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CASE REPORT

Infectious proctitis: a necessary differential diagnosis in ulcerative colitis

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Abstract

Introduction In the last years, there was a rising in the incidence of sexually transmitted infections, including proctitis. Infectious proctitis (IP), mainly caused by agents like *Neisseria gonorrhea* and *Chlamydia trachomatis*, is an entity that should be considered when patients with suspected inflammatory bowel disease (IBD) are approached, mainly if they have risk factors such as anal intercourse.

Clinical cases/Discussion The symptoms of IP, like rectal blood, mucous discharge, and anorectal pain, may appear in other causes of proctitis, like IBD. Therefore, to establish the diagnosis, it is crucial to take a detailed history and perform a physical examination, with the diagnosis being supported by complementary tests such as rectosigmoidoscopy, histology, serology, and culture. Depending on the etiology, treatment of IP is based in antibiotics or antivirals, which may be empirically initiated. Co-infections, mainly those that are sexually transmitted, and HIV should be tested and sexual partners should be treated, accordingly. In this article, the authors report three cases of IP, referent to three different patients, and review the initial approach required in cases where there is a clinical and/or endoscopic suspicion of this pathology.

Keywords Sexually transmitted infections · Clinical history · Rectal inflammation

Introduction

Proctitis is a common problem in gastroenterology and, most frequently, it is associated with inflammatory bowel disease (IBD). In the recent years, there was a rise in infectious proctitis (IP) incidence, especially in men who have sex with men (MSM) [1]. These cases usually occur in healthy patients with rectal symptoms, and it is essential to perform a detailed clinical history approaching risk behaviors such as anal intercourse. Stool samples for microscopy and culture tests should be performed as a rectosigmoidoscopy to find mucosal changes and to take histological samples [2]. Additionally, cultural and molecular tests are necessary for an adequate diagnosis [3]. The most frequent agents involved are *Neisseria gonorrhoeae* (NG), *Chlamydia trachomatis* (CT), *Treponema pallidum* (TP), and herpes simplex virus type 2 (HSV-2). IBD proctitis may present with similar endoscopic findings as IP, such as erythema, friability of mucosa, erosions, or deep ulcers with mucopurulent exudate [4].

In this report, the authors present three cases of IP initially misdiagnosed as ulcerative colitis (UC). We intend to highlight the importance of consider IP in the differential diagnosis of all suspected cases of IBD [4]. We will also discuss the empiric treatment of suspected IP and the additional measures that should be performed, such as sexual partner's test and treatment and to report notifiable diseases to the competent instances.

Case 1

A 39-year-old man presented to the emergency department with complaints of rectal bleeding, tenesmus, weight loss, and fecal urgency for 3 months. The physical exam was unremarkable. One month before, he underwent rectosigmoidoscopy in another institution that revealed several erosions and edema of the distal rectum mucosa, suggestive of UC. Stool microscopy was negative for microorganisms. He was medicated with oral and topical

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mesalamine with only mild improvement. When asked, the patient referred past receptive anal intercourse as well as a known positivity for human immunodeficiency virus type 1 (HIV-1) infection. Rectosigmoidoscopy was repeated and showed several superficial ulcers and erosions with well-defined borders, some with a target appearance (Fig. 1a). Rectum biopsies revealed a lymphoplasmacytic infiltrate with histiocytes involving the submucosal (Fig. 2a). Empiric antibiotic therapy with doxycycline (100 mg 12/12 h) was initiated due to the suspicious of an infection by CT. The polymerase chain reaction (PCR) test confirmed a CT serotype L infection. The symptoms resolved after completing 15 days of antibiotic therapy.

Case 2

A 49-year-old man was admitted in the emergency department with rectal bleeding, tenesmus, and diarrhea with mucus, since 4 months before. A rectosigmoidoscopy was performed in other institution showing edema of the mucosa and erosions from the rectum to the distal sigmoid colon, suggestive of UC, and he was medicated with ciprofloxacin plus metronidazole, with partial resolution of symptoms. One month later, he returned due to symptomatic recurrence after he had stopped the antibiotherapy. He denied relevant past medical history (including previous infectious diseases, such as HIV) and sexual risk behaviors. The rectosigmoidoscopy showed edema and ulceration of the mucosa of distal rectum and biopsies were performed (Fig. 1b). On the histological exam, a lymphoplasmacytic infiltrate, in the absence of cryptic abscesses and granulomas, was noticed (Fig. 2b). The PCR of the biopsy specimen were positive for NG. After this result, the patient confessed that he had unprotected anal sex with men before symptoms occurrence. The HIV-1 test was positive. He was medicated with azithromycin (1 g) orally plus ceftriaxone (250 mg) intramuscular.

Case 3

A 23-year-old man, with a recent diagnosis of UC medicated with oral and topic mesalazine, recurred to the emergency department due to rectal bleeding, anal pain and constipation. He denied fever or abdominal pain. Risk behaviors, namely anal intercourse, and past sexually transmitted infections were initially denied. A rectosigmoidoscopy was performed and showed edema, erythema, and ulceration of the rectal mucosa up to 12 cm of the anal verge with spared areas (Fig. 1c). The histological exam revealed a lymphoplasmacytic infiltrate with gland architectural distortion and decreasing of mucus secretion; cryptic abscess were also present (Fig. 2c). The PCR of the biopsy specimen of rectum was positive for CT serotype L. A low reactivity in treponemal test (two dilutions on the venereal disease research laboratory test) and the HIV-1 serology were also positive. Facing these results, the patient confessed his knowledge for HIV infection and referred a past of neurosyphilis with ocular involvement, 4 years before. He was medicated with doxycycline (100 mg, 12/12 h), during 21 days, with clinical improvement.

Discussion

Proctitis is an inflammation of the mucosa of the rectum and it is most commonly associated with IBD. However, this entity has many other noninfectious and infectious causes and it is crucial to consider them in the differential diagnosis [2, 4]. IP is typically sexually acquired and mostly caused by NG (30%), CT (19%), HSV-2 (HSV, 16%), and TP (2%). No identifiable infectious source is found in up to 45% of cases [5].

Gastrointestinal manifestations of sexually transmitted infections are not always easily recognized. Due to their propensity for columnar epithelium, CT and NG are the main pathogens of anorectal disease [4]. In their review, Lamb C. et al. concluded that, among MSM, infection by CT is present in a high proportion of patients with confirmed gonococcal

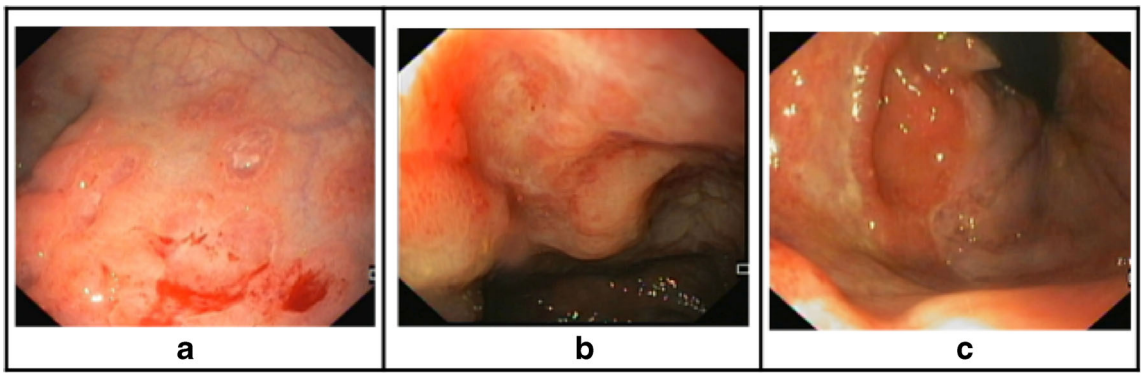

Fig. 1 Endoscopic findings of IBD proctitis

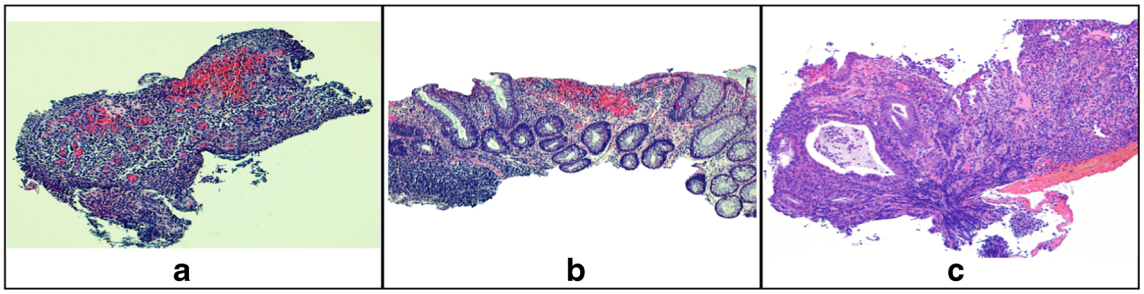

Fig. 2 Histologic findings of IBD proctitis

infection and in up to 85% of rectal infections with CT and NG were asymptomatic. When symptomatic, it may be indistinguishable of UC [1, 6].

In cases of high suspicion of IP, tests for NG, CT, TP, and HSV-2 should be performed as well as an anal smear. If HIV and hepatitis C virus serostatus are unknown, the screening tests for these viruses are also mandatory [3].

If perianal or mucosal ulcers are present, the empirical treatment for NG, CT, and HSV-2 may be initiated, as well as syphilis if the serology test is positive. The clinical response of patients who have been diagnosed with *CT* or *NG* infections must be assessed during its course, and 3 months after therapy. All recent sexual partners should also be screened (Table 1).

Lymphogranuloma venereum (LGV) is a systemic disease caused by CT serotypes L1-L3 and, in recent years, its incidence has increased in Western countries, especially in HIV-positive MSM [1, 6]. The clinical course of LGV can be divided into three stages. The primary lesion occurs 3–30 days after sexual contact and consists of a painless pustule, shallow ulcer, or erosion at the site of inoculation. A secondary stage can occur 3–6 months after exposure and manifests as an inguinal syndrome or an anogenitorectal syndrome. Both may be associated with systemic features, like fever or myalgia. Most frequent symptoms include anal discharge, which may be mucous, purulent, or bloody [8]. Tenesmus and constipation are common too. If the infection remains untreated, progression to tertiary stage may occur, causing a chronic inflammatory response and tissue destruction, including granulomas, colorectal fistulae, and fibrotic strictures, with histological, endoscopic, and radiological signs that can mimic IBD [1]. Reactive polyarthropathy, with or without conjunctivitis, has also been reported [6]. In LGV, the Gram stain of anorectal discharge smear commonly shows elevated white blood cell counts and the endoscopic exam typically reveals rectal ulcers with erythema and friability, with mucosal biopsies demonstrating lymphohistiocytic infiltrates, crypt abscesses, or granulomatous changes [7]. The diagnosis of LGV is typically based on epidemiological and clinical findings, confirmed by the positivity in PCR test [3, 5].

Treatment of LGV is often started empirically and consists in a course of doxycycline, 100 mg (twice daily) for 3 weeks. Alternatively, erythromycin (500 mg orally four times daily

Table 1 Common organism related to infectious proctitis

Organism	How to diagnose	How to treat/manage
Neisseria gonorrhea	Culture of anogenital and pharyngeal swabs (gold standard), Gram stain, NAAT (e.g., PCR)	Ceftriaxone 500 mg (i.m. single-dose) plus azithromycin 1 g (p.o., single-dose).
Chlamydia trachomatis (non-LGV serovars)	NAAT (e.g., PCR) and genotyping, culture	Azithromycin 1 g, (i.m., single-dose) or doxycycline 100 mg (p.o. twice a day, 2 weeks).
LGV	NAAT (e.g., PCR) and genotyping, culture, immunofluorescence	Doxycyline 100 mg (twice a day, 21 days) or erythromycin 500 mg (four times a day, 21 days). Sexual partners within the preceding 3 months should be notified and screened for infection.
Treponema pallidum	Dark ground microcopy. Serological tests: RPR/VDRL (primary syphilis), EIA/TPPA/TPHA (for secondary syphilis)	Penicillin G benzathine (2.4 million units, i.m., single-dose) or procaine penicillin (600,000 units a day, 10–14 days) or doxycycline 100 mg (twice a day, 14 days).
Herpes simplex virus type 2	NAAT (e.g., PCR), viral culture	Acyclovir 200 mg (p.o., 5 times daily, 5 days) or acyclovir (400 mg 3 times daily, 5 days) or valaciclovir 500 mg (twice a day, 5 days), famciclovir 125 mg (twice a day).

NAAT nucleic acid amplification tests, *PCR* polymerase chain reaction, *LGV* lymphogranuloma venereum, *P.o.* orally, *i.m.* intramuscular

for 3 weeks), can be considered, namely for pregnant women or patients with intolerance to doxycycline [8]. Asymptomatic sexual partners should also be treated with a course of doxycycline (100 mg twice daily for 1 week) [9, 10].

Gonorrhea's infection is caused by NG, a Gram-negative diplococcus, transmitted by direct contact of mucosal surfaces and so, proctitis is commonest in patients participating in receptive anal intercourse [4]. Rectal gonorrhea is common and asymptomatic in a high proportion of cases [6]. The symptoms of disease, which may arise 5–10 days after exposure, may include lower abdominal pain, diarrhea or constipation, mucopurulent anal discharge, tenesmus, pruritus, and rectal bleeding [3, 4]. Endoscopically, the rectal mucosa may appear normal, or there may be pus with erythematous mucosa and friability. The presence of Gram-negative diplococcic in Gram stain of mucosal biopsies or purulent discharge is suggestive of the diagnosis with a sensitivity of 90–95% [4], although the culture is the preferred method for the diagnosis [3]. The treatment of uncomplicated rectal infection consists in a single intramuscular dose of ceftriaxone (250 mg) plus azithromycin (1 g, orally, single-dose) [3]. Recent sexual partners should be treated since untreated infection can lead to complications, such as an abscess formation [5].

Conclusion

In the recent years, there was a rise of IP, mainly in HIV-infected patients with sexual risk behaviors, with CT and NG being the main causes of this infection. The symptoms of IP may mimic IBD and so, it should be considered in all cases. A complete clinical history and physical exam should include sexual habits, like receptive anal intercourse, anogenital lesions, and lymphadenopathy. Furthermore, in these cases, HIV test should also be performed. Also, in cases of infections by CT and NG, it is compulsory to report them.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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