Teicoplanin-induced Thrombocytopenia

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tests for SLE disease, presence of an acute viral illness or dysfunction of the bone marrow were negative. On the sixth day of teicoplanin therapy the serum level was 32.6 mg/1, measured 5 h after administration. After discontinuation of teicoplanin, leukocytopenia and thrombocytopenia recovered within 5 and 8 days respectively (fig. 1).

Dear Sir,

Teicoplanin is a glycopeptide antibiotic structurally related to vancomycin and effective against gram-positive microorganisms. Reported side effects are fever, allergic reactions, local pain at the infusion site, elevation of serum transaminase and creatinine levels, reversible eosinophilia, vestibulo-cochlear complaints and neutropenia [1, 2]. Thus far, only 1 case concerning thrombocytopenia associated with teicoplanin has been reported [3]. Herewith we present a second patient in whom this serious adverse event occurred.

A 24-year old woman with a past medical history of SLE, hypertension and end-stage renal disease, was admitted because of fever after transplantectomy of a kidney. Four weeks earlier, a postmortal kidney had been transplanted in the left iliac fossa, but had been readily removed because of infarction 10 days later. Her medication on admission comprised prednisone 10 mg q.d., pravastatin 10 mg q.d. and hydroxychloroquine 200 mg. With respect to the physical examination only fever (39.3 °C) and local tenderness in the left iliac region were present. Ultrasound investigation revealed a fluid collection in the left iliac fossa which could be evacuated in one session. Initial antibiotic treatment consisted of flucloxacillin intravenously during 4 days, which was replaced by teicoplanin intravenously (loading dose: 400 mg, followed by 200 mg once a day), because final cultures yielded a coagulase-negative staphylococcus. Fever as well as severe thrombocytopenia (8-10^9/1) and leukocytopenia (1.5 · 10^9/1, 49% granulo-cytes and 33% lymphocytes) occurred on the tenth day of teicoplanin therapy. Ancillary

Flucloxa- cillin Teicoplanin < x

6 8 10 12 14 16 18 20 22 24 Days Leukocytes Thrombocytes

Fig. 1. Number of leukocytes and thrombocytes in relation to teicoplanin therapy.

Both sera from the patient during treatment and after stopping the drug were tested for teicoplanin-induced antibodies reactive with autologous platelets by indirect immu-
During treatment, patient’s platelets were already in vivo covered with antibodies as shown by a positive immunofluorescence assay. This indicates an immunological mechanism involved in the thrombocytopenia. However, during treatment, we could not demonstrate the drug dependency of these antibodies at this point. After stopping the drug, direct immunofluorescence became negative and we could indeed demonstrate the presence of teicoplanin-dependent platelet autoantibodies. This was only shown when the drug was incubated with the patient serum before adding the platelets to the test system, which supports an immune complex-mediated reaction. Preincubating patient’s platelets with teicoplanin did not result in a positive assay.

A toxic reaction due to teicoplanin is improbable, as its serum level did not exceed one third of the peak level normally measured after intravenous administration. Concomitant use of the other drugs seems an unlikely explanation too, as all drugs except the flucloxacillin were continued during recovery of the thrombo- and leukocytopenia.

The in vitro tests provide sufficient evidence, in concordance with the normalization of the cell counts and the temperature after withdrawal of teicoplanin administration, to conclude to a causal relationship. Therefore, a rechallenge was judged as inappropriate and unethical. However, the first report on teicoplanin-associated thrombocytopenia validated the relationship with a positive rechallenge. In addition, the long plasma half-life of teicoplanin (especially in patients with renal insufficiency) offers a suitable explanation for the slow recovery of the thrombocytopenia and leukocytopenia seen in our patient.

In conclusion, leukocytopenia and thrombocytopenia appear to be very rare, but serious adverse events in patients treated with teicoplanin. Taking into account the increasing need for antibiotics as teicoplanin, one should be aware of these clinically important side effects.

### References


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