incidence of O25b-ST131 among antimicrobial-susceptible (as defined by susceptibility to all of ciprofloxacin, co-trimoxazole and gentamicin) isolates was low (2.9%, 5/175). PCR and sequencing showed that the only extended-spectrum β-lactamase (ESBL)-producing O25b-ST131 isolate had blaCTX-M-14.

Our results showed that O25b-ST131 exhibited a wide range of susceptibility patterns. Similar to previous studies,1,5 our findings showed that O25b-ST131 isolates were often multi-drug resistant and one was a CTX-M producer. However, the only ESBL-producing O25b-ST131 isolate was found to have blaCTX-M-14 instead of blaCTX-M-15.1,5 Among blood culture E. coli isolates collected in 2007–08, our recent work showed that O25b-ST131 accounted for 25.6% of the ESBL-producing isolates.3 All ESBL-producing O25b-ST131 isolates had blaCTX-M-14 and none had blaCTX-M-15.1 As our previous studies revealed, the dissemination of blaCTX-M-14 in O25b-ST131 isolates was associated with the acquisition of an epidemic pHK01 plasmid with FII replicon.3 In conclusion, this study showed that O25b-ST131 clonal group is widely distributed among antimicrobial-resistant and one was a CTX-M producer. However, the findings showed that O25b-ST131 isolates were often multi-drug resistant and one was a CTX-M producer. However, the only ESBL-producing O25b-ST131 isolate had blaCTX-M-14.

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Transparency declarations
None to declare.

References
Doses over 4 days without a clinically evident reaction. Ethambutol, pyrazinamide and isoniazid were not reintroduced on the assumption that they were the likeliest offenders. He was discharged from hospital on the four antituberculosis drugs.

Six weeks later he presented again with a 3 week history of the same rash. In the meantime his sputum reverted to culture-negative, and his tuberculosis symptoms and radiological features had improved. We thought rifampicin was the likeliest offender, but decided not to replace it with another second-line drug or rechallenge with the three first-line drugs initially omitted. This was informed by the patient’s unwillingness to restart the rechallenge process, the clinical improvement and the delay in clinical manifestation of LDR, possibly due to topical steroids. We continued treatment under cover of clobetasol. The rash improved and he was discharged from hospital.

He presented again 3 weeks later with worsening hyperpigmentation, depigmentation and diffuse alopecia, despite topical steroids. We introduced thrice weekly bath psoralen and ultraviolet A (PUVA). His skin gradually improved; however, 1 month later he developed photo-distributed rash with painful fissures, which we attributed to excessive sun exposure (see Figure 1). PUVA was suspended for 1 week and he was advised to minimize sun exposure. Sunscreen was prescribed, and he was advised to wear a hat and gloves on the day he received psoralen, a potent photosensitizer. He completed 12 months of treatment, and continued steroids and PUVA for 3 months thereafter. His skin has clinically improved with only residual hyperpigmentation and leucoderma (see Figure 1).

LDR presents as purple itchy papules becoming confluent and hyperpigmented with continuing exposure to the offending drug. The interval between initiating the drug and the rash ranges from days to years, with most cases occurring within months. On withdrawing the drug, the lesions resolve with persistent hyperpigmentation, often lasting for many years.\(^4\)

The lack of acute markers, insidious onset of the rash, and varying intervals between drug initiation and a clinically detectable rash make it difficult to establish a temporal relationship with the drug and ascribe causality in LDR. This is more so in patients receiving multiple drugs. The limited number of effective antituberculosis drugs, the cessation of which is associated with a higher mortality, increases risk of drug resistance, longer duration of therapy and public health concerns, make it necessary to balance the interruption of therapy against treating through the ADRs.\(^1,5\)

PUVA is used to treat a wide variety of inflammatory dermatological conditions, such as scleroderma, lichen planus, psoriasis, vitiligo, cutaneous T cell lymphoma and atopic dermatitis. It is also effective for pruritus associated with systemic disease. Psoralen is administered orally or topically by soaking in bathwater, followed by irradiation.

The first-line therapy generally used for LDRs is high-potency topical steroids, although there are no clinical trials supporting their use. There are better data supporting the use of acitretin, systemic steroids and other immunosuppressants.\(^6\) However, considering our patient’s marked immunosuppression and concurrent tuberculosis, we decided to use only topical steroids.

This case illustrates practical dilemmas in managing tuberculosis-associated ADRs. Should suboptimal treatment be used or should a potentially life-threatening therapy be continued despite serious side effects? We decided to continue treatment and manage the side effects, as the alternative would likely result in a poorer outcome. Phototherapy, in combination with topical steroids, is an option in the management of LDRs when the offending drug cannot be identified.

Written permission was given by the patient to publish the case and images.

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Teicoplanin therapy leading to a significant decrease in viral load in a patient with chronic hepatitis C

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Sir,

We read with interest the paper by Obeid et al.,1 ‘Inhibition of hepatitis C virus replication by semi-synthetic derivatives of glycopeptide antibiotics’. It provided us with a possible explanation for a clinical observation that we made.

We would like to report an elderly patient with chronic hepatitis C. The patient’s alanine aminotransferase levels were consistently ~120 U/L and a Fibroscan showed liver stiffness of 43.5 kPa correlating with stage IV fibrosis in 2010. The patient had completed a total of three antiviral treatment cycles with pegylated interferon and weight-based ribavirin. The last course of therapy had been maintained for 72 weeks and was finished in April 2010. Although the patient experienced on-treatment response, relapse occurred very shortly after the end of each therapy.

In April 2010, the patient received a right hip joint replacement in another hospital, which was complicated by delayed wound healing. On 31 May 2010, the patient fell on their hip and had to have repeat surgery. During the following days a fever developed and on 4 June two blood cultures were positive for Staphylococcus aureus. The surgical site was presumed the focus of infection and an antimicrobial therapy with ampicillin/sublactam was initiated. The patient was then transferred to the gastroenterology ward of our hospital on 28 June 2010. In consultation with infectious diseases specialists and orthopaedic surgeons, we decided to switch the antimicrobial therapy to long-term teicoplanin starting on 7 July. We administered 1600 mg of teicoplanin intravenously two to three times a week for a total of 10 weeks (trough level 9.2–19.9 mg/L). Surprisingly, 12 days after the initiation of teicoplanin treatment, normal serum transaminase levels were measured for the first time in 30 years. Hepatitis C viral load measurement on 13 August showed a significant decrease in the patient’s RNA load to 2.0 log10 IU/mL (previous measurement on 28 June: 6.9 log10 IU/mL). Subsequent measurements yielded RNA loads of ~<15 IU/mL on 27 August and 2.9 log10 IU/mL on 17 September, which was the last day of teicoplanin therapy (Figure 1). Transaminase levels remained normal until 1 October, but have been elevated since. Also, the patient’s hepatitis C RNA levels returned to the usual baseline levels of ~6.0 log10 IU/mL.

There is some evidence that glycopeptides and their derivatives show antiviral effects against retroviruses and coronaviruses,2,3 but Obeid et al.1 were the first to report activity of teicoplanin derivatives against hepatitis C virus replicons in an in vitro model. The mechanism of action of these compounds and the exact molecular substructures responsible for inhibition of viral replication have not yet been elucidated. However, the authors speculate that the peptide scaffold common to all these substances might play a major role in their antiviral activity.

Our patient showed significant decreases in the hepatitis C viral load and transaminase levels during teicoplanin therapy. Teicoplanin has been shown to enter human cells4 and therefore a post-entry interaction with the hepatitis C virus replication cycle, as proposed by Obeid et al.1 for their compound LCTA-949, may be a possible explanation for the observed effect. Another conceivable mechanism might be interference of teicoplanin with host cell factors such as lipid metabolism and membrane organization, which are both important for hepatitis C virus replication.5

It has been suggested that heterologous viral infections may trigger hepatitis C virus-specific T cell responses6;7 however, hepatitis B virus and HIV infection were excluded in our patient. Furthermore, our patient did not show any clinical signs of influenza and there was no influenza activity in Austria at that time. In the absence of any other explanation, we speculate that teicoplanin interfered with hepatitis C virus replication and led to the observed decrease in the viral load.

Unfortunately, our patient was not available for a trial of repeat exposure to teicoplanin, because the patient is currently undergoing treatment with triple antiviral therapy. To the best of our knowledge this is the first description of a possible effect of teicoplanin on in vivo hepatitis C virus replication.

References


None to declare.