

## Case report

# *Giardia intestinalis* diarrhea in a HIV-positive patient with *Pneumocystis jiroveci* pneumonia, as a possible symptom of IRIS

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**ABSTRACT.** Human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) still have a detrimental effect on public health. Lack of adequate therapy inevitably leads to the decrease in lymphocyte T CD4+ population and emergence of opportunistic infections (OIs) and AIDS-indicators. *Pneumocystis jiroveci* pneumonia (PjP) is recognized as one of the most common OIs in people living with HIV. *Giardia intestinalis* is a protozoan parasite, commonly reported throughout the world as the most important non-viral cause of human diarrhea. Immunocompromised patients are a high risk group for parasitic infections. Giardiasis usually is self-limiting, however it can cause severe dehydration and malnutrition, especially in immunocompromised individuals. In this work we described a case of 46-year old men, who stopped ART and expanded IRIS symptoms due to PjP and *Giardia intestinalis* infections. We concluded that parasitic stool examination in HIV/AIDS individuals should be performed to detect asymptomatic protozoa infections, which can lead to diarrhea during ARV treatment. Moreover, determination of the IRIS risk factors may have a detrimental effect on the prevention of severe complications in patients living with AIDS.

**Keywords:** AIDS, *Giardia intestinalis*, pneumonia, diarrhoea, CAART

## Introduction

Human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) still have a detrimental effect on public health, despite the introduction of highly active antiretroviral therapy (HAART, antiretrovirals ARV) which lead to immense decrease in mortality [1]. In developed countries AIDS is mainly seen as a consequence of non-compliance to treatment or insufficient testing. Lack of adequate therapy inevitably leads to the decrease in lymphocyte T CD4+ population and emergence of opportunistic infections (OIs) and AIDS-indicators. *Pneumocystis jiroveci* pneumonia (PjP) is recognized as one of the most common OIs in people living with HIV and an important primary

presentation of AIDS-related immunosuppression with CD4+ count below 200 cell/mm<sup>3</sup> [2]. *Giardia intestinalis* is a protozoan parasite, commonly reported throughout the world as the most important non-viral cause of human diarrhea. Annually, it affects approximately 280 million people worldwide. The prevalence of giardiasis varies from 2% in developed countries to 70% in developing ones [3]. Although stool antigen testing and PCR-gastrointestinal panels can detect different enteropathogens including parasites and are helpful in diagnostics procedures, the gold standard for *Giardia intestinalis* diagnosis is stool microscopy with 90% sensitivity when 3 stool samples are examined [4]. Immunocompromised patients are a high risk group for parasitic infections. Giardiasis

usually is self-limiting, however it can cause severe dehydration and malnutrition, especially in immunocompromised individuals. Several studies have reported that patients with immune deficiencies such as HIV infection and AIDS are more likely to suffer from *Giardia intestinalis* invasion [5]. *Giardia intestinalis* is a parasitic protozoan that inhabits the vertebrate hosts upper small intestine and is the most common cause of waterborne diarrhea worldwide [6]. *Giardia intestinalis* infection causes enterocytes damage which leads to watery diarrhea, steatorrhea, nausea, abdominal pain, vomiting with following weight loss. The main consequence of *Giardia intestinalis* infection is malabsorption syndrome [7]. We present a case report of a 46-year old male who presented with severe PjP and developed an acute diarrhea of *Giardia intestinalis* etiology. Unusual course, exacerbation of symptoms and the need for advanced treatment resulted in the suspicion of immunological reconstitution inflammatory syndrome (IRIS) diagnosis in this patient.

### Case description

A 46-year-old male patient was admitted to the Infectious Diseases, Immunodeficiency and Hepatology Department of Poznan University of Medical Sciences, Poland, due to severe dyspnoea, persistent dry cough, general weakness and 10 kg weight loss. He was transferred from a pulmonary ward with the diagnosis of pneumonia. Thoracic high-resolution computed tomography (HRCT) revealed the presence of disseminated interstitial changes, which occupied almost 80% of the lungs. Infection of *Mycobacterium tuberculosis* was ruled out with negative interferon-gamma release assay (IGRA). *Pneumocystis jirovecii* was detected due to positive molecular sputum analysis and the patient received 120 mg/kg trimethoprim-sulfamethoxazole (TMP-SMX) intravenously with oral prednisolone 40 mg daily. The patient had been diagnosed with HIV infection in 2013 and was successfully treated with emtricitabine, tenofovir and dolutegravir. He also was diagnosed with chronic hepatitis B (anti-HBc total positive, HBs Ag negative). In 2021 the patient abandoned ARV due to travelling and lack of AIDS symptoms. On admission to the infectious ward, the respiratory effort was observed and the physical examination revealed presence of disseminated crackles, tachycardia and subcutaneous tissue retardation.

Laboratory tests resulted in elevated levels of the inflammatory markers: CRP – 83 mg/l (0.0 – 5.0), IL-6 – 89.8 pg/ml (0.0 – 7.0), ferritin – 755 ng/ml (30 – 400), fibrinogen 601 mg/dl (170 – 420), WBC count – 14.2 G/l (4.0 – 11.0) with neutrophilia 92% (40 – 75)], hypoalbuminemia 18 g/l (35 – 52) and vitamin D deficiency 16.2 ng/ml (31 – 50). Lymphocyte CD4<sup>+</sup> cell count was reduced to 25 cells/mm<sup>3</sup> and viral load was established at 655 000 copies/ml. Presence of IgG anti-CMV 77.8 AU/ml and anti-*Toxoplasma gondii* – 14.8 IU/ml were also detected suggesting previous infections. Previous syphilis infection serology markers were detected as well [RPR 1:4 (n:<1:4), TPHA 1:320 (n:<1:100), FTA 1:100 (n:<1:10)]. The treatment was continued with prednisolone, TMP-SMX with additional 500 mg of clarithromycin twice a day and 1000 mg meropenem 3 times a day. Negative cryptococcal antigen (CrAg) led to initiation of ARV therapy with emtricitabine/tenofovir (Tivicay) and darunavir/cobicistat (Rezolsta). The patient required persistent high flow therapy (Airvo HFNC system) and symptomatic treatment. Despite accurate therapy and the patient's condition slowly improving with the reduction of inflammatory markers, three weeks after the admission the patient started to present with abdominal pains and diarrhea. Microbiological stool examination ruled out *Clostridium difficile* infection with LDH and A/B toxins being negative. Molecular stool section (digestive Multiplex PCR) detected the nucleic acid of *Giardia*. The parasitic microscopic stool examination revealed the presence of numerous *Giardia intestinalis* cysts. In addition, repeated blood serology showed probable reactivation of the chronic hepatitis B with high HBsAg level (3082,66) as well as increased level of anti-CMV IgG (> 2500AU/ml, reactive > 6.0). The patient was given metronidazole 250 mg 3 times a day for 7 days and tinidazole 2 g for 4 days, which led to a decrease in the number of stools. Oral paromomycin (Humatine) treatment 500 mg 3 times daily was initiated to eradicate the parasite. The patient was discharged and followed up in the Outpatient Parasitic Ward. The stool examination did not reveal any parasite life stages.

### Discussion

Various intestinal parasitic infections are known to be associated with severe diarrhea in AIDS patients in both underdeveloped and industrialized countries and *Giardia intestinalis* is the main agent

(8%). The prevalence of giardiasis is 1–2 times higher in patients not treated with ARV than those who undergo therapy [8]. Protozoa parasites are known to be responsible for gastroenteritis leading to high morbidity and mortality particularly in people living with HIV/AIDS [9]. *Giardia intestinalis* is a zoonotic endoparasite which invades the small intestine of vertebrate hosts causing diarrheal disease. Almost all mammals can be infected [10]. In humans most common symptoms of acute and chronic illness include abdominal cramps, gas, nausea, flatulence and weight loss. All these may cause malabsorption diarrhea with fatty bulky stools [4]. *Giardia* colonization and proliferation in the small intestine of the host may disrupt the ecological homeostasis of gastrointestinal commensal microbes and contribute to diarrheal disease. Prolonged presence of the parasite in the small intestine can be responsible for dysbiosis, which probably is mediated directly via the parasite's metabolism or indirectly via induction of the host responses which probably is enhanced by immunological system improvement during IRIS which is a rapid deterioration of patient's clinical status due to hyperactive immunological response after implementing therapy (in HIV patients) or putting away immunosuppressive agents (eg. in patients with autoimmune syndromes) [11]. A sudden increase in lymphocyte CD4+ cell counts leads to rise in interleukin and interferon concentrations that activate macrophages and other inflammatory cells. This uncontrolled reaction is often triggered by antigens of opportunistic infection pathogens. In people living with HIV/AIDS the most common etiology factors of IRIS are *Cryptococcus neoformans*, *Mycobacterium* spp., *Cytomegalovirus* and John Cunningham Virus [12]. Also protozoa infection, such as *Giardia intestinalis* which are often asymptomatic can change to fully symptomatic ones. To diagnose IRIS criteria proposed by French et al. [13], eventually those created by Shelburne are used [14]. Depending on the presentation of IRIS underlying cause, the syndrome can be described as “paradoxical” or “unmasking” [15]. Paradoxical IRIS is deterioration of a known disease, present before ART admission, unmasking IRIS unveils a subclinical infection that the patient was not diagnosed with before. Low CD4+ lymphocytes cell count (< 100 cells/ $\mu$ l) prior to ART, as in our case, administration and a quick drop in HIV viremia after the ART are considered risk factors of IRIS in

general, regardless of etiology [16]. Diarrhea is a common complication in hospitalized immuno-compromised patients and is associated with significant morbidity and sometimes mortality. It is worth mentioning the necessity for parasitic stool examination in such individuals' diagnostics in order to quickly introduce specific and more aggressive treatment to achieve parasite eradication [17].

## Conclusions

Parasitic stool examination in HIV/AIDS individuals should be performed to detect asymptomatic protozoa infections, which can lead to diarrhea during ARV treatment. Availability of antiparasitic agents like paromomycin is crucial in the *Giardia intestinalis* eradication which shorten time of gastrointestinal symptoms and prevent later relapses of the infection in immunocompromised patients. Determination of the IRIS risk factors may have a detrimental effect on the prevention of severe complications in patients with AIDS.

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