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Case Report

Whipple's disease associated with HIV – case report

Doença de whipple associada ao HIV – relato de caso

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ABSTRACT: Despite the lack of literature discussing the topic, the Whipple's Disease (WD) presents higher prevalence in people with compromised immunity, as it happens in HIV. This association can be seen in the current case, which reports a male patient, middle-aged, positive sorologic status for HIV with irregular use of antiretroviral therapy (ART) who presented symptoms of diarrhea and malabsorption during a previous hospitalization for pneumothorax treatment. In a biopsy of the small intestine, by upper gastrointestinal endoscopy, the diagnosis of *Tropheryma whipplei* infection was possible through immunohistochemical examination for periodic-Shiff acid (PSA), with evidence of foamy macrophages with cytoplasm rich in PSA positive granules. The medical conduct was the empirical treatment for pseudomembranous colitis, which includes association of Meropenem, Vancomycin and Metronidazole. With the improvement of the clinical of malabsorption and the decrease of diarrheal episodes the patient got hospital discharge. Yet underdiagnosed in people living with HIV, the WD should be considered in the arise of compatible symptoms, because when treated on time the prognosis of the disease is usually favorable.

KEY WORDS: HIV; Whipple's Disease; HIV Enteropathy; AIDS-Related Opportunistic Infections.

RESUMO: Apesar da escassa literatura abordando o tema, a Doença de Whipple (DW) apresenta maior prevalência em pessoas com a imunidade comprometida, como acontece no HIV. Essa associação pode ser vista no presente caso, que faz relato do paciente de sexo masculino, meia idade, status sorológico positivo para HIV com uso irregular de terapia antirretroviral (TARV) que apresentou sintomas de diarreia e malabsorção durante internação hospitalar prévia para tratamento de pneumotórax. Em biópsia do intestino delgado, via endoscopia digestiva alta, o diagnóstico de infecção por *Tropheryma whipplei* foi possível através de exame imuno-histoquímico para ácido periódico-Shiff (PAS) com evidências de macrófagos espumosos com citoplasma rico em grânulos PAS positivos. A conduta médica foi o tratamento empírico para colite pseudomembranosa que inclui associação de Meropenem, Vancomicina e Metronidazol. Com a melhora do quadro clínico de malabsorção e diminuição dos episódios diarreicos o paciente obteve alta hospitalar. Ainda subdiagnosticado em pessoas vivendo com HIV, a DW deve ser considerada no surgimento de sintomática compatível, pois quando tratada a tempo o prognóstico da doença costuma ser favorável

PALAVRAS-CHAVE: HIV; Doença de Whipple; Enteropatia por HIV; Infecções Oportunistas Relacionadas com a AIDS.

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INTRODUCTION

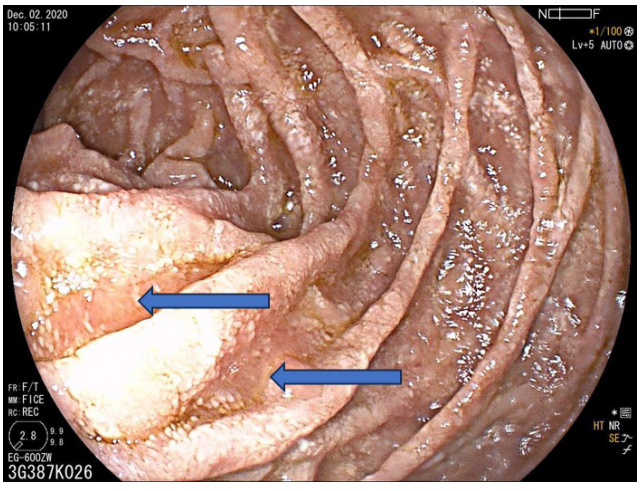
Caused by infection of the gram-positive bacteria *Tropheryma whipplei,* the Whipple's disease (WD) presents symptoms like weight loss, diarrhea and malabsorption because it usually affects the small intestine[1]. As it is a systemic threat, it's not uncommon to infect heart, lungs and brain[2]. If not treated, there is a possibility of gradual worsening and death[2]. It is suspected that can be caused by genetics or acquired immunologic predispositions, such as Acquired Immunodeficiency Syndrome (AIDS) which acts through immunosuppression by the lower counting of Lymphocytes-T CD4+, since the virus utilizes the alteration of the DNA of those cells to multiply and to continue disseminating[3]. The association between WD and HIV still lacks literature, in searches throughout the main portal accesses to scientific articles using the key words "whipple" and "hiv" together only five relevant results about it came up, among these, 4 other case reports[9-12] and 1 transversal study in Ghana[5].

CASE REPORT

We present the case of a person living with HIV, diagnosed with the virus infection for four years, male gender, 48 years old, body weight of 75 kilograms, caucasian, in manifestation of AIDS and in disordered antiretroviral treatment with Lamivudine, Tenofovir and Efavirenz combined. Furthermore, it was noticed in his exams a viral load of 1.890.685 copies and a count of lymphocytes T CD4+ of 17 cels/mm³. The patient presented a clinical picture of ponderal weight loss, fever, abdominal pain, malabsorption and watery diarrhea without the presence of mucus or pus reaching 10 episodes per day which persisted for one month during hospital stay for treatment of a right-sided pneumothorax.

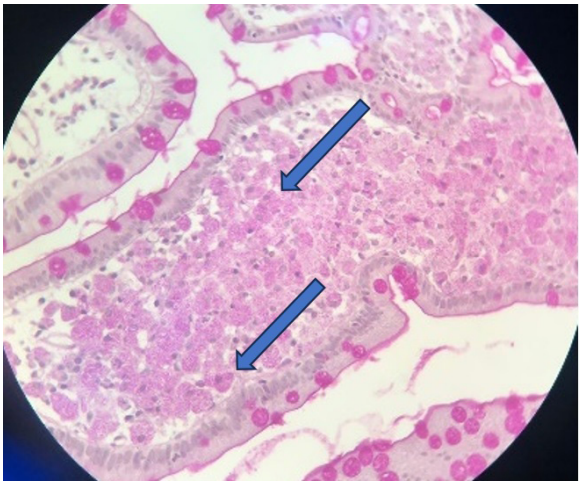
In the clinical investigation, during the exam of upper gastrointestinal endoscopy, it was already possible to observe big areas of deterioration of the duodenal mucosal villi, a compatible WD manifestation characteristic (Figure 1).

Figure 1 - Areas of deterioration of the duodenal mucosal villi



Duodenal biopsy was collected for realization of histopathological exam and immunohistochemical analysis, the analyzed histology suggested typical infection by *Tropheryma whipplei*. In conjunction, the positive coloration for periodic-Shiff acid in immunohistochemistry (Figure 2), gold standard for the disease confirmation[4], closed the diagnosis for WD.

Figure 2 - Macrophages with cytoplasm rich in PSA positive granules



With the confirmation of the clinical status in the eleventh day of hospitalization, empirical treatment for pseudomembranous colitis was initiated (one week of Metronidazole 1500mg/day + Meropenem 500mg/day for 30 days + Vancomycin 500mg/day for 30 days), which results in the clinical and radiological improvement plus reduction in the number of evacuations to a maximum of two times per day, culminating in the hospital discharge after 47 days of institutionalization, with the prophylactic use of Sulfamethoxazole associated with Trimethoprim orally for one year. In followed track at multidisciplinary and specialized outpatient, had significant improvement of the viral load for 474.829 copies, however the count of lymphocytes T CD4+ established in 20 cels/mm³ and his weight kept at 70 kilograms six months after discharge.

DISCUSSION

Although the infection by T. *whipplei* is vastly known and treatable, its association with HIV is still little known and described in literature. A study realized in Ghana, at the Ashanti region by the Department of Medicine of the University of Science and technology of Kwame Nkrumah between november of 2011 and november of 2012 compared the incidence of WD in people living with HIV (PLHIV) and people not infected by HIV. The result enlightened the need of a screening of WD in the PLHIV since it observed a higher susceptibility of these to infection due the WD bacteria[5]. The prevalence of WD was more than double in PLHIV, 5,85% against 2,08% in people with negative sorologic status for HIV. The outlook is even more concerning considering associated comorbidities, because the prevalence of WD came up to 12,31% in obese PLHIV[5].

The pathophysiology of WD is not clearly reported yet, however the cited research is important because it defines parameters in the epidemiology of the disease and

in the prevention of its active infection, such as the higher predisposition of WD in specific cases, like in HIV and obesity, or in milder cases, such as geographicals or assistencials.

From this perspective, what is understood regarding the pathophysiological process of small intestine, is that after the exposition to lamina propria foamy macrophages of the enteric mucosal tissue to *Tropheryma whipplei*, these cells phagocytize the bacteria and influenced the release of activated factors of host's immune response, which have potential to generate local inflammation[6]. This infection-induced inflammatory process destroys the intestinal villi and microvilli, typically at jejunoileal level[7], contributing to the most common symptoms of the disease such as malabsorption, diarrhea and weight loss[8].

The diagnosis comes through a intestinal mucosa biopsy associated with PSA immunohistochemistry. The result is positive when we can observe macrophages rich in PAS-positive granules cytoplasm due to the considerable bacterial infiltration[9]. Cardiac, pulmonary and nervous manifestations are possible and must be considered in the medical conduct[10]. Its important to observe that difficulty to adhering to ART can lead to a severe immune compromised caused by HIV, turning the patient more susceptible to development of WD[11-12].

CONCLUSION

The importance of asking wether symptoms such as weight loss, diarrhea and malabsorption allied to the count of lymphocytes T CD4+ with values lower than 200 cels/mm³ in PLHIV[13] can be related with WD. Its relevant to referral for the differencial diagnosis per upper gastrointestinal endoscopy with duodenal biopsy and immunohistochemical analysis.

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REFERÊNCIAS

1. Fuerle G. Doença de Whipple. https://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=PT&Expert=3452.
2. Atenodoro JR, Ruiz R. Doença de Whipple. https://www.msdmanuals.com/pt-br/casa/dist%C3%BArbios-digestivos/m%C3%A1-absor%C3%A7%C3%A3o/doen%C3%A7a-de-whipple.
3. Brasil. Ministério da Saúde. Departamento de Condições Crônicas e Infecções Sexualmente Transmissíveis. http://www.aids.gov.br/pt-br/faq/17-como-que-o-hiv-age-na-gente.
4. Hujoel IA, Johnson DH, Lebwohl B, Leffler D, Kupfer S, Wu TT, Murray JA, Rubio-Tapia A. Tropheryma whipplei Infection (Whipple Disease) in the USA. Dig Dis Sci. 2019;64(1):213-223. Doi: https://doi.org/10.1007/s10620-018-5033-4.
5. Eberhardt KA, Sarfo FS, Klupp EM, Dompreh A, Di Cristanziano V, Osei Kuffour E, et al. Intestinal Colonization with *Tropheryma whipplei* - Clinical and Immunological Implications for HIV Positive Adults in Ghana. Microorganisms 2021;9(8): 1781. Doi: https://doi.org/10.3390/microorganisms9081781.
6. Dolmans RA, Boel CH, Lacle MM, Kusters JG. Clinical Manifestations, Treatment, and Diagnosis of Tropheryma whipplei Infections. Clin Microbiol Rev. 2017;30(2):529-55. Doi: https://doi.org/10.1128/CMR.00033-16.
7. Antunes C, SinghalM. Johns Hopkins Hospital. Whipple Disease. https://www.ncbi.nlm.nih.gov/books/NBK441937/.
8. Marins TM, Silva LHV, Ferraz AR Doença de Whipple. *Rev Eletr Acervo Médico*. 23(1):e11704. Doi: https://doi.org/10.25248/reamed.e11704.2023
9. Rocha HC, Martins WRM, Carvalho MR, Amaral LM. Manifestações clínicas e diagnóstico da doença de whipple: relato de caso. Rev Med Minas Gerais 2015; 25(2): 296-300. Doi: https://dx.doi.org/10.5935/2238-3182.20150051.
10. Silva M, BRagança I, Parreira M, Pedroso E, Miranda C. Doença de Whipple – um caso. Med Interna. 2002;87(9):2. https://www.spmi.pt/revista/vol09/v09_n2_Whipple.pdf.
11. Khrais A, Han B, Ramasamy D, Kumar S. Whipple's Disease (WD) Without Arthropathy in an Immunocompromised Patient. Cureus 14(11): e31659. Doi: https://dx.doi.org/10.7759/cureus.31659
12. Duani H, Silva BR, Thomazi OB, Arantes FE, Azevedo LB, Moreira CM, et al. Doença de Whipple em paciente HIV positive. http://www.sbmt.org.br/medtrop2016/wp-content/uploads/2016/11/9807-Doenc%CC%A7a-de-Whipple-em-paciente-HIV-positivo.pdf.
13. LAB REDE, Acessoria Científica. HIV – Carga Viral. http://www.proexame.com.br/painel/informativos/images/NDE=/Lab.com%20_%20CARG A%20VIRAL%20HIV%201_fev_2016.pdf.

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