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LETTER TO THE EDITOR

# Acute renal failure caused by severe coagulopathy induced by the interaction between warfarin potassium and levofloxacin: a case report

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To the Editor:

A 30-year-old man took warfarin potassium (4 mg/day) for several years because of idiopathic dilated cardiomyopathy (ejection fraction was 48 %, and no arrhythmia was observed).

His medical regimen included aspirin (100 mg/day), digoxin (0.25 mg/day), pimobendan (20 mg/day), and atenolol (50 mg/day); glimepiride (4 mg/day), voglibose (2.7 mg/day), and allopurinol (900 mg/day) (for diabetes mellitus and hyperuricemia); and milnacipran hydrochloride (25 mg/day), fluvoxamine maleate (200 mg/day), risperidone (2 mg/day), and sodium valproate (800 mg/day) (for Asperger's syndrome). Despite the long-term use of these medicines, neither renal disorders nor bleeding tendencies were observed [prothrombin time (PT)-international normalized ratio (INR) (PT-INR) was controlled around 1.5].

The patient presented to the emergency room with hematuria. Laboratory analyses indicated elevated white blood cell counts (20,500 cells/$m^3$) and C-reactive protein levels (4.5 mg/dl), but no anemia. We suspected urinary tract infection; therefore, levofloxacin (900 mg/day) was prescribed.

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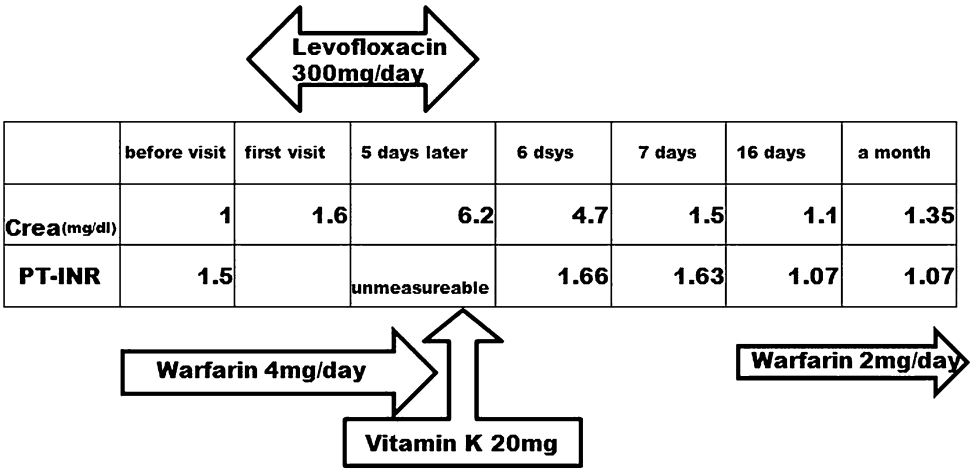
After 6 days, the patient was brought to the emergency room because of hypovolemic shock resulting from nasal hemorrhage (Hb 3.7 mg/dl, Hct 10.9 %). Prothrombin time (PT) could not be determined. Acute renal failure (ARF) was suspected because of elevated blood urea nitrogen (100 mg/dl), creatinine (6.2 mg/dl), and serum potassium (6.2 mmol/l) levels. Severe hematuria with a distinct blood clot was observed. Warfarin and aspirin were discontinued; vitamin K (20 mg) was administered. Under strict observation for volume overload, Ringer's solution and washed red cells were administered. Sufficient spontaneous urine production was maintained. Renal function recovered without hemodialysis. The hypovolemic shock caused by nasal bleeding and severe hematuria resulted in prerenal ARF; the hematoma that obstructed the urinary tract resulted in postrenal ARF. We believed both pre- and postrenal ARF were present. The patient's course of PT-INR and creatinine values is shown in Fig. 1.

The patient had been taking warfarin for 3 years. Bleeding improved with vitamin K; therefore, the cause of coagulopathy was thought to be reinforced by the effects of warfarin. Several drugs interact with warfarin [1]. We suspected that valproate, allopurinol, and levofloxacin could interact with warfarin. ARF may have caused elevated plasma valproate and allopurinol concentrations, which could have then interacted with warfarin. However, valproate and allopurinol previously had been taken routinely, without bleeding tendencies. Thus, the newly prescribed levofloxacin was mainly responsible for this coagulopathy.

Ofloxacin suppress the propagation of vitamin K-producing enteric bacteria, and thus the effects of warfarin would be enhanced. Also, warfarin and ofloxacin competitively bind with protein. Thus, the free effect of warfarin increases with the use of ofloxacin [2]. Levofloxacin and ofloxacin are both




| | before visit | first visit | 5 days later | 6 dsys | 7 days | 16 days | a month |
|---|---|---|---|---|---|---|---|
| Crea(mg/dl) | 1 | 1.6 | 6.2 | 4.7 | 1.5 | 1.1 | 1.35 |
| PT-INR | 1.5 | | unmeasureable | 1.66 | 1.63 | 1.07 | 1.07 |

**Fig. 1** Patient's course of creatinine (*Crea*) and prothrombin time-international normalized ratio (*PT-INR*) levels. PT-INR could not be measured when the patient was brought to the hospital after taking levofloxacin

quinolones, and we think that the mechanism of interaction with warfarin and ofloxacin is similar to that with levofloxacin. Jones and Fugate [3] reported that the warfarin–levofloxacin interaction elevated INR and warranted a 19 % warfarin dose reduction during levofloxacin treatment. Glasheen et al. [4] advised caution regarding oral levofloxacin intake by patients receiving warfarin therapy. Levofloxacin also significantly increases the PT-INR.

Considering the interaction between warfarin and levofloxacin, the warfarin dose may need to be reduced. Therefore, PT should be evaluated before determining the levofloxacin dosage and should be monitored at regular intervals.

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