

Diagnostic and Therapeutic Difficulties of Chronic Diarrhea with *Cystoisospora belli* Inaugural Infection by the HIV at the NTHC-HKM of Cotonou: Literature Review

Angèle Azon Kouanou^{1,*}, Yolande Sissinto Savi De Tovè², Agbodandé Kouessi Anthelme¹, Adélakoun Ange Géoffroy Falade¹, Yves Morel Sokadjo¹, Mahoutin Semassa Ghislain Missiho¹, Olamidé Gloria Marlene Marie Dénise Kouanou¹, Marcelle Vodounou¹, Richard Oba¹, Djimon Marcel Zannou¹

¹Unit of Internal Medicine-Medical Oncology, National Teaching Hospital Center (NTHC)-Hubert Koutougou Maga (HKM), Cotonou, Republic of Benin

²Parasitology-Mycology Laboratory, National Teaching Hospital Center (NTHC)-Hubert Koutougou Maga (HKM), Cotonou, Republic of Benin

Email address:

angele.azonkouanou@gmail.com (A. A. Kouanou)

*Corresponding author

To cite this article:

Angèle Azon Kouanou, Yolande Sissinto Savi De Tovè, Agbodandé Kouessi Anthelme, Adélakoun Ange Géoffroy Falade, Yves Morel Sokadjo, Mahoutin Semassa Ghislain Missiho, Olamidé Gloria Marlene Marie Dénise Kouanou, Marcelle Vodounou, Richard Oba, Djimon Marcel Zannou. Diagnostic and Therapeutic Difficulties of Chronic Diarrhea with *Cystoisospora belli* Inaugural Infection by the HIV at the NTHC-HKM of Cotonou: Literature Review. *International Journal of Infectious Diseases and Therapy*. Vol. 6, No. 4, 2021, pp. 161-164. doi: 10.11648/j.ijidt.20210604.17

Received: November 22, 2021; Accepted: December 17, 2021; Published: December 29, 2021

Abstract: Isosporosis is an opportunistic parasitosis caused by *Cystoisospora belli*. It was more or less frequently found during HIV immunodepression. Its prevalence has considerably decreased since the democratization of antiretroviral treatments and the implementation of a strategy of systematic global management of People Living with HIV (PLWH) and opportunistic infections. We report the case of a 49-year-old PLWH patient discovered during the exploration of recurrent diarrhea. This diarrhea was found to be due to *Cystoisospora belli*. The patient was allergic to cotrimoxazole and was therefore initially treated with ciprofloxacin and tinidazole with poor evolution. The other treatments selected are limited by the lack of access to drugs, both geographically and financially. In view of the persistence of the clinical picture and the continuous presence of the parasite in the stools, several hypotheses have been put forward. That of an under-dosage of the molecule used, of a lack of therapeutic compliance, or of the resistance of the germ to the prescribed molecule. Although the coproculture and antibiogram revealed the sensitivity of the germ to the Ciprofloxacin already prescribed, and to the Cotrimoxazole to which the patient is very allergic, and which can therefore no longer be prescribed. After a second opinion and a review of the literature, the patient was put on Pyrimethamine tablets and Albendazole with folic acid. The evolution was favorable with a significant regression of stools, resumption of appetite, and weight gain after one month. A last coproculture of control did not find any more oocysts of *cystoisospora belli*. In the face of chronic diarrhea, the systematic search for opportunistic germs in PLWHIV is essential. Management is possible.

Keywords: Chronic Diarrhea, NTHC-HKM Cotonou, *Cystoisospora Belli*, Internal Medicine

1. Introduction

Isosporosis is an opportunistic parasitosis caused by *Cystoisospora belli*. It is characterized by chronic recurrent diarrhea [1]. Positive diagnosis is based on the detection of

oocysts in the stool. It is often responsible for severe malnutrition due to dehydration and malabsorption. It is a cosmopolitan disease but is most often found in tropical environments [2]. Its detection should lead to a search for an immunosuppressed environment, in particular HIV. With the

free access and effectiveness of Anti Retro Viral (ARV) treatment, several diseases and opportunistic infections are in the process of regression [3]. However, *cystoisospora belli* infection still poses problems of diagnosis and management in sub-Saharan Africa [4, 5]. Diagnosis is often delayed after failure of several treatments, partly due to the lack of adequate technical facilities [6]. Although management is well codified, there are still difficulties in managing this disease, particularly in PLWHA, even when under antiretroviral treatment (ARV). Indeed, isosporiasis is characterized by an evolution marked by recurrence over several years, even after initiation of an effective ARV treatment and curative treatment [7]. The latter is currently based on cotrimoxazole [8]. However, its use may be limited in many patients with hypersensitivity to this molecule. We report here a case of isosporiasis revealing an HIV infection, characterized by diagnostic but especially therapeutic difficulties.

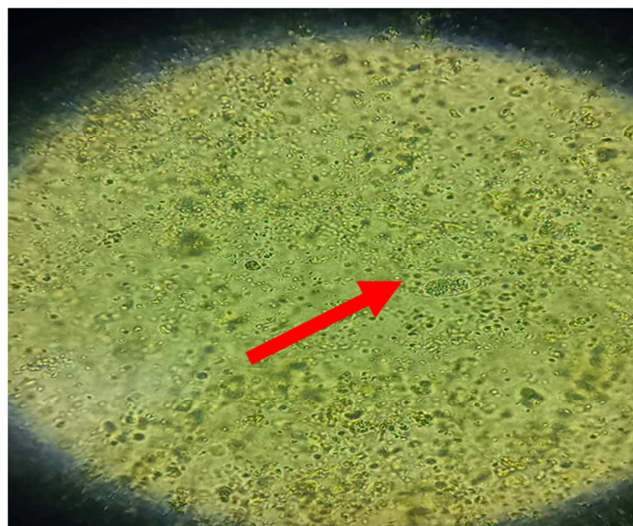
2. Medical Observations

This is a 49-year-old female patient, a reseller, divorced for several years. Infected with HIV, discovered about a year ago, after chronic non-febrile diarrhea. She is currently on Tenofovir, Lamivudine, and Dolutegravir.

The diarrhea was made up of liquid stools that were not bloody, yellowish in color, ranging from 3 to 10 exonerations per day, leading to dehydration and significant weight loss. This required several previous consultations and hospitalizations without success despite a well-conducted empirical antibiotic therapy. It should be noted that the patient is allergic to cotrimoxazole, which limited the empirical antibiotic therapy in the therapeutic arsenal available for the treatment of chronic diarrhea in PLWH. She consulted Internal Medicine for better management.

At the first consultation, she was very asthenic and cachectic. Her weight was 39 kg with a height of 1.60 m. The Body Mass Index (BMI) was 15 kg/m² (thinness). The rest of the physical examination was unremarkable. A stool culture was ordered to check for opportunistic germs: cryptosporidium, *cystoisospora belli*, *Candida albicans*, and mycobacterium tuberculosis. While waiting for the results, she was put on a combination (Ciprofloxacin and Tinidazole). The coproculture performed allowed the identification of *cystoisospora belli* oocysts (figures 1 and 2), which are sensitive to Ciprofloxacin, the first line treatment being Cotrimoxazole.

The evolution was initially favorable for about 10 days, with regression of diarrhea, recovery of body weight, and appetite. However, the resumption of diarrhea required a second consultation. The coproculture was still positive, with identification of *cystoisospora belli* oocysts. Given the persistence of the clinical and biological symptoms, a therapeutic failure was suspected. The HIV viral load performed for this purpose had returned undetectable. Other tests for hyperthyroidism, chronic inflammatory bowel disease, and other intestinal parasitosis were negative.



Source: Parasitology and Mycology Laboratory of NTHC-HKM

Figure 1. Oocysts of *Cystoisospora belli* seen under the electron microscope Olympus CX21.



Source: Laboratory of Parasitology and Mycology of NTHC-HKM

Figure 2. Oocysts of *Cystoisospora belli* seen under the electron microscope Olympus CX21 enlarged.

In view of the persistence of the clinical picture and the continuous presence of the parasite in the stools, several hypotheses have been put forward. That of an under-dosage of the molecule used, of a lack of therapeutic compliance, or of the resistance of the germ to the prescribed molecule. Although the coproculture and antibiogram revealed the sensitivity of the germ to the Ciprofloxacin already prescribed, and to the Cotrimoxazole to which the patient is very allergic, and which can therefore no longer be prescribed.

The control of the molecule showed that the molecule was well dosed, and the patient was very compliant. There was a precious counting of the tablets and the management of the stock of medicines. After a second opinion and a review of the literature, the patient was put on Pyrimethamine tablets and Albendazole with folic acid. The evolution was favorable

with a significant regression of stools, resumption of appetite, and weight gain after one month. A last coproculture of control did not find any more oocysts of *cystoisospora belli*.

3. Discussion

The prevalence of opportunistic parasitosis in PLWHA has decreased considerably [9-11]. *Isospora belli* infection in particular is one of the least frequently encountered [2, 12]. In Benin, it has become almost exceptional. We report here a case of chronic *Isospora belli* diarrhea in a 49-year-old HIV infected woman. The diagnostic and therapeutic course of this patient was characterized by several months of wandering.

3.1. On the Diagnostic Level

Isospora belli can be easily detected by examining stools under light microscopy. This requires that the stool be fresh and that the biologist be well trained. The diagnostic difficulties observed in this patient could be explained on the one hand by the lack of knowledge of the pathology by the different caregivers encountered during her treatment, and on the other hand, by the lack of availability of technical support in many countries. The NTHC-HKM of Cotonou, which is a university hospital center, has a high technical platform and all medical specialties are encountered there. These difficulties are not necessarily exclusive to our working environment. The systematic search for opportunistic germs in the presence of chronic diarrhea in a person living with HIV is essential. Kirkoyun Uysal et al, had underlined the necessity of systematic screening for opportunistic parasites during chronic diarrhea in PLWHA [3, 5].

3.2. On the Therapeutic Level

Currently, the reference treatment for isosporosis is based on the use of trimethoprim/sulfamethoxazole, which has been shown to be superior to other treatments [1, 7, 13]. In this case, the patient was allergic to trimethoprim/sulfamethoxazole. This could explain the long diagnostic and especially therapeutic erraticity in our context where trimethoprim/sulfamethoxazole represents one of the first-line treatments in the management of chronic diarrhoea in PLWHA. In case of allergy to this treatment, the main alternatives are pyrimethamine and ciprofloxacin. The alternative of choice is pyrimethamine, whose efficacy is similar to that of trimethoprim/sulfamethoxazole [7, 14]. However, its cost and lack of local availability initially limited its use in the patient. The patient was therefore treated with ciprofloxacin. A short clinical and parasitological remission was obtained, followed by a rapid relapse. Indeed, studies have shown that recurrence and/or treatment failure were more frequent with ciprofloxacin, and that secondary chemoprophylaxis with trimethoprim/sulfamethoxazole or pyrimethamine was necessary to obtain a better response [1, 13]. Thus, ciprofloxacin reduced the intensity of diarrhea but did not eradicate the germ. In view of the resumption of diarrhea and the presence of *Isospora belli* oocytes on the

second stool sample, the patient was put on pyrimethamine and albendazole, despite the cost and accessibility, with a favorable evolution after one month.

Isosporiasis remains a difficult parasitosis to treat with risk of failure and or recurrence in both immunocompetent and immunocompromised patients [1]. In HIV immunocompromised subjects, the infection would evolve towards a latent phase which would be influenced by the rise in CD4 count and not the viral load [15]. This would justify the persistence of diarrhoea in this patient even though her viral load was undetectable at six months on antiretroviral treatment. The evolution is often slow and complete remission of diarrhea may take several years [3].

4. Conclusion

The case reported is that of a 49-year-old female patient whose chronic diarrhea revealed HIV infection. Isosporosis was identified as the cause of this diarrhea after several months of diagnostic wandering. The ignorance of the practitioners encountered during his treatment, the lack of reference laboratories specialized in this field in many countries, and the concentration of specialists in this field at the CNHU-HKM of Cotonou, which is a university hospital center, explain the diagnostic difficulty. All this explains the lack of systematic search for opportunistic germs in the stools in the face of chronic diarrhea in this patient. The patient was allergic to cotrimoxazole, thus contraindicating her treatment by the reference treatment. Other therapeutic alternatives, which were not available, were prescribed for her management with a favorable outcome. In the face of chronic diarrhea, the systematic search for opportunistic germs in PLWHIV is essential. Management is possible.

References

- [1] Bartelt LA, Dillingham RA. *Cystoisospora belli* (syn. *Isospora belli*). In: Hunter's Tropical Medicine and Emerging Infectious Diseases. Elsevier. 2020; 722-4.
- [2] Getachew T, Hailu T, Alemu M. Prevalence of Opportunistic Intestinal Parasitic Infections Among HIV/AIDS Patients Before and After Commencement of Antiretroviral Treatment at Felege Hiwot Referral Hospital: A Follow-up Study. HIV. 2021; 13: 767-74.
- [3] Kirkoyun Uysal H, Oner YA, Akgül Ö, Kart Yaşar K, Gursoy S, Çağlar S. *Isospora belli* associated recurrent diarrhea in a patient with AIDS. International Journal of Infectious Diseases. 2016; 45: 363-4.
- [4] *Isospora belli* infection in HIV positive patients. Report of two cases and literature review. Rev chil infectol. 2010; 27 (3): 219-27.
- [5] Tefera T, Abera D, Teklu DS, Wolde M. Intestinal parasites and risk awareness of people living with HIV/AIDS in Debre Brehan Referral Hospital, Debre Brehan, Ethiopia: Intestinal parasites and risk awareness of people living with HIV/AIDS in Debre Brehan Referral Hospital, Debre Brehan, Ethiopia *Ethiop Med J*. 2021; 59 (04): 325-36.

- [6] Gebrecherkos T, Kebede H, Gelagay AA. Intestinal parasites among HIV/AIDS patients attending University of Gondar Hospital, northwest Ethiopia. *Ethiop J Health Dev.* 2019; 33 (2): 64-72.
- [7] Pape JW, Verdier RI, Johnson WD Jr. Treatment and prophylaxis of *Isospora belli* infection in patients with the acquired immunodeficiency syndrome. *N Engl J Med.* 1989; 320: 1044-7.
- [8] Straatmann A, Bahia F, Pedral-Sampaio D, Brites C. A randomized, pilot trial comparing full versus escalating dose regimens for the desensitization of AIDS patients allergic to sulfonamides. *Braz J Infect Dis.* 2002; 6 (6): 276-80.
- [9] Wang Z-D, Liu Q, Liu H-H, Li S, Zhang L, Zhao Y-K, et al. Prevalence of *Cryptosporidium*, microsporidia and *Isospora* infection in HIV-infected people: a global systematic review and meta-analysis. *Parasites Vectors.* 2018; 11 (1): 28.
- [10] Guiget M, Furco A, Tattevin P, Costagliola D, Molina J M, French Hospital database on HIV Clinical Epidemiology Group. HIV-associated *Isospora belli* infection: incidence and risk factors in the French Hospital database on HIV. *HIV Medicine* 2007; 8: 124-30.
- [11] Batista FS, de Souza Miranda L, de Oliveira Silva MB, Taborda RLM, Soares MGF and Matos NB. Chronic *Cystoisospora belli* infection in an HIV/AIDS patient treated at the specialized assistance service in Porto Velho County – Rondônia. *Rev Soc Bras Med Trop.* 2019; 52: e20180204.
- [12] Alemu A, Shiferaw Y, Getnet G, Yalew A, Addis Z. Opportunistic and other intestinal parasites among HIV/AIDS patients attending Gambi higher clinic in Bahir Dar city, North West Ethiopia. *Asian Pacific Journal of Tropical Medicine.* 2011; 4 (8): 661-5.
- [13] Verdier R-I, Fitzgerald DW, Johnson WD, Pape JW. Trimethoprim-Sulfamethoxazole Compared with Ciprofloxacin for Treatment and Prophylaxis of *Isospora belli* and *Cyclospora cayentanensis* Infection in HIV-Infected Patients: A Randomized, Controlled Trial. *Ann Intern Med.* 2000; 132 (11): 885.
- [14] Weiss LM. *Isospora belli* Infection: Treatment with Pyrimethamine. *Ann Intern Med.* 1988; 109 (6): 474.
- [15] Maggi P, Larocca A, Quarto M, Serio G, Brandonisio O, Angarano G, et al. Effect of antiretroviral therapy on cryptosporidiosis and microsporidiosis in patients infected with human immunodeficiency virus type 1. *European Journal of Clinical Microbiology and Infectious Diseases.* 2000; 19 (3): 213-7.