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Case Report Open Access

A Case of Anaphylaxis Following Administration of Garenoxacin Mesylate Hydrate

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Abstract

A 64-year-old woman took Garenoxacin Mesylate Hydrate (GRN) 400 mg and several drugs for the treatment of upper respiratory tract infection. Two and a half hours later and soon after bathing, she suddenly noticed pruritis on her face and hands. After her arrival at emergency unit of our hospital, she developed dyspnea and wheezing accompanied by generalized erythema and wheals. Within one hour following treatment with methylprednisolone sodium succinate and chlorpheniramine maleate, her cutaneous and respiratory symptoms subsided. Prick tests using diluted saline solution of these drugs showed positive results with GRN, whereas the other drugs were negative. Oral challenge tests, which were performed with all the drugs except for GRN, showed negative results at therapeutic doses. Based on these results, she was diagnosed as anaphylaxis related to GRN. During one-year follow up period after avoiding quinolones, she has not experienced any episode of anaphylaxis. Although quinolone-related anaphylaxis is not uncommon, our case is the first case report describing precise clinical history of anaphylaxis related to GRN.

Keywords: Quinolones; Anaphylaxis; Hypersensitivity; Garenoxacin Mesylate Hydrate; Prick test

Introduction

Garenoxacin mesylate hydrate (GRN) is a quinolone antibiotic with potent antimicrobial activity against common respiratory pathogens, including resistant strains, such as penicillin-resistant *Streptococcus pneumoniae* and beta-lactamase-negative ampicillin-resistant *Haemophilus influenzae* [1]. Quinolones are generally safe and well tolerated; however, anaphylactic reactions have been reported [2]. Here, we report a case of anaphylaxis related to GRN.

A 64-year-old woman took GRN 400 mg, montelukast 10 mg, carbocisteine 500 mg, eprazinone hydrochloride 20 mg and tranexamic acid 250 mg for the treatment of upper respiratory tract infection after dinner containing pickled scallops. She had occasionally taken levofloxacin or GRN for respiratory infections since 2 years before. This was the fourth time that she had taken GRN. She had never experienced of general anesthesia and had no other significant medical history except for mild bronchial asthma, which was occasionally treated by inhaled corticosteroids. Two and a half hours after taking these drugs and soon after bathing followed by applying moisturizer on her face, she suddenly noticed pruritis on her face and hands, and visited emergency unit of our hospital. On arrival, her consciousness was alert, blood pressure was 169/99 mmHg and oxygen saturation (SpO_2) level was 97% (with room air). Cutaneous findings revealed diffuse erythema and wheals on her face, arms and abdomen (Figures 1a-c). Within 20 min after her arrival, she developed dyspnea, wheezing and low SpO_2 92% (with room temperature).

According to world allergy organization guidelines for the assessment and management of anaphylaxis, [3] she was diagnosed with anaphylaxis and treated with intravenous administration of methylprednisolone sodium succinate 125 mg, chlorpheniramine maleate 10 mg, and acetated ringer's solution 500 mg, combined with nebulised salbutamol sulfate 0.3 mg and supplementary oxygen. Within one hour, her cutaneous and respiratory symptoms subsided.

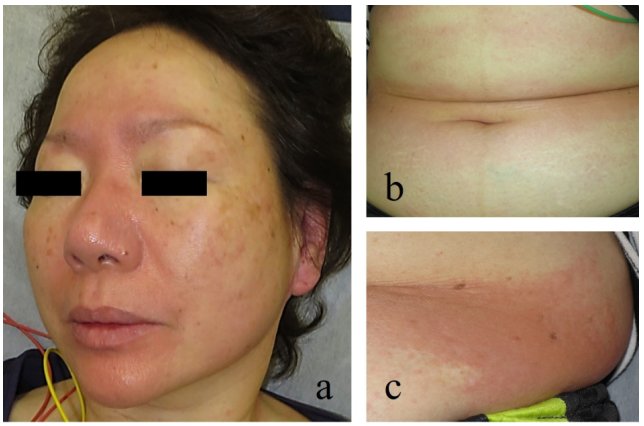

Figure 1: Diffuse erythema and wheals on face (a) and abdomen (b, c).

Laboratory test results were not significant: white blood cell count, 6,480/mm^3 (43.7% neutrophils, 1.4% eosinophils) ; C-reactive protein 0.20 mg/dL; Asperate aminotransferase, 24 U/L; Alanine aminotransferase, 20 U/L; Alkaline phoshatase, 176 U/L; Total bilirubin, 0.29 mg/dL; Lactate dehydrogenase, 206 U/L; creatinine 0.51 mg/dL; Antinuclear antibody, <1/40; 50% Hemolytic complement (CH50) activity, 32.0 SI; Complement component 3 (C3), 96 mg/dl ; C4, 27 mg/dl ; Immunoglobulin E, 88 IU/mL; Radio-allergosorbent test of scallops, <0.10 UA.

Four weeks later, prick tests using 1% saline solution of the suspicious drugs, as well as prick to prick tests with a pickled scallop and the moisturizer were conducted. Normal saline and 1% histamine dihydrochloride were used as a negative and a positive control, respectively. A positive result with 1% GRN at 15 min was obtained (2+), (6 × 6 mm wheal, 12 × 13 mm erythema) (Figure 2a), while the other results were all negative. The positive result was reproducible with 2% GRN (2+), (5 × 6 mm wheal, 9 × 10 mm erythema) (Figure 2b). Three healthy volunteers showed no reaction to 1% GRN. Oral challenge tests, which were performed with all the drugs except for the most suspicious GRN, showed negative results at therapeutic doses. Likewise, ingestion of pickled scallops and applying the moisturizer on her face did not provoke any reaction. We subsequently performed prick tests with 1% saline solution of levofloxacin tablet and 1.2 mg/ml ciprofloxacin. Weakly positive results with 1% levofloxacin (1+), (3 × 3 mm wheal, 9 × 12 mm erythema) and 1.2 mg/ml ciprofloxacin (1+), (2 × 2 mm wheal, 8 × 9 mm erythema) were obtained (Table 1).

	Wheal (mm)	Erythema (mm)	Interpretation
First test			
1% Garenoxacin mesylate hydrate	6 × 6	12 × 13	2+
1% Tranexamic acid	0 × 0	4 × 4	-
1% Eprazinone hydrochloride	0 × 0	4 × 5	-
1% Montelukast	0 × 0	3 × 3	-
1% Carbocisteine	0 × 0	3 × 3	-
Pickled scallop	0 × 0	3 × 3	-
Moisturizer	0 × 0	3 × 3	-
1% Histamine dihydrochloride	10 × 10	26 × 24	Positive control
Normal saline	0 × 0	3 × 3	Negative control
Second test			
2% Garenoxacin mesylate hydrate	5 × 6	9 × 10	2+
1% Histamine dihydrochloride	6 × 7	15 × 17	Positive control
Normal saline	0 × 0	0 × 0	Negative control
Third test			
1% Levofloxacin	3 × 3	9 × 12	1+
1.2 mg/ml Ciprofloxacin	2 × 2	8 × 9	1+
1% Histamine dihydrochloride	10 × 10	40 × 45	Positive control
Normal saline	0 × 0	0 × 0	Negative control

Table 1: Results of the skin prick tests.

Basophil activation test (BAT), which was performed using an Allergenicity Kit (Beckman Coulter, Fullerton, CA, USA) to quantify basophil CD203 expression, showed negative result with GRN. The Naranjo adverse drug reaction probability scale [4] demonstrated a probable relationship between anaphylaxis and GRN with a score of 6, whereas the other medications, pickled scallops, and moisturizer demonstrated a possible adverse drug reaction with scores of 1 or 2. Based on these results, she was diagnosed as anaphylaxis related to GRN. During one-year follow up period after avoiding quinolones, she has not experienced any episode of anaphylaxis.

Quinolone-related anaphylaxis is not uncommon. According to the analysis of 333 cases with severe drug-induced anaphylaxis in France, quinolones were the second most common incriminated antibiotics (15 cases) after beta-lactams (138 cases). They were attributed to moxifloxaxin (eight cases), ofloxacin (three cases), lomefloxacin (two cases), norfloxacin (one case) and flumequine (one case), respectively, and diagnosed by prick test (46.7%), or intradermal test (13.3%), or clinical criteria, such as chronology and single drug intake (40%) [2]. Adverese cutaneous reaction against GRN has not been reported except for a case report of fixed drug eruption due to GRN [5]. Although statistical data of the Pharmaceutical Affairs Act in Japan in 2008 indicates 21 cases of anaphylaxis due to GRN, [6] our case is the first report describing precise clicial history of anaphylaxis related to GRN.

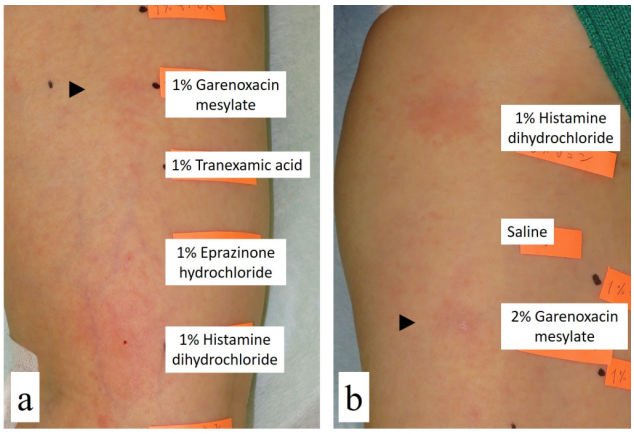

Figure 2: Results of skin prick tests. Positive reactions to (a) 1% and (b) 2% garenoxacin mesylate were observed (arrow head).

Evaluations of prick tests in quinolones are controversial because prick tests in quinolones are known to display both false negative [7] and false positive results [8]. Rouzaire et al. performed BATs in 34 patients who were being evaluated for quinolone hypersensitivity. They found that 50% of their subjects had negative BATs. Subsequently, they were able to successfully reintroduce quinolones in 15 of the 17 patients. They stated that 13 patients with positivite results for both BAT and skin test had high probability of allergic hypersensitivity [8]. However, reliability of BAT in quinolone is still not validated and its sensitivity has been reported 36.0-79.2% [9]. The allergic nature of the reaction in our case was not able to clarify because the result of BAT was negative and provacation test with GRN was not performed due to ethical considerations concerning the severity of the initial reaction. Nevertheless, since all the other possibities were excluded, hypersensitivity to GRN in our case seemed to be undeniable.

Immediate-type hypersensitivity reactions to quinolone often occur within 1 h after the intake of quinolones [8]. The time to onset of reaction in our case was rather delayed. Pharmacokinetics revealed that time to maximum plasma concentration (t max) of 400 mg GRN

was 2.46 h, [1] while tmax of 500 mg levofloxacin was shorter (1.23 h) [10]. Thus, the delayed t max of GRN may explain the late onset of anaphylaxis in our case. In addition, increased body temperature due to bathing might have accelerated mast cell degranulation through an unknown mechanism.

Cross-sensitivity between quinolone derivatives has been reported between ciprofloxacin and levofloxacin [11]. On the other hand, there is a case report of anaphylaxis due to levofloxacin with tolerance to GRN [12]. Although we advised our patient to avoid all quinolone derivatives because anaphylactic reactions are potentially life threatening, the evaluation of cross-sensitivity in our case seems to be controversial due to the weakly positive results of ciprofloxacin and levofloxacin with prick tests.

In conclusion, we have reported a first case of anaplylaxis following administration of GRN. We should keep in mind that GRN can develop anaphylaxis as shown in other quinolone derivatives. Further accumulation of case reports is required in order to clarify the diagnostic procedure.

References

1. Takagi H, Tanaka K, Tsuda H, Kobayashi H (2008) Clinical studies of garenoxacin. Int J Antimicrob Agents 32: 468-474.
2. Renaudin JM, Beaudouin E, Ponvert C, Demoly P, Moneret-Vautrin DA, et al. (2013) Severe drug-induced anaphylaxis: analysis of 333 cases recorded by the Allergy Vigilance Network from 2002 to 2010. Allergy 68: 929-937.
3. Simons FE, Ardusso LR, Bilò MB, Dimov V, Ebisawa M, et al. (2012) 2012 Update: World Allergy Organization Guidelines for the assessment and management of anaphylaxis. Curr Opin Allergy Clin Immunol 12: 389-399.
4. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, et al. (1981) A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 30: 239-245.
5. Miyake M, Oiso N, Yoshinaga E, Kawada A (2013) Fixed drug eruption due to garenoxacin mesilate hydrate. Eur J Dermatol 23: 111-112.
6. Horikawa T (2014) Anaphylaxis caused by drugs. Yakuji (in Japanese) 56: 51-55.
7. Valdivieso R, Pola J, Losada E, Subiza J, Armentia A, et al. (1988) Severe anaphylactoid reaction to nalidixic acid. Allergy 43: 71-73.
8. Rouzaire P, Nosbaum A, Denis L, Bienvenu F, Bérard F, et al. (2012) Negativity of the basophil activation test in quinolone hypersensitivity: a breakthrough for provocation test decision-making. Int Arch Allergy Immunol. 157: 299-302.
9. Doña I, Torres MJ, Montañez MI, Fernández TD (2017) In Vitro Diagnostic Testing for Antibiotic Allergy. Allergy Asthma Immunol Res. 9: 288-298.
10. Furlanut M, Brollo L, Lugatti E, Di Qual E, Dolcet F, et al. (2003) Pharmacokinetic aspects of levofloxacin 500 mg once daily during sequential intravenous/oral therapy in patients with lower respiratory tract infections. J Antimicrob Chemother. 51: 101-106.
11. Anovadiya AP, Barvaliya MJ, Patel TK, Tripathi CB (2011) Cross sensitivity between ciprofloxacin and levofloxacin for an immediate hypersensitivity reaction. J Pharmacol Pharmacother 2: 187-188.
12. Fukushima, Nakatsubo M, Noda M (2012) Anaphylaxis due to intravenous levofloxacin with tolerance to garenoxacin. Intern Med 51: 1769-1772.