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Case Report
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Acute Kidney Injury by Ciprofloxacin Simulating Rapidly Progressive Glomerulonephritis

*Isabella Maria Costada Cunha[1], Pedro Pannunzio Maranzano[1] and Cassio José de Oliveira Rodrigues[1,2]**

[1]Santo Amaro University, São Paulo, Brazil

[2]Federal University of São Paulo, São Paulo, Brazil

Abstract

Ciprofloxacin is a quinolone widely used for the treatment of gastrointestinal, respiratory and genitourinary tract infections. Acute kidney injury is a rare adverse effect determined by ciprofloxacin crystal nephropathy or acute interstitial nephritis. They are associated with good prognosis mainly after discontinuation of the drug. Although renal biopsy is the main diagnostic tool in both cases, it is often not performed, since the evolution is potentially favorable.

We present a case of a young woman that received ciprofloxacin for treatment of a urinary tract infection. The patient evolved with severe renal impairment and hemodialysis was initiated. Because of the presence of hematuria, proteinuria and leukocyturia, she was diagnosed as presenting a rapidly progressive glomerulonephritis. Although, the complete remission of clinical and laboratory findings after withdrawal of the drug pointed to a reversible cause of acute renal failure.

Here, we review the possible causes of acute renal injury related with ciprofloxacin and emphasizes the importance of to be aware of this potential complication of therapy.

Introduction

Ciprofloxacin is a quinolone widely used for the treatment of gastrointestinal, respiratory and genitourinary tract infections [1]. Although its most common adverse effects involve the gastrointestinal tract, renal function alterations have been observed.

One possible form of Acute Kidney Injury (AKI) by ciprofloxacin is determined by the intratubular precipitation of ciprofloxacin crystals, leading to tubular obstruction [2]. It is usually characterized by reversible clinical cases after discontinuation of the drug, vigorous hydration and maintenance of urinary pH at reduced values.

Acute interstitial nephritis is a frequent cause of AKI, and is found in 15%-27% of renal biopsies in patients with this diagnosis [3]. The most common etiology is drug-induced and the most known agents are non-steroidal anti-inflammatories and antibiotics, with ciprofloxacin being one of the most frequent causing agents [4-6]. Its treatment involves stopping the drug and eventually corticosteroid. The prognosis is good in most cases.

Clinical data, such as the evidence of hyper sensibility, and findings of ciprofloxacin crystals help to distinguish the causes of AKI related to ciprofloxacin. Although renal biopsy is the main diagnostic tool in both cases [6,7], it is often not performed, since the evolution is potentially favorable.

Case Presentation

A 21-year-old woman with a history of allergic rhinitis and recurrent nephrolithiasis sought medical care due to dysuria and hypogastric pain, and ciprofloxacin 500 mg twice daily was initiated. After seven days of treatment, she sought the hospital with persistent abdominal pain and nausea, vomiting and periorbital edema. She was a febrile, in good general condition, with normal cardiovascular and respiratory exams, and there was no evidence of sepsis. Laboratory tests on admission were: creatinine 6.8 mg/dL, urea 89 mg/dL, potassium 4.7 mEq/L, sodium 137 mEq/L and the urinalysis showed 2+/4 proteins, 75,000 white blood cells/mL, 144,000 red blood cells /mL and no crystals.

Intravenous hydration and ciprofloxacin suspension were performed. The hypothesis of acute

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Correspondence:
Cassio José de Oliveira Rodrigues, Santo Amaro University, Federal University of São Paulo, São Paulo, Brazil, 04128081, Tel: (55)(11) 999526294;
E-mail: cjorodrigues@uol.com.br

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interstitial nephritis, rapidly progressive glomerulonephritis or acute kidney injury by crystals of ciprofloxacin was considered.

The patient evolved with renal function worsening on the following four days, presenting oliguria, increase of serum creatinine (up to 16 mg/dL), and serum urea (up to 180 mg/dL) and difficult-to-control hyperkalemia. Hemodialysis was initiated and pulse therapy with methylprednisolone was performed for three days, being subsequently replaced by prednisone 1mg/kg/day. Except for the presence of nuclear dots ANA in low titers, the whole search for secondary glomerulopathies was negative.

The patient underwent hemodialysis for a few days, which was suspended due to recovery of renal function. After two weeks of hospitalization, the patient was discharged, with normal levels of serum creatinine and urinalysis without protein, leukocyturia or hematuria. Due to complete clinical and laboratorial remission, no renal biopsy was performed.

Discussion

We reported the case of a young woman with no history of kidney disease who presented Acute Kidney Injury (AKI) after treatment of a urinary tract infection with ciprofloxacin. The initial hypothesis was a rapidly progressive glomerulonephritis, having received treatment for this pathology. The full recovery of renal function combined with the complete disappearance of alterations in the urinalysis after drug discontinuation determined AKI directly associated with ciprofloxacin to be considered the most likely hypothesis.

In our patient, the presence of hematuria, proteinuria and acute loss of renal function led to the initial diagnosis of rapidly progressive glomerulonephritis. Due to the severity of the condition, immediate treatment with corticosteroid at high doses was justified, even before renal biopsy and confirmation of the diagnosis. Although only the long-term follow-up of the patient allows a complete exclusion of a glomerular condition, the complete disappearance of urinary alterations, probably secondary to the infectious condition, along with the normalization of renal function, point to a low probability of this diagnosis.

Renal changes associated with ciprofloxacin are uncommon and generally disregarded. One of the forms of affection described is characterized by the formation of crystals of ciprofloxacin with consequent acute loss of renal function, determining crystaluria and intratubular crystal precipitation with consequent tubular obstruction. Crystal-induced AKI due to ciprofloxacin occurs especially in association with alkaline urine [4,8], or use of high doses of the ciprofloxacin, although it has been described even at doses within the therapeutic ranges and in the presence of urinary pH below 6.8 [9]. As expected in patients with crystal-induced AKI due to ciprofloxacin, our patient had hematuria and leukocyturia without evidence of anatomical alterations. Although she did not use doses higher than those recommended and there is no description of ciprofloxacin crystals in the urine test, the patient's rapid and vigorous clinical improvement reinforces ciprofloxacin crystal nephropathy as a possible cause of the condition. The impossibility of carrying out more complex exams, such as erythrocyte dysmorphism evaluation and microscopic examination of the urinary sediment under polarizing light which would verify the presence of ciprofloxacin crystals [4] and the decision not to perform a renal biopsy after clinical improvement prevented this diagnosis from being confirmed, although quite probable.

Acute Interstitial Nephritis (AIN) is an important cause of AKI after drug use and was considered as an important hypothesis in this case. In fact, antibiotics are responsible for 49% of AIN cases, and there are reports that ciprofloxacin may be involved in up to 8% of them [10]. Our patient did not present with fever, skin rash and arthralgia, although there was a history of hypersensitivity. However, some studies have shown that the classic triad of fever, arthralgia and skin rash associated with elevated creatinine levels occurs in only a minority of cases [10]. The presence of urinary alterations, progressive clinical improvement after drug withdrawal and corticosteroids therapy reinforces AIN as an important hypothesis to be considered. Again, failure to perform renal biopsy prevented a definitive diagnosis.

The difficulty of obtaining better research conditions may also have contributed to the lack of a diagnostic definition. The case was completely led at a public hospital in the Grajaú district, in the city of São Paulo (Brazil). This is a low-income region with the seventh worst human development index of the metropolis.

In summary, we present a young patient with no major medical history who presented with an AKI case and consequent uremic syndrome after treatment of a urinary tract infection with ciprofloxacin. Although the presence of urinary changes had led to the initial diagnosis of rapidly progressive glomerulonephritis, the evolution with complete remission of the condition reinforced the possibility of typically acute changes associated with the drug. The possibility of one of the forms of AKI by ciprofloxacin was considered the most likely diagnosis. Clinicians should be aware of this potential complication of ciprofloxacin use and renal function should be closely monitored.

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