Tumor necrosis factor α (TNFα) plays a complex and even paradoxical role in the natural history of HIV infection. Serum levels of this cytokine are elevated prematurely after the acquisition of the virus and can exert a protective function, as it was shown to inhibit HIV-1 entry into primary macrophages *in vitro* [1]. Conversely, TNFα itself and HIV-1 proteins, which mimic TNFα signaling, have been reported to activate nuclear factor kappa B, thus stimulating viral replication and persistence [2,3]. Furthermore, TNFα-blocking agents are associated with an increased susceptibility to infectious complications, underlying the intimate involvement of this cytokine in the response to intracellular pathogens [4]. Hence, concerns arose regarding the use of those drugs in already immunocompromised patients, such as HIV-infected ones. Primary HIV infection during anti-TNFα therapy, which could influence therapeutic decisions and constitute a challenge in the management of such patient, was not addressed before in the literature.

A 16-year-old woman who was diagnosed with colonic and complex perianal Crohn's disease started infliximab (IFX) in 2008 (5 mg/kg, at 0, 2, and 6 weeks, followed by maintenance infusions every 8 weeks). Screening exams prior to anti-TNFα initiation, including HIV testing, were unremarkable. In July 2015, being in clinical remission for 1 year, she presented with a 24-h history of a nonpruriginous skin rash and fever, denying any gastrointestinal symptoms. She recalled unprotected intercourse during the last few weeks with a partner who had a recent diagnosis of urethritis. Laboratory studies demonstrated lymphopenia and a positive p24 antigen, with an undetectable anti-HIV 1/2 antibody. Further evaluation, performed 2 weeks later, confirmed HIV-1 seroconversion by Western blot, also showing a viral load of 74.941 copies/ml (4.87 log) and a $CD4^+$ T-cell count of 899 cells/μl. After careful consideration of benefits and risks, it was decided to start HAART with Emtricitabine/Tenofovir disoproxil fumarate (200 and 245 mg) and Darunavir/ritonavir (800 and 100 mg) and to maintain IFX maintenance therapy. Currently, with a follow-up of 18 months, no other complications were documented. $CD4^+$ T-cell levels remained stable and above 1.000 cells/μl throughout this period, having achieved an undetectable viral load (Fig. 1a,b). Regarding Crohn's disease, the patient maintained clinical and endoscopic remission without any IFX-related adverse events.

In a review of the literature, we identified 29 case reports of HIV-positive patients who received TNFα antagonists in the clinical practice [5–7]. Noteworthy, the vast majority of those study participants (86%) were also under HAART. In all cases, HIV infection preceded biological therapy initiation. Infectious complications were reported in five patients: a diagnosis of pulmonary and nodal tuberculosis; a facial abscess resolved with antibiotics; multiple bacterial infections culminating in sepsis and death; the development of septic shock a few weeks after influenza vaccination; and the occurrence of a *Listeria monocytogenes* meningitis. Remarkably, four of those five study participants had $CD4^+$ T-cell counts below 500 cells/μl, one of them – the patient who died from sepsis – having only 20 cells/μl. In a patient like ours, who had an extensive Crohn's disease and several predictive factors for relapse [8], stopping anti-TNFα treatment could have been deleterious. Additionally, anti-TNFα monoclonal antibodies induce leukocyte apoptosis in the intestinal lamina propria, especially of $CD4^+$ cells, which is one of the key mechanisms for the resolution of the inflammatory infiltrate and prevention of chronicity [4]. Data regarding a possible association between anti-TNFα therapy and variations in peripheral $CD4^+$ T-cell counts are conflicting [9–12]. In our case, it was possible to verify that, after an initial rise, the absolute levels of $CD4^+$ T cells stabilized above 1000 cells/μl, denoting small variations between measurements performed before and following drug's infusions (Fig. 1a,b). In fact, in patients who experienced resumption

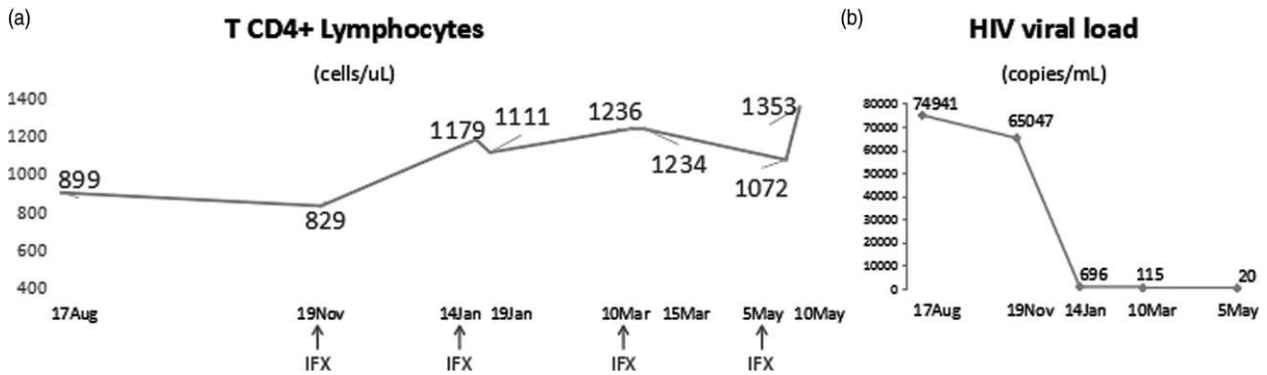

Fig. 1. Evolution of $CD4^+$ T-cell counts (a) and viral load (b) after IFX initiation. Arrows identify the timing of IFX administration. IFX, infliximab.

of HIV replication after HAART discontinuation, an increase in TNFα circulating levels was observed, which was shown to correlate with the degree of $CD4^+$ T-cell decline [13]. Based on the results from this randomized, controlled trial, we may hypothesize that TNFα blockage may have contributed to attenuate $CD4^+$ T-cell loss following HIV infection, allowing the maintenance of high cell counts even before HAART initiation.

Taking this into account, one can propose that TNFα inhibition may be well tolerated in patients who remain with high $CD4^+$ levels, such as the one we presented. With this purpose, early HAART should be considered in study participants with HIV who may require those agents in a near future. Accordingly, in some HIV patients with long-term remission of inflammatory bowel disease, the degree of immunosuppression may play a role in the decision of maintaining or stopping the treatment. In the case described, the clinical presentation of primary HIV infection and the course of the disease were not more severe despite TNFα suppression. Our report suggests that maintaining IFX treatment, when HAART is applied and under close monitoring, may be effective and well tolerated in patients presenting with acute HIV infection.

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Conflicts of interest

There are no conflicts of interest.

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