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Anaphylactoid Reaction Considered Ciprofloxacin Related: A Case Report and Literature Review

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Abstract

Background: Although ciprofloxacin is a generally well-tolerated fluoroquinolone antibiotic, serious and life-threatening adverse events such as anaphylaxis and pulmonary edema have been described with its use. However, there is a lack of data in the scientific literature regarding these events.

Objectives: This report describes a case of an anaphylactoid reaction, considered probably ciprofloxacin related, that manifested as angioedema and later as pulmonary edema. This report also summarizes the available scientific evidence regarding the epidemiology, pathogenesis, and outcome of ciprofloxacin-associated anaphylactoid reactions.

Methods: Previously reported cases were identified using a search of MEDLINE and EMBASE (years: 1960–June 2009; English-language articles; search terms: *ciprofloxacin, anaphylactoid reaction, anaphylaxis, angioedema,* and *pulmonary edema*). The references cited in these articles were examined to identify additional reports.

Case summary/Results: A 25-year-old healthy white woman with a weight of 65 kg and normal renal function presented with pyelonephritis. She was administered ciprofloxacin 500 mg BID PO and ibuprofen 400 mg q6h PO as needed for pain control. The following day, angioedema and pulmonary edema developed and were thought to be probably associated with ciprofloxacin use (Naranjo adverse drug reaction probability scale score, 6). Ciprofloxacin treatment was discontinued and supportive care with ceftriaxone 1 g/d IV was provided, and the patient recovered after 1 week of hospitalization. The adverse drug reactions associated with the intake of fluoroquinolones most commonly affect the gastrointestinal system, central nervous system, and skin. The literature search identified 64 cases of anaphylactoid reaction considered probably ciprofloxacin related. Forty-two of these cases were described in large studies, with no detailed data reported. Detailed information on the dose of ciprofloxacin, the time period between ciprofloxacin administration and anaphylactoid reaction, clinical manifestations, and outcomes of these reactions was available in 22 cases described in case reports. Twelve of these cases were described in HIV– patients; 10 cases were described in HIV+ patients. All of the patients

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recovered, with the exception of 2 patients with HIV infection, who died (unknown cause of death in 1 case and toxoplasma encephalitis in the other case). Fourteen patients (including all of the patients with HIV infection) required hospitalization in the intensive care unit. According to the manufacturer of ciprofloxacin, pulmonary edema has been described as an adverse event associated with ciprofloxacin in <1% of treated patients. However, a search of the MEDLINE and EMBASE databases did not identify any documented reports of ciprofloxacin-associated pulmonary edema.

Conclusions: The patient described in this case report experienced an anaphylactoid reaction likely associated with ciprofloxacin use. Although anaphylactoid/anaphylactic reactions are uncommon (<5% of cases) adverse events associated with ciprofloxacin and other fluoroquinolones, clinicians should be aware of this potentially life-threatening event, which might also lead to pulmonary edema even in the setting of normal renal function.

Keywords

ciprofloxacin; angioedema; pulmonary edema; anaphylactoid reaction; anaphylaxis

INTRODUCTION

Fluoroquinolones are generally well-tolerated antibiotics, with the most common (>3% of patients) adverse events being mild (without serious implications) and self-limiting.[1,2] However, serious and life-threatening adverse events, such as anaphylaxis, have been described with fluoroquinolone use.[1] Anaphylactoid reactions have been reported with ciprofloxacin use in the general population.[3] However, based on the findings from a literature search, there is a paucity of data in the scientific literature regarding this association.

This report describes a case of an anaphylactoid reaction that manifested as angioedema and later as pulmonary edema and was considered probably ciprofloxacin related. This report also summarizes the available scientific evidence regarding the epidemiology, pathogenesis, and outcome of anaphylactoid reactions considered probably ciprofloxacin related.

CASE SUMMARY

A 25-year-old healthy white woman weighing 65 kg with an unremarkable medical history presented at Caritas St. Elizabeth's Medical Center, Boston, Massachusetts, with left flank pain, dysuria, and leukocytosis (white blood cell count, 11.8×10^9 cells/L with 83% polymorphonuclear cells) and was diagnosed with pyelonephritis. The patient provided written informed consent to publish the information about her case. The patient had no known drug allergies. She was treated as an outpatient with ciprofloxacin 500 mg BID PO and ibuprofen 400 mg q6h PO as needed for pain control. The patient received 2 tablets of ciprofloxacin and 3 tablets of ibuprofen, in total. She had not previously received fluoroquinolones. The following day, she presented with angioedema and pulmonary edema thought to be probably associated with ciprofloxacin use (Naranjo adverse reaction probability scale score, 6), facial and lip swelling, shortness of breath, and intermittent nausea and vomiting. On physical examination, she was afebrile (oral temperature, 37°C)

and hemodynamically stable (blood pressure, 125/80 mm Hg; heart rate, 110 beats/min). She was tachypneic, with a respiratory rate of 27 breaths/min, and her oxygen saturation was 90% on room air. She had edematous lips and face, bibasilar crackles on auscultation, and leg edema. There was no stridor. Pertinent laboratory data included a white cell count of 12.5×10^9 cells/L with 76% polymorphonuclear cells, 19% lymphocytes, and 2.6% monocytes; blood urea nitrogen, 26 mg/dL; and creatinine, 0.9 mg/mL. Her initial urine culture was negative. On chest radiography, mildly increased interstitial markings suggesting early pulmonary edema were found. The patient was treated with intravenous corticosteroids (methylprednisolone 125 mg/d IV for 3 days followed by a taper of oral prednisone starting from 60 mg/d PO and by 10 mg every 2 days), antihistamines (diphenhydramine 25 mg q4h PO for the first 3 days), and oxygen. Her presentation was attributed to an anaphylactoid reaction to ciprofloxacin, which was discontinued, and the patient was treated with 1 g/d IV ceftriaxone for 10 days. No further treatment with any medications was initiated. The only other medication that the patient was receiving on admission was ibuprofen, but she had been previously exposed to NSAIDs, including ibuprofen, with no reported adverse events. There were no recognized insect bites or inhalation exposure to chemical toxins.

During the next day of hospitalization, the patient became progressively more dyspneic, and the hypoxemia worsened (oxygen saturation, 92% on 4-L nasal cannula). Due to increased respiratory distress, the patient was intubated and transferred to the intensive care unit. Computed tomography (CT) of the chest with intravenous contrast was used to rule out pulmonary embolism and identified bilateral ground-glass opacities and vascular congestion, with normal size of the heart. CT of the abdomen identified mild left hydronephrosis and hydroureter with bilateral renal calculi. Azithromycin 500 mg/d PO for 7 days and vancomycin 1 g/d IV for 7 days were added for the treatment of possible pneumonia. Cardiac echocardiography was used to identify an ejection fraction of 70%, with no wall-motion abnormalities and absence of valvular disease. Serial blood cultures and 2 nasal swabs for influenza A were negative. Bronchoscopy identified no endobronchial lesions. No white blood cells were found on a Gram stain of bronchoalveolar lavage, and cultures were negative for bacteria, mycobacteria, and fungi. Serology was negative for atypical pathogens such as *Mycoplasma, Legionella,* and *Chlamydia*. The patient improved progressively after diuresis with intravenous furosemide (she had a negative fluid balance of 2 L/d) and was extubated after 4 days. She was discharged after 1 week of hospitalization.

DISCUSSION

Fluoroquinolones are broad-spectrum antimicrobial agents used for the treatment of urinary tract infections, respiratory tract infections, sexually transmitted diseases, and skin and soft-tissue infections.[2] As a class, fluoroquinolones are generally well tolerated, with the most common (>3% of patients) adverse events including mild and self-limiting gastrointestinal effects, skin rashes, dizziness, and headache.[1,2] However, serious adverse events, such as anaphylaxis,[2] have been reported with fluoroquinolone use in postmarketing surveillance studies rather than in clinical trials or premarketing experience.[3] Anaphylactoid reactions considered related to fluoroquinolone use might manifest as facial edema, dyspnea, wheezing, hypotension, tachycardia, fever, pruritus, and/or diffuse erythroderma.[4,5] Anaphylaxis has been reported to have occurred after the first intake of ciprofloxacin.[6]

Anaphylactoid reactions, which are nonimmune-logically mediated, have been reported in <5% of cases with orally and intravenously administered fluoroquinolones and mostly with ciprofloxacin.[4–7] Possible cross-reactivity with other quinolones has been suggested.[7]

Cases of anaphylactoid reactions considered related to fluoroquinolone use have been described over the past 2 decades.[6,8–20] Anaphylactoid reactions associated with ciprofloxacin use might be associated with pulmonary edema, as has been described in 2 cases.[14,18] According to the manufacturer of ciprofloxacin, pulmonary edema has been described as a ciprofloxacin-related adverse event in <1% of treated patients.[21] Because ciprofloxacin is a commonly used antibiotic,[6] and because its use might lead to or be related to pulmonary edema, clinicians should be aware of the epidemiology, mechanism, and clinical characteristics of ciprofloxacin-associated angioedema. The literature on ciprofloxacin-associated anaphylactoid reactions is reviewed.

Literature review

Previously reported cases of anaphylactoid reactions associated with ciprofloxacin use were found using a search of MEDLINE and EMBASE (years: 1960–June 2009; English-language articles; search terms: *ciprofloxacin, anaphylactoid reaction, anaphylaxis, angioedema,* and *pulmonary edema*). The references cited in all of the identified articles were reviewed to identify additional reports. Based on the different immunologic profiles of patients with HIV infection and their increased susceptibility to allergic reactions from medications including ciprofloxacin,[22] HIV+ patients were assessed separately.

Results

Sixty-four cases of ciprofloxacin-related anaphylactoid reactions considered probably related to treatment, based on Naranjo score, were identified based on data from 20 studies.[3,5–20,23–25] In 42 of these cases, which were described in large studies, detailed data were not reported.[3,6,20,25] Detailed information on the dose of ciprofloxacin, the time period between ciprofloxacin administration and anaphylactoid reaction, clinical manifestations, and outcomes of these reactions was available in 22 cases described in case reports and is summarized in Tables I and II. Twelve cases in HIV– patients (Table I) and 10 cases in HIV +patients were described (Table II).[9,12,14,16,18,19]

Based on 12 cases with available data on HIV–patients, the mean age of the patients was 35 years (range, 15–79 years), and 5 of 12 (41.7%) were male. Moreover, based on 7 cases with available data on HIV+ patients, the mean age of the patients was 35.6 years (range, 31–44 years) and 6 of 7 (85.7%) were male. Ciprofloxacin was given intravenously in 3 of 22 cases (13.6%).[5,7,24] In all HIV+ patients with anaphylactoid reactions occurring with ciprofloxacin use, symptoms occurred after the first dose of the second course of therapy,[9,14,16,18,19] whereas symptoms of anaphylaxis occurred after re-exposure to ciprofloxacin in 4 HIV–patients.[8,12,15,17] Concentrations of immunoglobulin E (IgE) were determined in 2 cases[7,24] and were elevated (>100 IU/mL). C4-, C3-, and C1-inhibitor levels were documented in 1 case report and were repeatedly normal.[7] Intradermal testing with ciprofloxacin was documented in 1 case and was positive.[7] All patients recovered, with the exception of 2 HIV+ patients, who died (causes of death, unknown in 1 case and toxoplasma

encephalitis in the other case).[12,16] In 5 patients, no data on outcome were reported.[15,19,24] Fourteen patients (including all of the HIV+ patients) required hospitalization in the intensive care unit.[5,7,9,12,14,16–19] According to the manufacturer, pulmonary edema has been described as an adverse event associated with ciprofloxacin in <1% of treated patients.[21] However, the literature search of the MEDLINE and EMBASE databases did not identify any published reports of ciprofloxacin-associated pulmonary edema.

Epidemiology of Fluoroquinolone-Associated Angioedema

Data on the occurrence of serious allergic reactions with fluoroquinolone use are limited but have been reported with ciprofloxacin use, with a prevalence of 0.46 to 1.2 per 100,000 patients treated.[4–6,26] Based on a spontaneous adverse-events report, the frequency of fluoroquinolone-associated anaphylaxis has been estimated to be 1.8 to 23 per 10 million patient–days of treatment, depending on the fluoroquinolone studied.[27] A previously published literature review of 384 case reports of unpredictable adverse reactions to fluoroquinolones reported that anaphylactic reactions occurring within 1 hour after fluoroquinolone ingestion have been reported in 167 individuals, with 39 cases of anaphylactic shock.[28] However, in a retrospective study of 262 cases of adverse reactions to ciprofloxacin (acquired from a US Food and Drug Administration outpatient-based database), 15 anaphylactoid reactions (5.7%) were reported.[6] In 1 retrospective study based on the database of spontaneous adverse drug reactions of the Federal Institute for Drugs and Medical Devices in Germany, ciprofloxacin accounted for 21 of 166 cases (13%) of anaphylactic/anaphylactoid reactions, and the corresponding reporting rate per 1 million defined daily doses was 0.2 for ciprofloxacin.[25] In an epidemiologic report that documented the adverse events experienced in 3863 postal employees who used antimicrobial agents (89% on ciprofloxacin) for anthrax prophylaxis, 2% of the persons who received antimicrobial agents experienced symptoms that may have been associated with anaphylaxis.[21] Anaphylactoid reactions to fluoroquinolones have been reported in patients of all ages (29 months to 79 years).[27,28]

Based on the absence of data from clinical trials, and variations in terminology used in various investigations (eg, *anaphylaxis, anaphylactic shock, anaphylactic/anaphylactoid reaction*), it is unclear whether the various fluoroquinolones are associated with different rates of individual occurrence and reporting of anaphylaxis, although evidence from retrospective studies suggests that these reactions are more common with moxifloxacin.[5,8,25] In 1 retrospective study of the incidence per 10,000 first diagnoses of any allergy made in the hospital or emergency department, the incidences of anaphylactic/anaphylactoid reactions did not appear to differ substantially between fluoroquinolones, penicillin, and cephalosporins.[3] Moreover, estimating prevalence based on spontaneous reporting is problematic because underreporting of cases was likely, and the size of the exposed population from which the cases arose is difficult to determine. More data are needed on the prevalence of anaphylactoid reactions related to fluoroquinolone use.

Mechanism of Ciprofloxacin-Related Anaphylactoid Reactions

In general, angioedema can be allergic or nonallergic, which basically means IgE mediated or not IgE mediated (ie, by direct stimulation of the effector cells), respectively.[5,7] Both

mechanisms produce the same clinical picture. However, no sensitization phase is necessary for non–immune-mediated reactions, which may occur after first-ever intake. Although non–immune-mediated reactions were formerly also referred to as *anaphylactoid reactions,* in contrast to *IgE-mediated anaphylactic reactions,*[29] the terms might be used interchangeably. There have been reports of anaphylactoid reactions in HIV– patients with the use of certain fluoroquinolones, such as levofloxacin (500 mg/d IV), ciprofloxacin (400 mg IV q12h), and moxifloxacin (400 mg/d IV), without the presence of drug-specific IgE or evidence of cross-reactivity with other fluoroquinolones.[3]

Nonallergic angioedema might be caused by hereditary disposition, be of iatrogenic origin, or result from the use of drugs that may increase bradykinin concentrations.[30] Clarification of the underlying mechanism in fluoroquinolone-associated immediate reactions is difficult because there is no routine test for the detection of fluoroquinolone-specific IgE, and skin tests have been found to be false-positive in healthy control subjects and false-negative in affected individuals.[28,31] The exact mechanism of fluoroquinolone-associated anaphylactoid reaction is unknown. However, based on findings from pharmacokinetic studies, it has been suggested that the high intracellular penetration characteristic of this drug class and its ability to release mediators, such as histamine and/or its complements and kinin activation from mast cells, may be important mechanisms.[13,19] Findings from an in vitro study suggested that the potency of fluoroquinolones to induce the release of vasoactive substances might induce non–immune-mediated, pseudoallergic reactions.[28]

According to a retrospective study analysis, a history of fluoroquinolone use and a short time to the onset of the reaction suggest underlying non–immune-mediated mechanisms in a considerable number of cases, based on the assumption that with non–immune-mediated reactions, no sensitization phase is necessary.[3] In a review of 384 cases of unpredictable adverse reactions to fluoroquinolones, Campi and Pichler[28] found that fluoroquinolone-specific IgE was detected in 55% of patients (30/55) with a history of immediate reactions to fluoroquinolones, suggesting underlying non–immune-mediated mechanisms in the other 45% of patients. Drug-related rashes have been estimated to be 100-fold more common in HIV+ patients than in the general population.[22] Anaphylactoid reactions associated with ciprofloxacin are more common in HIV+ patients, an occurrence that is poorly understood but might be due to disturbances in cytokine profiles, such as overexpression of interferon-γ and immune hyperactivation.[22]

Time Between First Administration of Ciprofloxacin and Anaphylactoid Reaction

In a retrospective study based on the database of spontaneous adverse drug reactions in Germany, in 21 of 166 cases (13%) of ciprofloxacin-related anaphylactic/anaphylactoid reactions, the reactions occurred within the first 3 days of ciprofloxacin administration, and it was stated that the particular fluoroquinolone had never been used before but that the possibility of use of a previous fluoroquinolone was not entirely ruled out.[25] In this study of 166 cases, 2 cases (1%) of anaphylaxis occurred after first use or within the first 3 days of use in reportedly fluoroquinolone-naive patients, suggesting non–immune-mediated mechanisms for the reaction in these 2 cases.[25] In HIV+ patients with anaphylactoid reactions considered likely related to ciprofloxacin, symptom presentation may occur within

minutes after administration of the first dose of the second course of therapy,[9,14,16,18,19] whereas in HIV– patients, reactions can develop within 1 hour of the administration of the initial dose.[6] The time to onset of anaphylactoid reactions with intravenous infusion of fluoroquinolone varied from 15 to 30 minutes after the start of infusion to 5.5 hours after the end of drug administration.[6,8–19] In a retrospective study in 307 patients identified in a database of spontaneous reports of adverse drug reactions, drug-associated anaphylaxis was reported more often after intravenous compared with oral administration of drugs (59.1% vs 40.9%).[29] However, in the German retrospective study, fluoroquinolone was administered intravenously in 3% of reports of anaphylaxis (5/166), and 2% of the reports (3/166) in that study were associated with a fatal outcome.[25] These observations may be of importance because fluoroquinolones typically are administered orally, and in cases of anaphylaxis/anaphylactoid reaction, immediate care may not be available, unlike with intravenous drug application, which may take place under a physician's surveillance.

A temporal relationship was noted between the start of ciprofloxacin treatment and the onset of clinical manifestations consistent with fluoroquinolone-associated anaphylactoid reaction. Angioedema has been reported with NSAID use.[32] Angioedema might be related to ciprofloxacin use in combination with other drugs such as angiotensin-converting enzyme inhibitors.[33] However, based on the literature search, this association has not been previously described with NSAIDs. It is unclear whether ibuprofen had a synergistic effect with ciprofloxacin in inducing angioedema. However, the patient in the present report had received ibuprofen in the past without any reported reaction. Noncardiogenic pulmonary edema has been reported with ibuprofen use in a 38-year-old healthy person who received ibuprofen 600 mg PO TID for 2 weeks postoperatively.[34] However, in that case, there was a genetic predisposition for the reaction. The patient in the present case report had previously received ibuprofen for premenstrual pain and had no family history of a similar reaction.

The reaction in the patient in this case report was considered anaphylactoid because the condition occurred with the first exposure to the drug, and the patient experienced a complete recovery after ciprofloxacin treatment was discontinued and supportive care with ceftriaxone was provided. The ciprofloxacin reaction in this patient was likely anaphylactoid, but anaphylaxis cannot be ruled out because the symptoms are indistinguishable. Anaphylactoid reactions are clinically similar to anaphylactic reactions but may occur after first exposure to a drug and are not mediated by IgE. The 2 terms are often used interchangeably because both reactions lead to the activation of mast cells and the release of mediators, including histamine.[3,5] There are reports of anaphylactoid reactions to certain fluoroquinolones without the presence of drug-specific IgE or evidence of cross-reactivity to other quinolones.[3,5] Because this patient did not undergo an intradermal skin test with ciprofloxacin, IgE release could not be determined in this reaction. Application of the Naranjo adverse drug reaction probability scale for angioedema and pulmonary edema (score of 6 for ciprofloxacin and 2 for ibuprofen) suggested that these adverse events were probably related to ciprofloxacin use. The pulmonary edema was of unclear etiology, and diffuse opacification was found on chest radiography, suggesting pulmonary capillary leak. Pulmonary edema has also been previously described in 2 cases of ciprofloxacin-associated anaphylactoid reaction.[14,18] Although pulmonary edema has also been described as a direct effect of ciprofloxacin,[21] the bilateral ground-glass opacities in the absence of white blood

cells and negative cultures from bronchoalveolar lavage, the normal cardiac function (ejection fraction, 70%), and the timing of events after angioedema might suggest pulmonary capillary leak as the cause of noncardiogenic pulmonary edema, as part of a systemic anaphylactoid reaction resulting from ciprofloxacin use. In this case, the pulmonary edema was detected after the onset of angioedema. However, a retrospective study of 166 cases of fluoroquinolone-related anaphylactic/anaphylactoid reactions in Germany reported that a ciprofloxacin-related anaphylactoid reaction might manifest even after a prolonged time period of days.[25]

Treatment of Anaphylactoid Reaction

Corticosteroids, antihistamines, epinephrine, and supportive care have been used to treat anaphylactoid reaction or anaphylaxis associated with ciprofloxacin.[3] However, the best "treatment" for anaphylaxis is prevention. Although a desensitization protocol has been tried, caution should be used when applying this protocol in individual patients.[35] These patients also may wear an identifying medical bracelet and carry an emergency kit. Because anaphylactoid reactions are potentially life threatening, the administration of fluoroquinolones should be avoided in patients who have experienced a reaction to any of these agents.

CONCLUSIONS

The patient described in this case report experienced an anaphylactoid reaction likely associated with ciprofloxacin use. Although anaphylactoid/anaphylactic reactions are uncommon (<5% of cases) adverse events associated with the use of ciprofloxacin and other fluoroquinolones, clinicians should be aware of this potentially life-threatening event, which might also lead to pulmonary edema even in the setting of normal renal function.

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Table I.

Anaphylactoid reactions considered ciprofloxacin related in HIV– patients.

Report	Age	Sex	Patient Characteristics	Ciprofloxacin Administration/Onset of Anaphylactoid Reaction	Presentation	Outcome
Lobera et al (2008)[24]	41	F	NR	Administered preoperatively (IV; dose NR); during induction of anesthesia	Cutaneous (erythema, rash, urticaria/angioedema)	NR
Kothur et al (2006)[23]	15	F	Healthy adolescent	PO (dose NR); within a few minutes of administration	Patient developed pruritus and urticaria, shortness of breath and angioedema that progressively worsened, and she became unconscious	Patient regained consciousness within a few hours of treatment
Ho et al (2003)[5]	79	M	Repair of an abdominal aortic aneurysm, hypercholesterolemia, hypertension, peripheral vascular disease, and diverticulosis	400 mg IV q12h;~30 minutes after the start of infusion of the first dose	Initially, a local area of erythema and pruritus was noted and the patient then developed respiratory distress and rigors. The infusion of ciprofloxacin was terminated immediately. His respiratory status worsened rapidly, and he developed severe tachypnea and wheezing	Pyelonephritis resolved; patient was discharged on day 4 of hospitalization; on follow-up, no further symptoms and an HIV test was negative
Erdem et al (1999)[13]	29	F	NR	15 mg/kg IV; 15 minutes after the start of infusion of the first dose	Fever, tachycardia, tremors, headache, flushing, vomiting	Symptoms resolved spontaneously within 1 hour after infusion was discontinued
Clutterbuck and McMillan (1997)[10]	35	M	Eczema	Single dose of 500 mg PO; 10 minutes after administration	Lightheaded, urticaria, choking	Symptoms resolved 30 minutes after administration of chlorpheniramine
Salon et al (1997)[17]	47	F	Systemic lupus erythematosus	500 mg PO; 30 minutes after administration (patient had received ciprofloxacin 250 mg BID PO 1 week earlier)	Hypotension, generalized erythematous rash	Hospitalized; required vasopressors + fluid resuscitation; discharged after 5 days
Vidal et al (1995)[7]	50	M	Type 1 diabetes, patient was receiving captopril for hypertension	400 mg IV; within 30 to 60 minutes after the start of infusion	The patient experienced generalized pruritus, erythema, and prominent facial, lip, and genital swelling with upper dyspnea. Four hours later, patient noted a change in voice with hoarseness, inspiratory stridor, and asphyxia	Recovered
Assouad et al (1995)[8]	21	F	NR	(Dose/route of administration/duration NR) 30 minutes after administration; patient had received ciprofloxacin (dose/route of administration/duration NR) 2 weeks prior and experienced a milder reaction	Shortness of breath, generalized pruritus, facial swelling, hives	Angioedema; hospitalized overnight
Dâvila et al (1993)[11]	26	F	Atopy	Single dose of 250 mg PO; 2–3 minutes after administration	Dysphonia, generalized urticaria, angioedema	Treated in the emergency department
Deamer et al (1992)[12]	46	M	NR	PO (dose/duration NR) (restart; patient had received a 10-day course [earlier dose/route of earlier course NR]); within 24 hours	Hypotension, tachycardia, fever, erythema	Discharged after 3 days of hospitalization

Report	Age	Sex	Patient Characteristics	Ciprofloxacin Administration/Onset of Anaphylactoid Reaction	Presentation	Outcome
Miller et al (1991)[15]	15	F	Cystic fibrosis	PO (dose/duration NR);1 hour after administration of the first dose	Urticaria, headache, fever, vomiting	NR
Miller et al (1991)[15]	16	M	Cystic fibrosis	PO (dose/duration NR);30 minutes after administration of the first dose (patient had received a 14-day course 6 months earlier [dose/route of earlier course NR])	Generalized pruritus, angioedema, shortness of breath, urticaria	Treated in the emergency department

F = female; NR = not reported; M = male.

Table II.

Anaphylactoid reactions considered ciprofloxacin related in HIV+ patients.

Report	Age	Sex	PatientCharacteristics	Ciprofloxacin Administration/Onset of Anaphylactoid Reaction	Presentation	Outcome
Soetikno et al (1993)[18]	44	M	AIDS	750 mg BID PO; 5 days after start of administration (a similar reaction occurred in the past 2 weeks after receiving ciprofloxacin)	Hypotension, fever, diffuse erythroderma	Hospitalized in ICU, required fluid resuscitation and vasopressors; discharged 21 days later
Deamer et al (1992)[12]	35	M	HIV	PO (dose/duration NR); 2 days after treatment initiation (patient had received 10-day course 3 days earlier)	Hypotension, tachycardia, diffuse rash, fever, delirium	Died; toxoplasma encephalitis on autopsy
Deamer et al (1992)[12]	36	M	AIDS	(Dose/route/duration NR); reaction time after dose NR) Patient had received a 10-day course 6 months earlier	Mild, diffuse pruritus after first dose of ciprofloxacin; anaphylactoid reaction after second dose, with fever, hypotension, wheezing, and diffuse rash with marked swelling	Hospitalized; recovered at 3 days
Berger and Franklin (1992)[9]	38	M	AIDS	PO (dose/duration NR; 2 hours after dose (patient had received a course of oral ciprofloxacin 10 days earlier)	Hypotension, hypoxic, tachypneic, generalized erythematous rash, facial edema	Hospitalized in ICU; improved at 4 days
Kennedy et al (1990)[14]	33	F	HIV	PO (dose/duration NR); 5 minutes after administration of the first dose	Dyspnea, hypotension, stridor, cyanosis, pruritic rash	Hospitalized in ICU, intubated for 6 days and recovered
Kennedy et al (1990)[14]	31	M	AIDS, chronic osteomyelitis	PO (dose/duration NR);15 minutes after administration of the first oral dose of third course of ciprofloxacin (patient had experienced erythematous rash with first and second courses 4 days prior)	Shortness of breath, total body erythroderma, hypotension, tachycardia	Hospitalized, improved over 2 days
Wurtz et al (1989)[19]	3Patients (age NR)	NR	AIDS	(Dose/route/duration NR); 2nd time received ciprofloxacin (patient had received a 10- to 14-day course in the past)	Hypotension, pruritus, wheezing, erythroderma, fever	NR
Peters andPinching(1989)[16]	32	M	AIDS	500 mg PO; 10 minutes after administration of the first dose of the 2nd course (patient had received 10-day course of ciprofloxacin 4 weeks prior)	Hypotension, dyspnea, anuria, tachycardia, epigastric pain, vomiting	Died after cardiac arrest and resuscitation

M = male; ICU = intensive care unit; NR = not reported; F = female.