antibiotic therapy and therapeutic drug monitoring is available for only a handful of antibiotics. This is important, as suboptimal antibiotic therapy is associated with worse outcomes. Systematic research using ex vivo circuits, large animal models and population PK studies are indicated to improve antibiotic prescription and, hence, patient outcomes during ECMO.

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Transparency declarations
None to declare.

References
8.4 mm internal diameter). The patient received symptomatic treatment with spiramycin, metronidazole, prednisone and acetaminophen; in addition, opioid analgesia was necessary. At day 3, a salivary stone was spontaneously released and collected to determine its composition.

After solubilization of the yellowish calculus in acid aqueous solvent (10.2 mg stone weight; 3.4 mm internal diameter), the antiretroviral concentration was determined using liquid chromatography coupled with tandem mass spectrometry, as previously described. Atazanavir was identified as the main component of the salivary stone at 1400 mg/g. At the time of calculi collection, the atazanavir plasma concentration 24 h after the last intake (C24h) was 1775 ng/mL, which is consistent with the median (IQR) value of the atazanavir C24h obtained in frozen plasma during the past 78 months: 1349 ng/mL (1155–1597; n = 7). During this follow-up, the intrapatient variability of the atazanavir C24h was 25% (Figure 1).

To our knowledge, only one case of lithiasis in the salivary glands has been described in an HIV-infected patient treated with an atazanavir/ritonavir-containing regimen. However, no pharmacokinetic data were reported in that case to illustrate a potential atazanavir overdose.

Here, we report a second case of sialolithiasis with obstruction of the parotid duct in an HIV-infected patient without any previous occurrence of renal or biliary lithiasis. Atazanavir was identified in the extracted stone and the median atazanavir C24h was ~10-fold higher than the effective target atazanavir C24h (150 ng/mL). Moreover, since the introduction of atazanavir/ritonavir in this patient’s treatment, the atazanavir C24h was always >850 ng/mL, which is considered the upper limit of safety for the atazanavir C24h.

Since its approval in HIV treatment in June 2003, atazanavir/ritonavir has been known to be associated with renal and biliary lithiasis. Given the literature on this subject, the mechanistic hypothesis of atazanavir stone formation is in situ precipitation consecutive to the pH-dependent solubilization of atazanavir, enhanced by high plasma concentrations, saturation or inhibition of efflux transporters and waning renal (diuresis) and biliary (metabolic) clearances.

The mechanism of atazanavir-related sialolithiasis occurrence is not well established, but among the possible factors we can list are those that might be connected with the present case: bacterial infection increasing the salivary pH, dry mouth worsened by HIV infection and tobacco/cannabis use. In addition, regarding our findings, we suggest adding the high atazanavir C24h as another potential factor.

Given the wide use of atazanavir in the medical management of HIV, knowledge of sialolithiasis as a potential long-term atazanavir-associated complication is important for physicians and patients, and our results should encourage prescribers to be more vigilant for antiretroviral pharmacokinetic variations.

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**References**


