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Ciprofloxacin-induced Hematuria

Summary: We used ciprofloxacin, a quinolone-derivative, to treat a lung infection due to *Pseudomonas aeruginosa* in an adult cystic fibrosis patient. On three different occasions the use of ciprofloxacin was associated with the development of an asymptomatic hematuria with red blood cell casts. The mechanism responsible for this hematuria is presently unknown, but clinicians should be aware of this potential adverse effect of ciprofloxacin.

Zusammenfassung: *Ciprofloxacin-induzierte Hämaturie.* Wir behandelten einen erwachsenen Patienten mit zystischer Fibrose wegen seiner durch *Pseudomonas aeruginosa* verursachten Lungeninfektion mit Ciprofloxacin, einem Quinolonderivat. Die Einnahme von Ciprofloxacin war wiederholt mit dem Auftreten einer asymptomatischen Hämaturie verbunden. Obwohl der dafür verantwortliche pathogenetische Mechanismus zur Zeit unbekannt ist, sollte auf diese mögliche Nebenwirkung von Ciprofloxacin geachtet werden.

Introduction

Ciprofloxacin, a quinoline-carboxylic acid, is a new antibiotic with excellent activity against gram-negative bacteria, including *Pseudomonas aeruginosa* (1). The drug can be administered orally and is usually well tolerated (2). We recently treated a cystic fibrosis patient with ciprofloxacin for pulmonary infection caused by *P. aeruginosa.* Treatment was repeatedly associated with the development of hematuria, a potentially serious adverse effect of ciprofloxacin that to our knowlege has not yet been described.

Case Report

A 24-year-old male patient with cystic fibrosis developed fever, increasing dyspnoe and a productive cough in July 1984. *P. aeruginosa* and *Staphylococcus aureus* were isolated from the sputum and therapy with flucloxacillin (4 × 1 g per day) and piperacillin (6 × 2 g per day) was instituted and resulted in an improvement of the patient's condition. Since *P. aeruginosa* was repeatedly isolated from bronchial secretions, treatment with ciprofloxacin (2 × 500 mg per day) orally was instituted instead. During therapy with ciprofloxacin, urinalysis revealed repeatedly amorphous salts on several occasions. Peak and trough concentrations in serum determined with a specific HPLC method (3), were 1.4 mg/l and 0.2 mg/l, respectively (Table 1). One month (on 6 September) after institution of ciprofloxacin therapy, asymptomatic microhematuria with excretion of red blood cell (RBC) casts was observed (Table 1). Other laboratory parameters, including serum creatinine, remained unchanged and the hematuria improved within five days after the discontinuation of ciprofloxacin. Twelve days after the drug had been stopped on 18 September, a second episode of hematuria with RBC casts was documented. By that time, the patient's condition had worsened and he had taken ciprofloxacin without medical advice, which was documented in a random serum specimen which showed a ciprofloxacin concentration of 1.1 mg/l. The patient was immediately switched to ceftazidime (2 g t.i.d.) with clinical improvement. At the patient's request, a third trial of ciprofloxacin was instituted in order to stabilize his condition. Therapy had to be stopped again after four days on 19 October because of the development of hematuria with RBC casts (Table 1). Three hours after an oral dose of 500 mg, the ciprofloxacin urine concentration (3) was 1962 mg/l. The hematuria resolved within three days after the discontinuation of ciprofloxacin. No proteinuria was observed during these episodes.

Table 1: Therapy, urinalysis and serum concentrations of ciprofloxacin in a patient with cystic fibrosis.

Therapy	Results			
		Urine		Ciprofloxacin concentration (mg/l)
From – To	Date	*RBC (per mm³)	*RBC casts	Serum Peak – Trough
Piperacillin Flucloxallin 11. 7.–30. 7. 1984	11. 7.	3–6	None	
Ciprofloxacin 2. 8.–6. 9. 1984	7. 8.	None	None	1.4 – 0.2
	28. 8.	3–4	None	
	6. 9.	189	Granular	1.0 – 0.5
	13. 9.	25	None	
	18. 9.	96	Granular	– 1.1 –
Ceftazidime 24. 9.–5. 10. 1984	5. 10.	None	None	
	10. 10.	1	None	
Ciprofloxacin 15. 10.–19. 10. 1984	19. 10.	172	Granular	
	22. 10.	0–2	None	

*RBC = Red blood cells.

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Discussion

The temporary coincidence of ciprofloxacin therapy and the development of microhematuria with RBC casts, which was observed on three occasions, presents a strong case for the etiologic role of ciprofloxacin. Since the hematuria was uniformly associated with RBC casts, it is likely that the antibiotic caused reversible glomerular damage. Serum creatinine concentrations remained normal throughout the observation period. The significance of the amorphous salts, which were observed initially during therapy, is not clear. Theoretically, ciprofloxacin could cause renal damage by crystallization in the renal tubules, a mechanism that has been described for certain sulfonamides (4). However, the urine concentration of ciprofloxacin, measured during the third episode of hematuria, did not exceed the solubility of the drug (data not shown).
Physicians using ciprofloxacin or related drugs, should be aware of the possibility of hematuria occuring during therapy. It is conceivable that hematuria may herald the development of potentially serious renal damage during therapy with ciprofloxacin.

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