

CASE REPORT

Ciprofloxacin-induced immune-mediated thrombocytopenia: No cross-reactivity with gemifloxacin

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Summary

What is known and objective: Fluoroquinolone-induced immune-mediated thrombocytopenia is uncommon, and no reports of cross-reactivity among fluoroquinolones exist. Here, we describe a case of ciprofloxacin-induced immune thrombocytopenia with no cross-reactivity with gemifloxacin.

Case description: A 77-year-old woman showed profound thrombocytopenia immediately after two ciprofloxacin injections for pneumonia. Platelet counts recovered rapidly after ciprofloxacin discontinuation. She had experienced thrombocytopenia after ciprofloxacin administration 4 years earlier, which was assumed to be ciprofloxacin-induced immune-related. Interestingly, no thrombocytopenia occurred following the subsequent exposure to another fluoroquinolone, gemifloxacin.

What is new and conclusion: No cross-reactivity occurred between ciprofloxacin and gemifloxacin in this fluoroquinolone-induced immune thrombocytopenia case.

KEYWORDS

ciprofloxacin, cross-reactivity, drug-induced immune thrombocytopenia, gemifloxacin

1 | WHAT IS KNOWN AND OBJECTIVE

Although drug-induced thrombocytopenia is a common clinical disorder, severe thrombocytopenia (platelet count $<50\,000/\mu\text{L}$) may lead to serious complications.¹ Because thrombocytopenia can be caused by several factors, drug-induced thrombocytopenia could easily be overlooked.¹ Most cases of drug-induced thrombocytopenia result from decreased platelet production and increased platelet destruction.² Immunosuppressive and chemotherapeutic agents cause cytotoxic myelosuppression, which is typically dose dependent and affects all cell lines.³ In contrast, drug-induced immune thrombocytopenia (DITP) involves antibody-mediated platelet destruction that leads to isolated thrombocytopenia without anaemia or leucopenia.⁴

DITP is thought to occur when drug-dependent antibodies bind to the platelet membrane glycoproteins to activate platelet consumption signalling.⁴ Several studies have reported that platelet nadir typically occurs between 1 and 7 days, and as late as 21 days after initiation of the culprit drugs.⁴ Consequently, antibody-mediated platelet destruction should be suspected in patients with an acute drop in platelet levels, usually within a week of starting a new medication.⁴

Many drugs have been associated with DITP, such as quinidine/quinine, salicylates, sulphamethoxazole/trimethoprim, aspirin, vancomycin, clopidogrel and glycoprotein IIb/IIIa receptor inhibitors.^{3,5} Until recently, only a few cases of fluoroquinolone-induced thrombocytopenia have been reported.⁶⁻¹³ However, a study has shown a correlation between thrombocytopenia and fluoroquinolone in intensive care unit patients.¹⁴ In addition, some cases of thrombotic thrombocytopenic purpura and DITP associated with fluoroquinolones have been reported.^{9,15} The structural similarities between quinine and fluoroquinolones could explain the DITP associated with the latter.¹³ Nevertheless, no cross-reactivity between fluoroquinolones has been reported in DITP induction. Here, we described a case of ciprofloxacin-induced DITP, which was not cross-reactive with gemifloxacin.

2 | CASE DESCRIPTION

A 77-year-old woman presented at our pulmonary clinic with fever, diaphoresis, headache and dyspnoea. She had been regularly monitored for known idiopathic pulmonary fibrosis but had

not been prescribed medications. Blood tests showed a leucocyte count of 6300/ μ L, haemoglobin level of 12.3 g/dL, platelet count of 220 000/ μ L and C-reactive protein level of 12.9 mg/dL. Contrast-enhanced computed tomography chest images revealed multiple, variably sized centrilobular nodules in both lungs, suggesting bacterial pneumonia.

She was admitted to our hospital and was empirically administered imipenem (Prepenem[®], JW Pharmaceutical, Seoul, Korea) and azithromycin (Zithromax[®], Pfizer Korea, Seoul, Korea). On day 6, a bronchoalveolar lavage fluid examination identified quinolone-susceptible *Pseudomonas aeruginosa*. On day 7, the antibiotics were changed to gemifloxacin (320 mg once daily), based on the above results. On day 8, gemifloxacin was replaced with ciprofloxacin due to a medical insurance issue. Immediately after the administration of two doses of ciprofloxacin (400 mg twice daily), the platelet counts decreased to 6000/ μ L. Initially, the thrombocytopenia was thought to have resulted from pneumonia. However, on day 11, the platelet counts remained extremely low, although the pneumonia had improved. She was referred to our allergy department for a possible drug allergy consultation. At that time, she was assumed to have DITP and ciprofloxacin was strongly suspected as the culprit drug. On day 12, ciprofloxacin was discontinued, and she was switched to cefepime. The platelet counts rapidly returned to normal, and on day 18, cefepime was again changed to oral gemifloxacin (320 mg once daily). However, thrombocytopenia was not noted after 2 days (Figure 1). She was discharged with a 2-week prescription for gemifloxacin oral medication, and even 2 weeks later, her platelet counts remained in the normal range at the outpatient clinic (platelet count, 245 000/ μ L).

We obtained her incomplete medical information on possible previous drug allergies, which revealed she had been administered some medications (L-carbocysteine, bromhexine, ciprofloxacin, hexoprenaline sulphate and codeine) at a local clinic 4 years earlier. After treatment with the medications for 4 days, her platelet count dropped

to 9000/ μ L from a premedication level of 220 000/ μ L. Even on the following day, the platelet count remained low (3000/ μ L) and sputum was blood-tinged sputum. Further evaluation of thrombocytopenia was not performed because the patient refused.

The present case could be diagnosed as ciprofloxacin-induced DITP, based on the DITP criteria¹⁶ and the Naranjo adverse drug reaction probability scale.¹⁷ The administration of ciprofloxacin was initiated prior to the onset of thrombocytopenia, and the patient's platelet count recovered following the discontinuation of ciprofloxacin, which was the only new medication administered. Furthermore, no other causes for the low platelet count were identified, and re-exposure to ciprofloxacin resulted in a concomitant drop in platelets. The patient's Naranjo score was 9, which indicates a definite association between ciprofloxacin administration and thrombocytopenia. Other diseases known to cause thrombocytopenia, including idiopathic thrombocytopenia purpura, sepsis, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, haemolytic anaemia and pseudothrombocytopenia, were excluded based on the clinical and laboratory findings. Drug-specific antibody tests have been used to detect the presence of markers for drug-induced antibodies. However, technical issues make these tests difficult to perform and they are not widely available.¹

The patient in this case may have been sensitized to ciprofloxacin 4 years ago, and the re-exposure to ciprofloxacin might have subsequently destroyed her blood platelets very rapidly by antibody-mediated mechanisms.

Our patient was given another fluoroquinolone, gemifloxacin, twice during admission (Figure 1). The first dose of gemifloxacin administered on day 7 might have induced DITP. However, our observation that the second dose administered on day 18 did not cause thrombocytopenia clearly excludes the possibility. Finally, gemifloxacin was well tolerated by the patient, suggesting that no cross-reactivity occurred between ciprofloxacin and gemifloxacin in the induction of DITP.

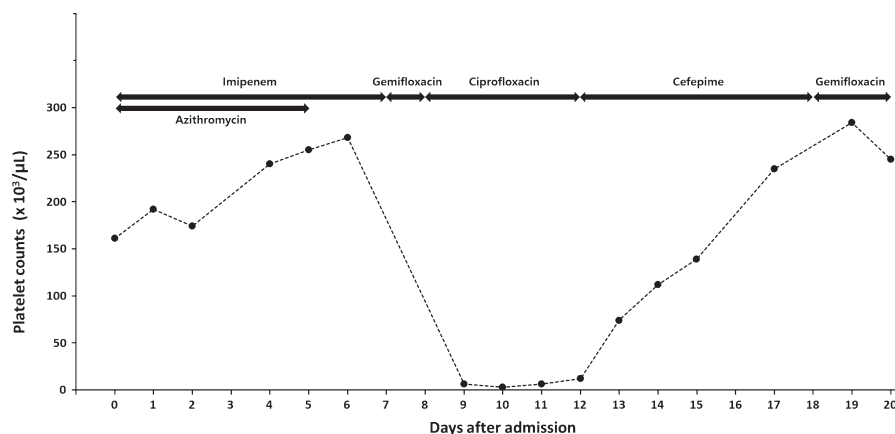


FIGURE 1 Changes in blood platelet count following the administration of various antibiotics during admission. Administered drugs were imipenem (500 mg intravenously every 6 h), azithromycin (500 mg orally on day 1, followed by 250 mg once daily on days 2-5), gemifloxacin (320 mg orally once daily), ciprofloxacin (400 mg intravenously every 12 h) and cefepime (1 g intravenously every 12 h)



3 | WHAT IS NEW AND CONCLUSION

To the best of our knowledge, this is the first reported case showing no cross-reactivity between ciprofloxacin and gemifloxacin in the induction of DITP, although a small trial reported low rates of cross-reactivity for IgE-mediated hypersensitivity reactions.¹⁸ We concluded that gemifloxacin could be administered safely in a patient with ciprofloxacin-induced DITP.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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