# Recurrent pericarditis in an adolescent with Crohn's colitis

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## ABSTRACT

**Extraintestinal manifestations are common complications of inflammatory bowel disease (IBD), whereas the recurrent pericarditis during remission of Crohn's disease is rarely reported. Chest pain developed in a 13-year-old adolescent male who had a history of Crohn's colitis since 9 years of age and was in remission for 4 years after treatment with infliximab, adalimumab, and vedolizumab. Physicians should be aware of the pericardial involvement in patients with a history of IBD. The literature on pericardial involvement in Crohn's disease is reviewed with emphasis on the management of recurrent pericardial effusion in the pediatric age group.**

**Keywords:** Crohn's disease, inflammatory bowel disease, pericardial effusion, pericarditis

## INTRODUCTION

Inflammatory bowel diseases (IBD), including Crohn's disease and ulcerative colitis, may be associated with extraintestinal disorders, often during an exacerbation of the disease.[1] Among the most common extraintestinal manifestations are other chronic immune-mediated diseases, such as erythema nodosum, ankylosing spondylitis, and primary sclerosing cholangitis. Pericarditis or myopericarditis may occur more often than currently appreciated. For example, up to one-third of patients may develop myocarditis or pleuropericarditis during the course of their IBD.[2] These conditions may resolve with corticosteroid therapy or rapidly evolve and progress to cardiogenic shock and death.[3] The exact mechanism of pericarditis is unknown, immune-mediated inflammation is thought to be responsible.[1] However, other causes may occur including drug reactions (e.g., mesalazine).[4] We describe a 13-year-old adolescent male who had Crohn's disease, and while he was in remission for 4 years presented with recurrent pericarditis.

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## CASE REPORT

In July of 2017, a 13-year-old adolescent male presented to the emergency room (ER) with left-sided and central chest pain that had been present for 1 day. The pain radiated to the left shoulder and back. Shortness of breath, fever, and malaise were also present. The clinical evaluation performed in the ER described a pale and lethargic adolescent with a heart rate of 80 beats/min. A pericardial rub was discovered on examination by a pediatric cardiologist, but all else was otherwise normal. A chest X-ray showed mild cardiomegaly but lungs were clear [Figure 1]. His electrocardiogram (ECG) showed ST-T wave changes consistent with pericarditis (Figure 2: Diffuse ST-T elevation compared to his baseline ECG [Figure 3]). Laboratory studies showed anemia (hemoglobin level of 11.4 g/dl) and elevated acute phase reactant (C-reactive protein [CRP] was 9.4 mg/l) (normal <3 mg/l), but his serum troponin level was normal (<0.1 $\mu$g/l). The patient's liver and renal function studies were normal.



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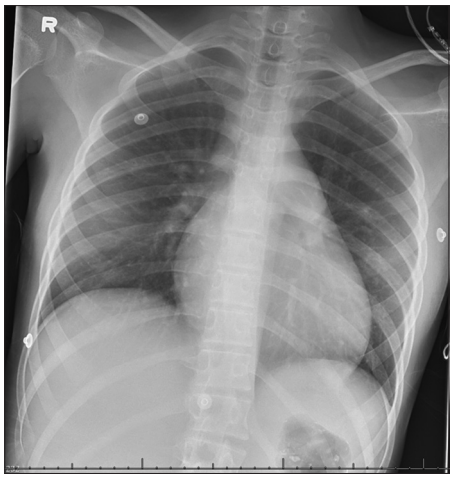


**Figure 1: Chest X-ray showing clear lungs but mild cardiomegaly**

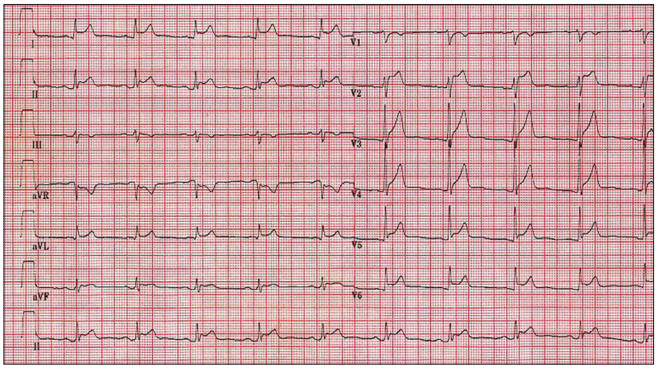


**Figure 2: Electrocardiogram showing ST elevation suggestive of pericarditis**

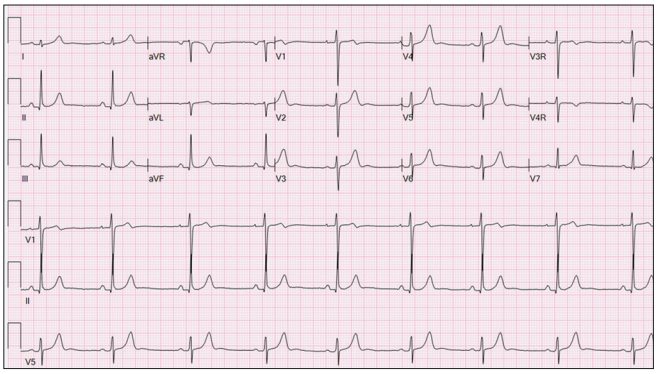


**Figure 3: Baseline electrocardiogram showing normal sinus rhythm**

The initial echocardiogram revealed pericardial effusion with normal biventricular systolic function. A chest CT was performed and revealed a bilateral pleural effusion along with a pericardial effusion but no thickening or calcification of pericardium. The patient was admitted to the hospital, and a pericardiocentesis was performed. A total of 265 ml of slightly turbid yellow fluid was drained, and the pericardial drain was removed a couple of days later. The Gram stain demonstrated moderate WBC's but no organisms. He was negative for candida, coccidioides, histoplasmosis, *Bartonella henselae*, and quintana antibodies. The pericarditis and pleural effusion responded to hydrocortisone 100 mg every 12 h for 3 days. Then, the patient was given oral prednisone with a several week wean. He had a negative rheumatologic workup, including antinuclear antibody, anti-chromatic antibody, antibody to single-stranded DNA and double-stranded DNA, anti-histone antibody, centromere antibody, JO-1 antibody, and antibodies to nRNP, Scl70, Sm, Ro (SSA) and La (SSB). His serum levels of complement (C3) was 121 mg/dl (normal 66–185 mg/dl), and levels of C5 was 25 mg/dl (normal 15–52 mg/dl). Endoscopic evaluation by gastroenterologists confirmed the remission of his Crohn's colitis. Four months later, in November of 2017, the patient presented to the ER with recurrent chest pain, fever, and elevated CRP. His ECG was again abnormal with ST-T changes, and the echocardiogram revealed normal function with a small pericardial effusion. The patient's symptoms improved after a short course of systemic steroids followed by ibuprofen. Shortly thereafter, he again presented with a chest pain. He was then given a several week prednisone wean. His echocardiogram showed no pericardial effusion, and his ECG was normalized in December 2017. In January 2018, he had another episode of chest pain and fever and was started on a short course of systemic steroids, followed by colchicine therapy 0.6 mg daily. He remained on colchicine for several months. He presented with severe weakness in October 2018 for which he was admitted to the hospital. A repeat colonoscopy was performed, which showed the patient's Crohn's disease was still in remission. He was investigated for myasthenia gravis and was ruled out. His brain magnetic resonance imaging was normal, and his symptoms attributed to having low ferritin and autonomic dysfunction. He received intravenous iron therapy. During this hospitalization, the possibility of fatigue and weakness being secondary to chronic colchicine was considered (although his creatine phosphokinase was normal), and he was weaned off colchicine. After 6 weeks off colchicine, he had recurrence of symptoms similar to the previous pericarditis episodes, with positional chest pain and shortness of breath. His echocardiogram showed a small pericardial effusion not seen on earlier surveillance studies. His symptoms responded promptly with steroid therapy and resumption of colchicine. He was last seen on September 2019, and he has been quite healthy while on colchicine therapy 0.6 mg daily.

The patient's history revealed extensive Crohn's colitis, which was diagnosed in March 2012, following 3 months of abdominal pain, bloody diarrhea, and weight loss. At that time, laboratory tests revealed anemia (hemoglobin level of 10.9 g/dL; normal is 13.5 g/L–17.5 g/L) and iron deficiency (ferritin level of 9 pmol/L; normal is 45 pmol/L–674 pmol/L). His white cell and eosinophil

counts were normal. Anti-neutrophil cytoplasmic antibody was positive with an atypical perinuclear pattern. He was negative for adenovirus, cytomegalovirus, Epstein–Barr virus, and hepatitis A, B, and C viruses. In addition, his *Clostridium difficile* and stool cultures were negative, ruling out other common causes of pancolitis. Endoscopic evaluation of the colon with biopsies confirmed extensive colitis. This was characterized by inflammatory lesions with skip areas, but nonpenetrating and nonstricturing type involving the cecum, ascending colon, sigmoid colon, and rectum. Initially, he was prescribed infliximab, an anti-tumor necrosis factor-alpha agent. His diarrhea resolved and weight returned to normal. Over the next 6 months, the patient's blood and biochemical studies along with colonoscopic appearance (including biopsies) became normal. He initially had two recurrences of his colitis after several months of the initial presentation. He was found to have a very high level of antibody to infliximab, and his infliximab level was zero. He was subsequently given adalimumab and vedolizumab infusions, which helped to control his symptoms. He was found to have latent tuberculosis and received 6 months of isoniazid and pyridoxine therapy. The family history is significant for Crohn's disease in mother, in addition, the mother has autoimmune hemolytic anemia, and the father has irritable bowel syndrome.

## DISCUSSION

The present case reports a single patient with recurrent pericarditis in an adolescent who had a history of Crohn's disease. Pericarditis or myopericarditis can be caused by infectious and noninfectious diseases. Infectious causes are the most common and include viral (e.g., influenza A and B, enteroviruses, cytomegalovirus, Epstein–Barr virus, adenovirus, and hepatitis C virus); bacterial (e.g., *Staphylococcus*, *Streptococcus*, and *Mycobacterium tuberculosis*); and fungal (e.g., candida, coccidioidomycosis, and histoplasmosis) pathogens. Noninfectious causes include hypersensitivity reactions (antibiotics, insect bites, and diuretics); systemic diseases (thyroid disorders, sarcoidosis, hypereosinophilia, rheumatoid arthritis, and collagen vascular diseases); and radiation exposure. In our patient, viral and fungal serologies were all negative. He displayed clinical (chest pain), acute phase reactant (elevated CRP), echocardiographic (pericardial effusion), and ECG (ST-T changes) evidence illustrating pericarditis. On at least, the first two episodes of pericarditis separated by a period of 4 months with a symptom-free interval in between, rapid resolution occurred with systemic steroid. The recurrence of pericarditis is significant without flare-up of his Crohn's disease and on the fourth occasion it recurred 6 weeks after stopping colchicine, which responded well to resumption of therapy. Complete resolution of cardiac findings with corticosteroids and colchicine suggested that immune-mediated factors played a role in recurrent pericarditis.

Cardiac manifestations of IBD flares are rare, and include pericarditis, pericardial effusion, myocarditis, endocarditis, arrhythmias, and conduction disturbances.[5] The relationship between IBD and cardiovascular disease has not been fully elucidated to date. In the findings from a number of meta-analyses and cohort studies in recent years, investigators have suggested that IBD patients have an increased risk of myocardial infarction, stroke, and cardiovascular mortality, particularly during periods of active bowel disease in adults.[6] There have been previous cases of Crohn's-associated pericarditis, but our case is different in several ways, as recurrent pericarditis was the reason for multiple hospital admissions while Crohn's disease is under remission. There are a number of case reports where pericarditis has been reported with mesalazine treatment in Crohn's disease.[4,7,8] Pericarditis has also been reported as a complication of infliximab therapy.[9,10] The decision whether pericarditis is a symptom of the underlying disease or a side effect of the drug used for the treatment of the disease is not always easy. Kupferschmidt *et al.* presented an analysis in a patient with Crohn's disease and pericarditis, showing the dilemma of pericarditis in chronic IBD and its therapy.[11]

Previously two studies including three patients, pericarditis preceded the onset of Crohn's disease.[12,13] Furthermore, Manomohan *et al.* reported an adolescent with severe pericarditis with flare-up of Crohn's disease.[14] In contrast to the above-mentioned studies, we present a case, in which our patient displayed recurrent pericarditis in the setting of established Crohn's colitis during prolonged remission. A similar case has been reported in an adult with recurrent myopericarditis in the setting of Crohn's disease and association with human lymphocyte antigen B27-positive.[15]

Idiopathic or viral pericardial effusion is most common in male adolescents.[16] The European Society of Cardiology Guidelines for the management of pericarditis recommend the use of colchicine in recurrent (Class 1 indication) and acute pericarditis (Class 2a indication); however, routine use of colchicine has not been yet translated to pediatric practice.[17] There is a large practice variation across centers, nonsteroidal anti-inflammatory drugs are used most commonly, followed by corticosteroid use; however, colchicine is not commonly administered in children with viral or idiopathic pericarditis.[16] The infrequent use of colchicine in children with viral or idiopathic pericarditis might be related to the paucity of published studies on its use or to a lack of familiarity with this drug in pediatric cardiology practice. Other immunosuppressants, such as anakinra, azathioprine,

cyclophosphamide, cyclosporine, and rituximab are rarely used in recalcitrant cases of pericarditis with recurrent pericardial effusion. Recurrence of pericarditis is common in children with reports ranging from 15% to 40%.[18] Higher recurrence rate has been observed in patients with a history of use of corticosteroid in the initial episode of pericarditis in adults.[19]

In summary, we present a unique case of recurrent pericarditis in an adolescent with a history of Crohn's colitis, who finally responded to prolonged colchicine administration along with conventional therapies. To our knowledge, this is the first such case of its type. Physicians should be aware of myopericardial involvement in patients with a history of IBD. Further studies to elucidate molecular mechanisms associated with these clinical phenomena are needed.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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