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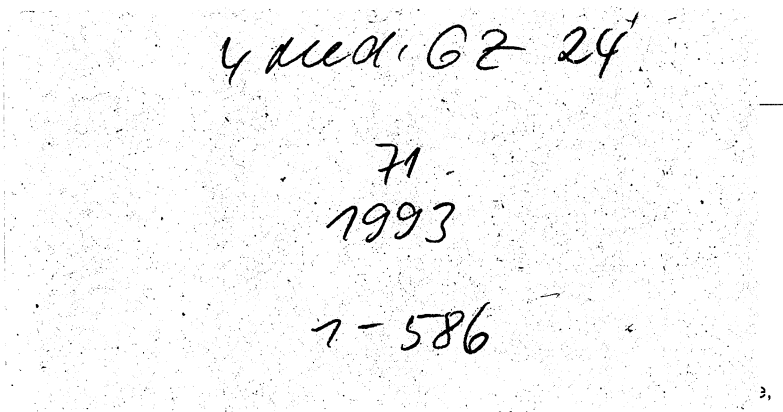

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Clinical Pharmacology **Case Report**

The Clinical Investigator

Cefotaxime desensitization*

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Summary. We report the successful desensitization to cefotaxime in a patient with severe lumbar osteomyelitis of unknown bacteriology and hypersentivity to the drug. Desensitization was carried out because of the unknown bacteriology, the favorable response to cefotaxime at that time, and hypersensitivity to other antibiotics. On the first day the patient received 1 mg cefotaxime intravenously. The dose was increased for 13 successive days to 4 g cefotaxime intravenously per day. No allergic reaction occurred during densitization or within 4 weeks of observation under this therapy. Patients with severe infections of unknown bacteriology might benefit from desensitization if therapy with a second-choice antibiotic is impossible.

Key words: Allergy – Cefotaxime – Cephalosporins – Desensitization

Allergic reactions against β-lactam antibiotics (penicillins, cephalosporins, monobactams, and carbapenems) are common causes of morbidity in patients treated with antibiotics [5, 9, 15, 18] and make the discontinuation of the drug indispensable. A second-choice antibiotic may be less effective and/or more toxic. Moreover, patients with a history of allergy to β-lactam antibiotics may develop life-threatening infections which require treatment with these drugs. Desensitization to penicillins has repeatedly been reported [7, 13, 14, 16, 19]. Cephalosporins are usually effective alternatives to penicillins in cases of hypersensitivity. However, penicillins are often insufficient for replacing cephalosporins, especially third-generation cephalosporins, in allergic patients with severe infections of unknown bacteriology. We could not find a single report of successful antigen-specific desensitization to cephalosporins in the literature. In this case report we report the first successful desensitization to cefotaxime, a widely used third-generation cephalosporin, in a patient with hypersensitivity to the drug.

* Dedicated to Prof. Dr. N. Zöllner on the occasion of his 70th birthday

Materials and methods

A 51-year-old man with severe lumbar spondylitis of unknown bacteriology developed an allergic reaction with generalized pruritic maculopapular skin rash, eosinophilia (1800 cells/mm^3) and unspecific IgE response after 25 days of therapy with 3×2 g cefotaxime (Claforan) daily and after 13 days of therapy with 3×5 g fosfomycin (Fosfocin) daily. After the discontinuation of both antibiotics all symptoms disappeared. A separate reexposure to fosfomycin 2 days after the disappearance of the pruritic skin rash led to the same cutaneous reaction. Four days after the disappearance of this cutaneous reaction a separate reexposure to cefotaxime led to the same pruritic skin rash. A radioallergosorbent test was not available for fosfomycin or for cefotaxime. On the basis of the criteria of Karch et al. [3], hypersensitivity against cefotaxime and fosfomycin was highly probable.

Desensitization to cefotaxime was decided because of the following reasons. (a) An antibiotic with good penetration into bony tissue and with broad spectrum was needed due to the unknown bacteriology of the lumbar osteomyelitis. (b) The clinical response under cefotaxime was favorable. (c) The patient had a history of allergic reaction to an unknown antibiotic, probably penicillin, many years ago.

Informed consent was obtained after description of the desensitization method and after explanation of the risks and benefits. The desensitization was carried out according to the protocol in Table 1 and under inpatient conditions. An intravenous infusion line was established, and emergency medications and equipment were at bedside. Nursing personnel were alerted to the possibility of severe allergic reactions.

Table 1. Intravenous desensitization to cefotaxime

Day	Solution A (ml)	Solution B (ml)	Dose (mg)
1	0.1–0– 0		1
2	0.1–0– 0.1		2
3	0.2–0– 0.2		4
4	0.4–0– 0.4		8
5	0.8–0– 0.8		16
6	1.6–0– 1.6		32
7	3.0–0– 3.0		60
8	6.0–0– 6.0		120
9	10 –0–10		200
10	20 –0–20		400
11		8.0–0– 8.0	800
12		16 –0–16	1600
13		32 –0–32	3200
14		40 –0–40	4000

Solution A: 0.5 g cefotaxime (Claforan) diluted in 50 ml isotonic saline; solution B: 2 g cefotaxime diluted in 40 ml isotonic saline. A fresh solution of cefotaxime was prepared daily

Results and discussion

During desensitization and after 4 weeks of therapy with 2×2 g cefotaxime no allergic reaction or other complication occurred. The outcome of the therapy was successful.

Cefotaxime is the third-generation cephalosporin with which there has been the most experience [1, 5, 6]. It provides a potent, broad spectrum of activity against aerobic gram-negative bacteria that is markedly greater than that provided by first- or second-generation cephalosporins [2] or extended-spectrum penicillins [1]. Hypersensitivity reactions against cefotaxime have an incidence of approximately 10% and include skin rash (1.8%), drug fever (0.4%), and eosinophilia (1.3%) [4]. Immediate reactions occur in 0.3% of patients treated with cefotaxime [4]. Cross-reactivity of penicillins and cephalosporins has been repeatedly reported in vitro [8] and in retrospective studies [10, 17]. However, in prospective studies the apparent cross-reactivity appears remarkably less often [11, 12] and seems to reflect concurrent but non-cross-reactive sensitivity in a small number of highly allergic individuals presumably due to IgE antibodies to side-chain structures rather than the bicyclic core [8, 11]. On this basis the apparent cross-reactivity between cefotaxime, fosfomycin, and perhaps penicillin (history of allergic reaction probably to penicillin many years ago) can be explained in our patient. Moreover the completely different molecular structure of cefotaxime and fosfomycin makes a true cross-reactivity impossible.

This case report demonstrates for the first time that antigen-specific desensitization to cephalosporins is possible. Because of the wide use of third-generation cephalosporins, especially cefotaxime, in severe infections of unknown bacteriology and because of the relatively high incidence of allergic reactions (10%) [4], many patients may benefit from desensitization. Nevertheless, the benefits must be carefully compared with potential risks, and therapy with a second-choice antibiotic should generally be preferred if it is possible. Patients with serious allergic reactions, such as anaphylactic shock, agranulocytosis, toxic epidermal necrolysis, or fibrosing alveolitis, should be excluded from desensitization. Moreover, desensitization must be discontinued immediately if signs of such a serious allergic reaction appear.

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