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Review Article

Evaluation and Management of Abdominal Pain in Patients with Human Immunodeficiency Virus: A Review of Literature

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Abstract

Abdominal pain is one of the main symptoms evaluated in patients with Human Immunodeficiency Virus (HIV) infection. This population is special because the differential diagnosis is broad and the clinical presentation is usually atypical. This article will review general information on the evaluation and management of abdominal pain in patients with human immunodeficiency virus infection.

Introduction

Abdominal pain is one of the most frequent causes of emergency department visits (approximately 7% to 10% of emergency visits) and is a symptom of a challenging diagnosis with a difficult approach [1-3].

Although the presentation is common, there are multiple causes of it ranging from benign diseases to fatal diseases if not diagnosed in a timely manner [4]. In the case of the immune-compromised population due to HIV infection, the diagnosis becomes even more complex due to the multiple pathologies that can cause it and the broad spectrum of clinical presentation of each pathology including atypical forms of presentation [5,6]. On the other hand, the differential diagnosis is broader than in the common population; mainly due to the infectious diseases that predominantly affect this special population [7-9].

It is not known the exactly incidence of gastrointestinal involvement in the HIV-infected population because is variable in each region. Prior to the era of Highly Active Antiretroviral Therapy (HAART) it was estimated that approximately 50% to 93% of HIV patients had involvement of the gastrointestinal tract [10]. It has been described in approximately 15% of cases of intense abdominal pain [11].

Evaluation of Abdominal Pain in a Patient with HIV

The first step in evaluating the patient with abdominal pain is clinical assessment. Based on the medical history, physical examination and initial laboratory parameters, it is possible to decide if further approach is required. Patients usually present with abdominal pain and other added symptoms such as nausea, vomiting, fever and diarrhea [12].

Infectious Diseases as Cause of Abdominal Pain in Patients with HIV

Patients with HIV infection are predisposed to opportunistic organisms. Although we currently have multiple antiretroviral drugs and the incidence of opportunistic infections has declined because of this, these infections continue to occur frequently.

Among the main differential diagnoses of infectious etiology as a cause of abdominal pain are *Cytomegalovirus, Mycobacterium Avium Complex, Histoplasmosis, Crytosporidium, Isospora, Microsporidia, Salmonella, Shigella, Campylobacter* and some other pathogens [13,14].

Cytomegalovirus infection is common in patients with human immunodeficiency virus infection. The most frequent symptoms are abdominal pain, anorexia, diarrhea and weight loss. This infection should be considered in patients with CD4 count below 50cells/mm^3 [15-18].

Infection with the mycobacterium avium complex is an opportunistic infection that also frequently affects the digestive tract. It is especially suspected in patients with a CD4 count below 100cells/mm^3 [19].

In developing countries, tuberculosis infection is a major cause of abdominal pain in this population and generally affects the ileocecal region with invasion of nearby lymph nodes [20-22].

Strongyloidosis has been reported as a cause of abdominal pain [23-25].

In endemic regions, visceral leishmaniasis is another important cause of abdominal pain [26].

Conditions Requiring Surgical Treatment

The main pathologies that warrant surgical intervention are the same as the general population; Intestinal obstruction, acute appendicitis, intestinal perforation, and acute cholecystitis, and occur in both treated and non-antiretroviral treated patients [27].

Acute cholecystitis occurs clinically in a similar way in patients with infection that without infection by human immunodeficiency virus [28], although acalculous cholecystitis occurs more frequently in this population. On the other hand these patients may present cholangitis or cholangiopathy; either by adverse effects of antiretroviral drugs or by infiltration by opportunistic organisms [29].

Acute appendicitis may be caused by pathogens such as cytomegalovirus and present milder symptomatology than in the common population. Appendectomy has been reported as the most frequent surgical procedure in this population [30].

Intestinal perforation occurs when there is invasion of microorganisms to the deeper layers of the intestinal wall with vasculitis and ulceration; the most frequently affected area is the terminal ileum and colon. Abdominal pain and fever are the most common symptoms [31], It can be caused by any opportunistic agent [32,33].

Clinical Manifestations

Gastropathy

The inflammatory processes of the stomach can occur in the same way as in the general population; such as pain or epigastric burning with varying intensity and occasionally with gastrointestinal bleeding. In patients with alarm data such as gastrointestinal bleeding, anemia, tachycardia and hypotension, an emergency diagnosis should be given as an endoscopy [34]. And in patients without alarm data, treatment based on proton pump inhibitors and therapeutic response could be initiated; if this treatment fails, an endoscopy should be considered to rule out gastropathy. As in the rest of the population, *H.pylori* infection should be ruled out in patients with HIV infection, and cytomegalovirus infection should be ruled out in patients with CD4 count below 50cells/mm^3 [35]. The definitive diagnosis of these infections is done by endoscopy. The differential diagnosis in epigastric abdominal pain should also include drug gastropathy (including antiretrovirals) and neoplasia such as Kaposi's sarcoma [36].

Enteritis in a patient with HIV infection

In this population, both the small and the large intestine can be affected; and both conditions can cause abdominal pain [37-39]. Abdominal pain include infections by bacteria such as salmonella, Shigella, campylobacter and Yersinia; fungi such as histoplasma and diseases caused by tuberculosis, as well as opportunistic infections such as isospora, microspora and cryptospora. In patients with large intestine involvement, the main microorganism to be considered is cytomegalovirus and may manifest as gastrointestinal bleeding, perforation or toxic megacolon [40]. Clostridium difficile infection, as in the common population, should be considered if there is a history of antibiotic treatment [14,41-43].

Intestinal occlusion

There have been reports of intestinal obstruction due to disseminated infection of some microorganisms such as histoplasmosis [44]. It can also be caused by Kaposi's sarcoma or intestinal lymphoma [45].

Acute pancreatitis

The incidence of acute pancreatitis in HIV patients is 4% to 22%.

In the case of the presence of acute pancreatitis in a patient with HIV infection, it should be treated in the same way as the general population, but clinicians must consider some special features such as antiretroviral treatment as a cause of acute pancreatitis in this population [46,47]. Although the exact mechanism by which these drugs cause acute pancreatitis is currently unknown, cases of pancreatitis associated with *Pentamidine*, *Ritonavir*, sulfonamides have been reported, but the greatest association so far has been with *Didanosine* [48].

In the case of acute pancreatitis, serum amylase and lipase will be elevated; without forgetting that in case of chronic pancreatitis these serum markers may not be elevated.

Peritonitis

Peritonitis may be secondary to perforation of viscera or to non-specific causes in the context of peritonitis without intestinal perforation. Infections associated with peritonitis in this population include peritoneal tuberculosis, mycobacterium avium complex, toxoplasmosis, and cryptococcosis. It should be kept in mind that leukocytosis may be absent due to the low CD4 cell count and, on the other hand, the classic signs of peritonitis may not be present [49].

Liver infection by opportunistic organisms as a cause of abdominal pain

Multiple hepatic infections have been described in patients with HIV including tuberculosis [50,51].

Liver infection in this population may occur as an abscess or as a form of cholangiopathy [52,53]. Population with HIV infection also tends to have more frequent amoeba infection [54,55] and in some cases fulminant forms of colonic infection have been reported [56].

Some entities such as tuberculosis infection can give pictures of severe abdominal pain simulating peritonitis [57-59].

HIV-related vasculitis

Cases of vasculitis associated with this infection have been described [60] and also cases associated with pseudoaneurysms due to vasculitis in this special population [61,62].

Lymphadenitis

Cases of abdominal pain have been reported by some opportunistic organisms that invade lymph nodes [63].

Abdominal pain due to antiretroviral drugs

Antiretroviral drugs can cause abdominal pain as a side effect and intolerance to it; so a good interrogation of the drugs consumed by the patient must always be carried out [64-67].

Some cases of acute intermittent porphyria secondary to the use of some antiretroviral drugs such as *Atazanavir* and *Ritonavir* have been reported [68].

There are also reports of paralytic ileus with the use of some combinations of antiretroviral therapy [69].

The production of renal lithiasis has typically been associated with the protease inhibitor *Indinavir* and the nucleoside reverse transcriptase inhibitors *Didanosine* with acute pancreatitis; both entities are cause of abdominal pain [48].

Diagnostic Approach

As in the non-HIV infected population, the initial approach to abdominal pain is very similar. The performance of computed tomography with venous contrast should be assessed if renal function allows [70].

Ultrasound has also been described for assessing intra-abdominal lymphadenopathy and splenic lesions; however, they would only guide HIV-associated pathology in the right context [71].

In chronic abdominal pain in this population, gastrointestinal endoscopy and biopsy of suspicious areas should be indicated [72].

In case no alterations were detected by endoscopy or colonoscopy, the endoscopic capsule could be used with good results to evaluate the small intestine [73].

Treatment

The treatment of abdominal pain in this special population should be directed to treat the cause itself. The indications for treating a patient with surgery are the same as in the common population. If surgery is performed, suspect tissues should be biopsied and cultured.

Infrequent conditions of abdominal pain in patients with HIV infection.

Even traumatic ruptures of spleen associated with HIV have been described [74,75].

Forms of abdominal aneurysms infected with opportunistic microorganisms have also been described [76]. There are some reports of pancreatic tuberculosis and it usually manifests as abdominal pain and fever [77-79].

Conclusions

The approach of the patient with abdominal pain and with HIV infection should focus on ruling out the most frequent opportunistic infectious pathologies in the first instance. Clinical manifestations depend on the site of infection. Abdominal computed tomography and abdominal ultrasound are the most useful diagnostic tests to initiate the assessment of abdominal pain in this special population. Gastrointestinal endoscopic is an excellent tool for ruling out gastrointestinal infection.

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