid (48 hours) than in the first occurrence. Since that reaction, the patient has tolerated penicillin, cephalosporins, imipenem, macrolides, and sulfonamides.

After obtaining informed consent, we performed allergologic evaluation 8 months after the last episode. Serial skin prick and intradermal tests were performed on the volar surface of the forearm with aztreonam and clindamycin on different days. Intradermal tests proved positive at delayed reading for both drugs (Table): an erythematous infiltrate about 2.5×1.5 cm was observed to last 48 hours. The same tests in 5 control patients were negative.

Drug	Prick, mg/mL	Intradermal, mg/mL	Immediate Reaction	Delayed Reaction
Aztreonam	2	2×10^{-4}	Negative	Negative
	20	2×10^{-3}	Negative	Negative
	200	2×10^{-2}	Negative	Negative
		2×10^{-1}	Negative	Positive (6-8 h)
		2	Negative	Positive (6-8 h)
Clindamycin	1.5	1.5×10^{-4}	Negative	Negative
	15	1.5×10^{-3}	Negative	Negative
	150	1.5×10^{-2}	Negative	Positive (12 h)
		1.5×10^{-1}	Negative	Positive (12 h)
		1.5	Negative	Positive (12 h)

Table. Skin Tests With Aztreonam and Clindamycin

Discussion

Skin rashes, which occur in fewer than 2% of patients, are the most commonly reported adverse effects with aztreonam; other dermatologic effects such as urticaria, toxic epidermal necrolysis, purpura, erythema multiforme, and petechiae have been described only rarely [3]. Skin rashes have also been reported following clindamycin therapy, but they are usually mild and self-limiting. This drug has also been implicated in some cases of contact dermatitis, Stevens-Johnson syndrome, and anaphylaxis [4].

Erythroderma is an uncommon clinical entity which could be life-threatening. This syndrome may be the result of many different causes: previous dermatoses (psoriasis, atopic dermatitis, pityriasis rubra pilaris, chronic actinic dermatitis, congenital ichthyosiform erythroderma), malignancies (Sézary syndrome, fungoid mycosis), drug reactions (systemic or topical medications), or undetermined [1]. The correlation between clinical presentation and histologic findings in erythroderma is usually poor, because the specific cutaneous changes of a dermatosis or a drug reaction are obscured by the nonspecific changes induced by erythroderma [1]. For diagnosis, besides clinical and chronological parameters, skin testing (patch testing and also prick and intradermal testing) with the suspected compound can be helpful in determining the cause [5]. Intradermal tests with aztreonam and clindamycin have been reported only rarely in the literature [4, 6]. In our case, they have been useful for diagnosis. The concentrations used by other authors have been similar to ours, although they have reported different results. De la Fuente et al [6] found positive results with aztreonam upon immediate reading in a patient who had had an immediate reaction with aztreonam. On the other hand, Mazur et al [4] found negative results with clindamycin in a patient who had experienced a delayed reaction to this drug.

On the basis of the results of the skin tests and clinical history, we identified aztreonam and clindamycin as the cause of the cutaneous reactions that occurred in our patient. Our findings confirm a delayed-type hypersensitivity reaction to both drugs, possibly involving

an immunologic mechanism involving T cells, as has been suggested [5]. There are no structural analogies between aztreonam and clindamycin, so we think that our results cannot be explained by cross-reactivity. Rather, coincidental sensitization seems more likely.

In conclusion, we report on a patient who developed an erythrodermic reaction with two drugs of different chemical structures: aztreonam and clindamycin. This is an uncommon coincidence not previously reported. Finally, intradermal tests have been useful for the diagnosis.

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