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Case Report

Acute Pericarditis as an Extraintestinal Manifestation of Inflammatory Bowel Disease: A Case Report

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Abstract

Inflammatory Bowel Disease (IBD) can have Extraintestinal Manifestations (EIM). Rarely, extraintestinal cardiac manifestations, such as Acute Pericarditis (AP), may occur. We report a case of a 19-year-old male patient with IBD, who was diagnosed with AP, confirmed by cardiac magnetic resonance. The final diagnosis was AP as an EIM of IBD. AP usually occurs following viral infections and, in IBD patients, it can occur as an adverse effect of drugs, especially Mesalamine, or as an EIM of the disease, anyway of its activity. Regardless of its etiology, it should be promptly recognized and treated in order to avoid serious outcomes.

Keywords: Inflammatory Bowel Disease (IBD); Ulcerative colitis; Pericarditis; Crohn disease

Introduction

Inflammatory Bowel Disease (IBD) is a chronic systemic inflammatory disease with an autoimmune background, with inflammation of the bowel that can be further categorized into Ulcerative Colitis (UC) and Crohn's Disease (CD) [1]. Approximately 10% to 15% of cases are indistinguishable between UC and CD in the colectomy specimen, thus named Indeterminate Colitis (IC). Currently this diagnosis was broadened to those cases in which UC or CD cannot be confirmed by colonoscopy, histopathological analysis or following colectomy [2].

Regardless of the type of IBD, it is known that there can be various extraintestinal manifestations. (EIM) EIM are manifestations of the disease that affect organs other than the gastrointestinal tract, such as cardiovascular, ophthalmic, genitourinary, respiratory, hepatobiliary, musculoskeletal and cutaneous [3,4].

Several cardiac EIM have been described: myocarditis, arterial and venous thromboembolism, left ventricular dysfunction, infective endocarditis, valve diseases, Takayasu´s arteritis and arrhythmias. These manifestations are rare and usually immune-mediated [4,5]. Acute pericarditis is possibly the most common of these disorders, and it is usually caused by immunosuppressants, anti-TNF and 5-ASA derivatives, notably mesalamine [6]. However, in literature there are described cases of AP as an EIM of IBD. The patient in this report had an episode of AP related to IBD, and other causes were excluded. Due to the rarity and importance of AP as an EIM, we decided to report this case.

Case Presentation

We performed a case of acute pericarditis in a 19-year-old man with IBD. He had no other comorbidities and no history of smoking, alcohol consumption or substance abuse. The patient had a diagnosis of Inflammatory Bowel Disease two years prior, following a colonoscopy which showed small ulcers in the ileum, cecum and ascending colon. Other colonic segments were normal. The histopathological examination showed ileal mucosa with chronic inflammation in moderate activity with cryptitis and crypt abscesses. The mucosa of the right colon, transverse colon, left colon and rectum showed active chronic inflammation, with cryptitis. The patient was followed up at another service and sulfasalazine was started as the first treatment, probably because it was initially a mild to moderate disease. In September 2019, he was admitted to our hospital due to diarrhea with mucus and blood, with no improvement after antibiotic therapy with ciprofloxacin 500 mg orally twice a day and metronidazole 500 mg orally every eight hours for 5 days. A new colonoscopy was performed, which showed ileal mucosa with aphthoid ulcers, cecum, ascending colon and transverse colon mucosa with ulceration, friability and intense exudation, with an endoscopic appearance suggestive of Clostridioides infection (Figure 1). The aspirate for Clostridioides toxin was negative, but given the suggestive endoscopic appearance, he was started on empirical treatment with oral vancomycin 125 mg orally 4 times daily. Following clinical improvement, the patient was discharged on mesalamine 4 g orally once a day and gradually tapered off prednisone. Six months later, due to the severe reactivation seen in this hospitalization, it was decided by our team to start vedolizumab 300 mg and proceed with the withdrawal of mesalamine.

In May 2020, he was readmitted due to toxic megacolon associated with Clostridioides infection, confirmed by positive fecal DNA (polymerase chain reaction). He received treatment with oral vancomycin 125 mg four times a day orally and intravenous metronidazole 500 mg three times a day orally, in addition to

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intravenous methylprednisolone 30 mg intravenous twice a day. He required rescue biological therapy with intravenous infliximab 5 mg/Kg, and due to his compromised nutritional status and the impossibility of using the oral nutrition, it was decided to start total parenteral nutrition, having evolved with a poor clinical response, requiring subtotal colectomy with ileostomy and sigmoid colon mucosal fistula. The anatomopathological examination revealed chronic suppurative and ulcerated inflammation throughout the extension of colonic segment, restricted in its majority the mucosa, displaying marked distortion architectural, countless pseudo-polyps inflammatories, cryptitis and cryptic abscesses. Ileal segment within the limits of normality. Absence of wall fibrosis, granulomas, and lymphoid hyperplasia associated with mucosa or perineuritis.

In September 2020, the presented to the emergency department due to pleuritic chest pain radiating to the clavicles, worsened by deep inspiration and lying flat. He had no other symptoms and had had no symptoms suggestive of viral diseases in the previous weeks. He was not on any medication. His cardiovascular examination was unremarkable, except for mild tachycardia of 110 bpm. His electrocardiogram revealed a sinus tachycardia without PR or ST segments abnormalities. His chest radiography, troponin, D-dimers, blood count and renal function were normal. His C-Reactive Protein (CRP) was increased at 9 mg/dL (Reference Value <1mg/dL). Echocardiogram and esophagogastroduodenoscopy were performed, which did not detect abnormalities. Computed tomography of the chest was performed, which showed a small pericardial effusion (Figure 2).

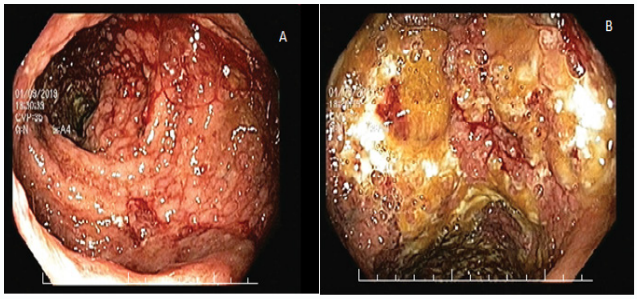

Figure 1: Colonoscopy showing ulceration, friability and intense exsudation, an endoscopic appearance suggestive of Clostridioides infection.

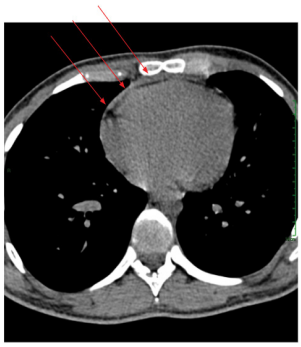

Figure 2: Chest CT showing small pericardial effusion.

Due to the persistence of chest pain and a high clinical suspicion of AP, he underwent a Cardiac Magnetic Resonance, which showed a diffuse late gadolinium enhancement on the pericardium, consistent with acute pericarditis (Figure 3). There was no myocardial involvement and his left ventricular ejection fraction was normal. An evaluation by the cardiology team was requested, which did not indicate the performance of serologies or other diagnostic tests, since their results would neither confirm nor exclude the cause of pericarditis. Due to the diagnosis of IBD, he was first started on oral colchicine 0.5 mg once daily with resolution of his chest pain and concurrent reduction of CRP to normal level (1.2 mg/dL) from the second day of use.

In December 2020, an ileorectal anastomosis was performed (the rectum was spared in previous endoscopic evaluations), requiring early reintervention due to intestinal obstruction due to adhesions and intra-abdominal hematoma. He underwent a new Colonoscopy in November 2021, which showed aphthoid ulcers in the neoterminal ileum and mild retitis (mucosa with an edematous appearance with reduced visibility of the submucosal vessels). His final diagnosis was IC and he was started on adalimumab 40 mg subcutaneously every 14 days. The patient had no chest pain relapse and is currently in clinical and endoscopic remission.

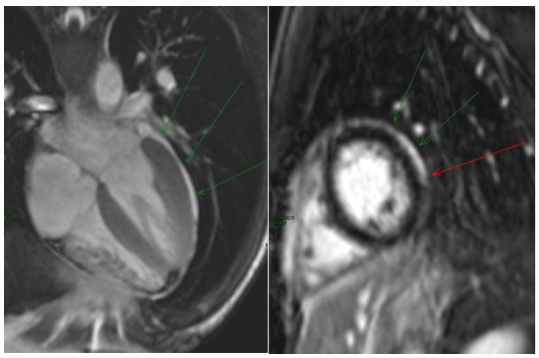

Figure 3: Four-chamber resonance cine, without contrast, demonstrating pericardial enhancement; Post-contrast short-axis - delayed enhancement.

Discussion

We report a case of a 19-year-old male with IBD, more specifically IC progressing to AP. This is a rare but important EIM. Pericarditis accounts for approximately 70% of cases of extraintestinal cardiac manifestations. The pathophysiology of IC is multifactorial and linked to an increase in expression of Toll-like receptor-4 leading to activation of nuclear factor kappa B (NF-kB). NF-kB regulates macrophage production of proinflammatory cytokines, like tumor necrosis factor-alpha, and Interleukin [IL]-1, and IL-6 [6]. A large population-based study showed incidence rates of 0.23% and 0.18% of pericarditis in UC and CD, respectively [7,8]. Most cases occur in men with UC [9].

It is unclear whether acute pericarditis is related to disease activity in IBD. Data from some studies suggest that there is no relationship with disease activity, but one study showed that during an episode of non-drug related myocarditis or pericarditis, 50% of patients had IBD activity [10-13]. However, there are case reports of pericarditis secondary to infliximab, from a lupus-like reaction or from direct pro-inflammatory damage to the pericardium [14]. There is a greater risk of myopericarditis occurring in patients with IBD than in the general population. This can happen due to an autoimmune response caused by exposure to self-antigens or drug toxicity following the use of 5-aminosalicylic acid (5-ASA) or other drugs [15].

Most cases of pericarditis caused by aminosalicylates have symptom onset within a few weeks (usually four) of initiation of therapy and resolve within two weeks of drug discontinuation and steroid treatment [15,16]. It is important to note that our patient had not been using Mesalamine for at least 6 months and did not present with lupus-like symptoms, like pleural effusion and to not having anti-histone antibodies or other alterations (as in reports secondary to the use of infliximab), in addition to having already performed the entire induction treatment and already using infliximab for more than 5 months, making the etiology secondary to drugs unlikely. In addition, he did not have any flu-like symptoms or even any other associated symptoms, making a viral etiology highly unlikely.

Transthoracic echocardiography and troponin assays need to be done immediately in all patients with suspected pericarditis, in order to further assess the disease and exclude concurrent myocarditis. The finding of a thickened pericardium with pericardial effusion should raise the suspicion for pericarditis, and the absence of these findings should not exclude the diagnosis. The findings of raised troponin levels alongside with left ventricular dysfunction, regional wall motion abnormalities, reduced ejection fraction associates with myocarditis. Furthermore, the echocardiogram can also evaluate severe complications of pericarditis, such as tamponade and constrictive pericarditis [16].

Cardiovascular Magnetic Resonance (CMR) evaluates both myocardium and pericardium non-invasively, and is usually sufficient for the diagnosis of both pericarditis and myocarditis. Focal or diffuse late gadolinium enhancements on the pericardium are the most frequent findings in CMR suggestive of pericarditis. Findings suggestive of concurrent myocarditis are myocardial hyperaemia or oedema (global or regional) and necrosis with non-related coronary artery distribution and focal fibrosis. Our patient had no myocardial involvement in any of the imaging tests and his troponin levels were normal [16].

The patient received oral colchicine treatment and had progressive clinical improvement (improvement of pain) and normalization of inflammatory markers (ESV and CPR). Other treatment options are Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), corticosteroids and immunosuppressants [5].

We chose not to use NSAIDs due to the risk of worsening IBD activity. Since there were no signs of constrictive physiology, we also chose not to use corticosteroids as a first-line treatment due to an increased risk of recurrent pericarditis. Since our patient improved on low-dose colchicine and his CRP returned to normal levels, he was kept on low dose. It is important to emphasize the diagnostic differentiation between UC and CD, which has implications for treatment, prognosis, chosen treatments and disease course.

In our patient, there was always greater disease activity in the right colon, in addition to ileal involvement, characteristic findings of Crohn's disease. On the other hand, there was clinical evolution to severe acute colitis (pancolitis), histopathological examination without granuloma, absence of strictures/fistulas and need for colectomy, common findings of Ulcerative Colitis. Given these considerations, the patient was categorized as having IC [2].

It is important to remember the increased incidence of Clostridioides difficile infection in patients with IBD, which happened to our patient, but who, fortunately, had a good clinical response with treatment with oral Vancomycin. We decided to report this case due to the rarity of inflammatory bowel disease-related pericarditis and its potential for severity. Although most cases are secondary to the use of mesalamine, cardiovascular manifestations, especially acute pericarditis, should be remembered as an EIM of IBD, which is unrelated to disease activity. The implication of recognizing the AP and its etiology involves choosing the appropriate treatment, which can be the suspension of the correlated drug (e.g., mesalamine) or, as in this case, the use of colchicine. We consider the use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) a poor option for the treatment of AP in these patients, due to the risk of damage to the gastrointestinal tract mucosa and activation of IBD [17-20].

Conclusions

Although acute pericarditis is most often secondary to the use of medications (notably 5-ASA derivatives), it can also be an EIM of IBD, which it is not clear if there is a relationship with disease activity. This requires attention from the medical team, so that the diagnosis and treatment is instituted early, with the aim of avoiding serious outcomes. If there are medications known to be related to the acute cardiovascular condition, they should be suspended. Among the treatment options, we highlight colchicine, due to its good response and gastrointestinal safety, not increasing the risk of disease flares.

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