Introduction

Human immunodeficiency virus (HIV)-associated immune reconstitution inflammatory syndrome (IRIS) has emerged as an important early complication of antiretroviral therapy (ART) initiation, associated with considerable morbidity and mortality.[1] In this condition, immune recovery following the ART initiation associates with a pathological inflammatory response, usually directed toward the microbial antigens. This was first noted following the introduction of zidovudine monotherapy in the early 1990s, when the localized forms of *Mycobacterium avium* ‑intracellulare infection were observed in association with the recovery rather than the failure of cellular immune responses.[2] Here, we present a 7-year-old HIV positive girl who developed IRIS as a complication of the initiation of ART.

Case Report

A 7-year-old HIV infected girl presented with chronic diarrhea and hypocalcemic tetany (serum calcium = 5.6 mg/dl [normal = 8.5 to 11 mg/dl]). She was on trimethoprim-sulfamethoxazole (TMP-SMX) prophylaxis. She had herpes zoster 2 years back. Both the parents were also HIV infected but not on ART. On examination, her weight was 12 kg, height was 103 cm, had generalized as nonsignificant lymphadenopathy with edema feet and pallor. On systemic examination, she had hepatosplenomegaly. Other systems were normal. Her mantoux test was negative; barium meal follow through was normal, and stool showed 20–25 pus cells/hpf. She was treated with intravenous (IV) ceftriaxone, metronidazole, nitazoxanide, and fluconazole to which she responded with calcium supplements. Her CD₄ count was 158 cells/cumm with CD₄:CD₈ of 0.22. She was started on ART consisting of stavudine, lamivudine, and nevirapine. After 1 month of ART, she was admitted with diarrhea. Stool showed the presence of giardiasis and budding yeast. She was treated with intravenous (IV) ceftaxone, metronidazole, nitazoxanide, and fluconazole to which she responded along with calcium supplements. Her CD₄ count was 158 cells/cumm with CD₄:CD₈ of 0.22. She was started on ART consisting of stavudine, lamivudine, and nevirapine. After 1 month of ART, she was admitted with diarrhea. Stool showed the presence of giardiasis and budding yeast. She was treated with IV cefotaxime, amikacin, TMP-SMX, and required inotropes in the form of dopamine and dobutamine, and also prednisolone to which she responded. She was subsequently tapered off the steroids and were doing well.

Keywords: Giardiasis, human immunodeficiency virus, immune reconstitution inflammatory syndrome
Discussion

Diarrhea in patients with acquired immune deficiency syndrome (AIDS) is significantly caused by intestinal parasites. Giardia intestinalis is one such pathogenic intestinal parasite. Studies in adults have demonstrated that enteritis due to G. intestinalis is a frequent event among the AIDS patients, especially in the most advanced stage of the disease. In a study of 75 HIV-infected adults in India, G. intestinalis was the most commonly isolated parasite, and patients with the lower CD4 cell counts presented with significantly more enteric disease and chronic diarrhea.

IRIS has been reported in association with a number of diseases and inflammatory conditions. These include tuberculosis, herpes zoster (shingles), Cryptococcus neoformans, Kaposi's sarcoma, Pneumocystis pneumonia, hepatitis B virus, hepatitis C virus, herpes simplex virus, Histoplasma capsulatum, human papillomavirus, and Cytomegalovirus. However, the immune reconstitution syndrome (IRIS) has never been documented with a giardiasis or its treatment.

Our patient was treated empirically with anti-bacterials such as ceftriaxone; anti/protozoal such as metronidazole and nitazoxanide; and anti-fungal agents such as fluconazole because the routine stool examination did not detect any particular organism and HIV-infected children are known to have polymicrobial infections. However, the post-ART, the preexisting infections which might have been partially treated or may have been subclinical was later unmasked by the patient’s regained capacity to mount an inflammatory response. Giardiasis was then diagnosed from the stool sample where it showed up as the causative organism. The patient’s symptoms, this time were more severe, and she went into sepsis for which she was given inotropic support.

A low baseline CD4+ T cell count has also been documented as a major risk factor for the development of IRIS. In a study conducted at a hospital in Mumbai, India, to evaluate incidence and risk factors for IRIS in 37 HIV-infected children, it was found that the patients with opportunistic infections before the antiretroviral treatment would have increased the incidence of IRIS. However, there was no correlation between the degree of immunosuppression and development of IRIS.

There may also be a genetic predisposition and certain genes have been associated with an increased susceptibility to the development of IRIS in the presence of mycobacteria and herpes viruses which might have been the case with our patient who had a prior history of herpes zoster infection.

Therefore, this case highlights that giardiasis may also be considered as a cause of IRIS in patients with HIV infection.

Learning points from the case in family medicine and the primary care:
• Always screen for IRIS in patients who present with infection post-ART
• IRIS may be associated with unusual infections.

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Conflicts of interest
There are no conflicts of interest.

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