**Unravelling recurrent heart inflammation: A case report**

**Keywords**

Myocarditis, pericarditis, myopericarditis, recurrent, Coxsackie

**Ethics**

* This case report adheres to ethical guidelines by ensuring patient confidentiality, obtaining informed consent, and prioritizing the welfare and rights of the patient throughout the study.

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**Data sharing**

* Data sharing not applicable – no new data generated

**Patient Permission/Consent statement**

In adherence to stringent ethical standards, I affirm that the research obtained informed written consent from participant, ensured data confidentiality without patient identifiers, and maintained transparency and objectivity throughout.

**Conflict of interest**

I, hereby declare that the research undertaken herein is free from any conflict of interest that could unduly influence the integrity or impartiality of the findings. As a researcher dedicated to upholding the highest standards of ethical conduct, I recognize the critical importance

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**1.Introduction**

Myopericarditis, according to 2015 ESC guidelines, is characterized by predominant pericarditis with myocardial involvement and can be clinically confirmed in patients meeting definite criteria for acute pericarditis, alongside elevated biomarkers of myocardial injury (troponin I or T, CK-MB). 1 2This diagnosis is established in the absence of newly developed impaired left ventricular function in echocardiography or Cardiovascular Magnetic Resonance (CMR).2 While pericarditis is found to be the cause of 0.1% hospitalizations and myocarditis occurred in 17 cases per 100,000 persons in a study involving military recruits, the exact incidence of myopericarditis remains unknown.3,4Initial manifestations of myopericarditis can include precordial positional chest pain, fever fatigue, dyspnea, and palpitations.5 It can be divided into infectious and non-infectious etiologies as shown in Table 1.6 Among these, Coxsackie virus is found in 50% of patients with myopericarditis 7 While recurrent pericarditis affects 15% to 50% of individuals with pericarditis in the US, amounting to around 20,000 people per year, the prevalence of recurrent myopericarditis is not clearly defined .8 We present the case of a 44-year-old man with recurrent myopericarditis due to Coxsackie virus who was treated with colchicine and tapering dose of ibuprofen.

**2.Case history**

A 44-year-old male, with a history of myopericarditis one year ago, initially came to the emergency department with fever and chest pain for four days. The patient presented with 8/10 non-exertional pressure-like chest pain localized to the mid-sternal region. The pain was described as radiating to the left shoulder and was alleviated by leaning forward and taking ibuprofen. He did not experience dyspnea, orthopnea, paroxysmal nocturnal dyspnea, changes in exercise tolerance, palpitations, diaphoresis, flu-like symptoms, sore throat, joint pain or rash. He had no recent travel history or exposure to sick contacts. His past medical history included non-ischemic cardiomyopathy, sickle cell trait and latent tuberculosis.

The patient had a temperature of 100.9°F and remained hemodynamically stable. On examination, he had trace bilateral edema, with clear lung exam, and normal heart sounds without any murmur.

This presentation closely resembled his previous admission a year ago, where the patient experienced fever, positional chest pain, dyspnea on exertion, and was subsequently diagnosed with Coxsackie virus-induced myopericarditis and pleuritis. In that admission, patient was also found to have pleural effusion, pericardial effusion without tamponade physiology along with non-ischemic cardiomyopathy with an ejection fraction (EF) of 45% The patient was started on colchicine 0.6mg per day for 3 months and ibuprofen 600mg three times a day for 7 days for myopericarditis with subsequent resolution of symptoms. He was also started on metoprolol succinate 12.5mg, lisinopril 2.5mg, and empagliflozin 10mg for his cardiomyopathy with improvement of EF to 55% 1 year later.

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**3.Methods**

**3.1 Investigations**

Significant laboratory findings included an initial elevation in high-sensitivity (hs) troponin to 34 ng/dl(n:0-22ng/dl) which decreased to 22 ng/dl. The patient was also found to have elevated inflammatory markers with an erythrocyte sedimentation rate (ESR) of 117mm/hour (n:0-15mm/hour) and a C-reactive protein (CRP) of 209 mg/L(n:0-5mg/L). Coxsackie virus titer was 1:800.

The Electrocardiogram (EKG) showed sinus rhythm with non-specific T wave inversions, without significant ST elevations or PR depressions, as shown in figure 1. Bilateral small pleural effusions were noted on the chest X-ray, as shown in Figure 2. Transthoracic echocardiogram (TTE) showed a small pericardial effusion of less than 1 cm in size, without respiratory variation in transaortic and trans tricuspid flow, and no indications of tamponade physiology, as shown in Figure 3. However, confirmation of the diagnosis of myocarditis by endomyocardial biopsy was not done as according to 2015 ESC guidelines, myopericarditis with no symptoms of acute decompensated heart failure does not clinically require endomyocardial biopsy. 2

Further investigations to rule out other etiologies, which included antinuclear antibody, rheumatoid factor, thyroid stimulating hormone (TSH) level, acid-fast bacilli sputum, antibody levels of viruses including Epstein Barr virus, herpes virus, parvovirus, influenza, hepatitis C, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS COV-2) and adenovirus, were negative. This effectively ruled out autoimmune, endocrine, malignant and infectious etiologies other than Coxsackie virus for myopericarditis.

**3.2 Differential diagnosis**

Initial potential differential diagnoses considered were recurrent myopericarditis, acute coronary syndrome (ACS), pneumonia, and pulmonary embolism. As per 2015 European Society of Cardiology (ESC) guidelines2, the patient tested positive for 2 out of 4 criteria for pericarditis: characteristic chest pain of pericarditis, and the presence of pericardial effusion observed on TTE, along with a new event following a symptom-free interval of 4-6 weeks for recurrence and elevated Troponin for myocarditis. Subsequently the patient was diagnosed with Coxsackie virus induced recurrent myopericarditis.

**3.3 Treatment**

According to 2015 ESC guidelines for recurrent pericarditis 2,the patient was initiated on a regimen of colchicine 0.6mg twice per day for a duration of 6 months and a tapering dose of ibuprofen starting at 600mg three times daily for 7days, followed by 600mg twice daily for 7 days, and finally 600mg once daily for 7 days, completing a total treatment duration of 21 days for recurrent myopericarditis.

**4. Conclusions and Results**

The patient's chest pain significantly improved, and the inflammatory markers, ESR (62 mm/hr) and CRP (33.5 mg/L), showed a decreasing trend. The patient was discharged with an outpatient cardiology follow up. At the follow-up visit two weeks later, the chest pain had completely resolved, and a notable reduction in pericardial effusion size (from less than 1 cm to trace) was observed in the repeat TTE, as shown in Figure 4. The case summary is summarized in Figure 5.

**5.Discussion**

We present a case of recurrent myopericarditis due to Coxsackie virus. Coxsackie virus is a notable factor in causing recurring myopericarditis, but there are no specific guidelines for treating it. However, using strategies meant for dealing with recurring pericarditis has shown promise in achieving good results. The way Coxsackie virus avoids the immune system is a key reason for its ability to cause repeat episodes of myopericarditis, emphasizing the importance of more research to better understand this process and potentially improve treatment methods.

There are multiple etiologies for new onset of myopericarditis which include infectious, autoimmune, neoplastic, metabolic, trauma, drug-related and other causes, as outlined in Table 11 Although there is lack of data on the exact prevalence of recurrent myopericarditis, recurrent pericarditis is observed in approximately 15–30% of patients.910 In instances of previous recurrences, prior corticosteroid use, or cases with a non-idiopathic etiology such as neoplastic causes, this rate may increase to 50%.910 There is limited data available regarding recurrent myopericarditis, and it is typically rare to identify Coxsackie virus as the culprit, adding uniqueness to this particular case.

According to 2015 ESC guidelines, the treatment of recurrent pericarditis primarily includes colchicine 0.5mg for 6months, aspirin and non-steroidal inflammatory drugs (NSAIDS) (Class I, Level A recommendation) 2. Corticosteroids are not recommended as the initial treatment (Class III, Level B), and the duration and response to treatment should be guided using CRP as a marker (Class IIa, Level C).2

The second line modalities of treatment include azathioprine11,IVIG 12and IL-1 receptor antagonists such as Anankira 13and Rilonacept14(Class IIb, Level C)2. Pericardiectomy should be contemplated as a final resort for individuals experiencing chronic constriction or pericarditis with symptoms that cannot be effectively treated.15 The treatment modalities are summarized in table 2. Few case reports16 17181920highlight the effectiveness of colchicine and indomethacin in recurrent myopericarditis; however currently, there are no established guidelines for managing recurrent myopericarditis or determining the duration of treatment. In our case, we followed the ESC guidelines for managing recurrent pericarditis, adapting them to recurrent myopericarditis. We administered colchicine for 6 months and ibuprofen for 21 days, aligning with the ESC recommendation for recurrent pericarditis, and observed promising results.

Coxsackievirus is believed to play a role in approximately 25 to 40 percent of initial instances of acute myopericarditis and dilated cardiomyopathy.21 There is limited data on the prevalence of Coxsackie virus induced recurrent myopericarditis and the pathophysiology is poorly understood. One possible hypothesis is that Coxsackie virus can evade the immune system and lead to recurrent myocardial and pericardial damage. Both cell surface and internal Toll-like receptors (TLR) have been implicated in the immune response to Coxsackie virus.22Furthermore, Coxsackie virus leads to impaired apoptosis by CD8+ T cells by having an inhibitory effect on antigen presentation via MHC Class I pathway.23 These interactions of Coxsackie virus with the immune system have led to long-term persistent infection in a variety of cell types, including human myocardial cells.2425

Hence Coxsackie virus should always be considered an important etiology in recurrent myopericarditis and treatment approaches established for recurrent pericarditis can be employed in managing recurrent myopericarditis.

**6.Key Clinical Message**

Acute recurrent myopericarditis is rare and lacks definitive guidelines, posing diagnostic and treatment challenges. A 44-year-old man with Coxsackie virus-induced myopericarditis responded well to colchicine and of ibuprofen employed in recurrent pericarditis. While management strategies for recurrent pericarditis utilized in recurrent myopericarditis show promise, Coxsackievirus's immune evasion underscores the need for further research.

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A screenshot of a graph

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Figure 1: EKG with sinus rhythm and non-specific T wave inversions

A x-ray of a person's chest

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Figure 2: Chest x ray showing bilateral small pleural effusions

A ultrasound of a baby

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Figure 3-TTE. Para-sternal long axis view showing pericardial effusion of <1cm (blue arrow) on initial presentation

A ultrasound of a baby

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Figure 4**-** TTE. Parasternal long axis view showing decrease in size of pericardial effusion to trace(arrow) after treatment in follow up

**A screenshot of a medical program

Description automatically generated** Figure 5:A summary of the clinical presentation

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| **Infectious causes** |
| Viral:  Coxsackievirus, echovirus, herpes virus, adenovirus, parvovirus B19 |
| Bacteria:  Mycobacterium tuberculosis, Coxiella burnetii, Borrelia burgdorferi |
| Fungal:  Histoplasma, Aspergillus, Candida, Blastomyces |
| **Autoimmune** |
| Systemic lupus erythematosus, rheumatoid arthritis, sarcoidosis, systemic vasculitis |
| **Neoplastic** |
| Primary cardiac tumor |
| Secondary metastatic tumors, commonly lung and breast cancer |
| **Metabolic** |
| Hypothyroidism, Uremia |
| **Trauma** |
| Post-radiation, post pericardiectomy syndrome |
| **Drug-related** |
| Procainamide, hydralazine,  doxorubicin, danorubicin, cyclophosphamide |
| **Vaccine** |
| SARS-Cov-2 |

**Table 1:** Common etiologies of new onset of myopericarditis

|  |  |  |
| --- | --- | --- |
| **ESC recommendation** | **Class** | **Level** |
| Colchicine | I | A |
| NSAIDS and aspirin | I | A |
| Azathioprine | IIb | C |
| IVIG | IIb | C |
| IL-1 receptor antagonist-Anankira, Rilonacept | IIb | C |
| Corticosteroids are not recommended as first line therapy | III | B |

**Table 2:** Summary of ESC guidelines for recurrent pericarditis.