Case Report

Aggressive Cholesterol Pericarditis With Minimal Effusion Masquerading as Treatment-Refractory Autoimmune Disease

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ABSTRACT

A middle-aged woman with rheumatoid arthritis presented with treatment-refractory pericarditis. Symptoms persisted despite escalation of immunosuppression, and she had recurrent admissions for heart failure. Imaging revealed minimal pericardial effusion and a thickened pericardium. Invasive hemodynamics confirmed constrictive physiology, and a pericardiectomy was required. Pathology testing confirmed cholesterol pericarditis, a rare condition of inflammatory cholesterol deposits within the pericardium. Previous reports describe moderate-to-large volumes of gold-coloured pericardial fluid. This case illustrates that cholesterol pericarditis can present with minimal pericardial effusion and rapidly progress to pericardial constriction.

RÉSUMÉ

Une femme d'âge moyen atteinte d'arthrite rhumatoïde a présenté une péricardite réfractaire. Les symptômes ont persisté en dépit de l'escalade de l'immunosuppression. Elle a été admise de façon répétitive en raison d'insuffisance cardiaque. L'imagerie a révélé un épanchement péricardique minimal et un péricarde épaissi. L'exploration hémodynamique invasive a permis de confirmer la physiologie constrictive. Une péricardectomie a été nécessaire. L'examen pathologique a permis de confirmer la péricardite cholestérolique, une affection inflammatoire rare due aux dépôts de cholestérol dans le péricarde. Les observations précédentes décrivent des volumes modérés à élevés de liquide péricardique doré. Ce cas illustre que la péricardite cholestérolique peut se traduire par un épanchement péricardique minimal et progresser rapidement vers la péricardite constrictive.

A 41-year-old woman was admitted to the coronary care unit with a non-ST elevation myocardial infarction after receiving one drug-eluting stent to the left circumflex artery. Her past medical history included multiple wrist surgeries, a spinal cord

stimulator for chronic joint pain, and chronic inappropriate tachycardia. Medications included ivabradine, gabapentin, and trazodone.

Within 1 week of presentation, she developed decompensated heart failure and new chest pain consistent with pericarditis. She had wrist swelling consistent with synovitis. A new diagnosis of rheumatoid arthritis (RA) was made based on the pericarditis, arthritis, and positive autoimmune bloodwork. She was treated for pericarditis with corticosteroids and received intravenous diuretics for heart failure. She was slow to improve, and after a 30-day stay, was discharged home on oral furosemide and prednisone.

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Ethics Statement: The research reported has adhered to the relevant ethical guidelines.

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See page 239 for disclosure information.

Novel Teaching Points

- Cholesterol pericarditis is a rare, but underdiagnosed, etiology of recurrent pericarditis and pericardial constriction. It is most often associated with RA, hypothyroidism, and tuberculosis.
- The pathogenesis of cholesterol pericarditis is poorly understood, but it is characterized by inflammatory cholesterol deposits within the pericardium.
- This case illustrates that cholesterol pericarditis can also present with only a small pericardial effusion.
- Cholesterol pericarditis can be successfully treated with pericardiectomy, and this case had sustained remission 1 year later.

However, over the next 8 months, she had recurrent clinic and emergency department visits for decompensated heart failure and pericarditis-like chest pain. At one such visit, the physical exam was consistent with constrictive pericarditis. Findings of this condition can include the presence of a pericardial rub, pericardial knock, elevated jugular venous pressure, paradoxical rise in jugular venous pressure on inspiration (Kussmaul's sign), bilateral pedal edema, and ascites. There was no wrist swelling.

Multiple investigations were completed over this time period. Laboratory investigations showed normal electrolytes, creatinine, complete blood count, and liver enzymes. Serum lipid values revealed a cholesterol level of 3.48 mmol/L (normal: < 5.20), a triglycerides level of 1.09 mmol/L (normal: < 1.70), and a low-density lipoprotein level of 2.03 mmol/L. Autoimmune bloodwork was positive for anti-cyclic citrullinated peptide, at 78 RU/mL (normal high: ≤ 5), and for rheumatoid factor, at 32 IU/mL (normal: < 14 IU/mL). The initial C-reactive protein level was 9.7 mg/L (normal high: ≤ 5.0), which peaked at 343.7 mg/L, and normalized thereafter.

An echocardiogram (Fig. 1A; Video 1 [\[video icon\]](#), view video online) revealed normal biventricular function with inferolateral hypokinesis, in keeping with the circumflex territory infarct. There was pericardial thickening and less than 10 mm

of pericardial effusion, consistent with minimal effusion. There was annulus reversus, with a lateral E' of 8.7 cm/s, a medial E' of 16.1 cm/s, and an elevated E/A ratio of 3.2. A dilated and noncompliant inferior vena cava was present. Computed tomography (CT) of the heart (Fig. 1B) revealed only 3-mm circumferential pericardial thickening. There was no calcification, so this imaging underestimated the true pericardial thickness. Cardiac magnetic resonance imaging was contraindicated due to her spinal cord stimulator. Invasive hemodynamics (Fig. 1C) revealed findings consistent with constrictive physiology.

The initial working diagnosis was constrictive pericarditis due to refractory RA. Initially, she was treated with intravenous methylprednisolone before being switched to oral prednisone. Subsequently, she was treated with escalating immunosuppression, including prednisone, methotrexate, leflunomide, and hydroxychloroquine. Symptoms persisted, and she appeared refractory to conventional immunosuppression. On multidisciplinary discussion with the rheumatology and cardiovascular surgery services, escalation to biologic therapy was felt unlikely to be effective without removal of the thickened pericardium that had not yet responded to already significant immunosuppression. A referral for pericardiectomy was made about 8 months after initial presentation.

In the operating theater, the pericardium was very thick (Fig. 2A). Pathology testing revealed pericardial tissue with extensive dense fibrosis with areas of calcification (Fig. 2, B and C). Multiple variably sized collections of cholesterol material were noted, some surrounded by chronic inflammatory cells and macrophages, in keeping with chronic cholesterol pericarditis.

Postoperatively, she did very well. She had an uncomplicated postoperative course. At the 1-year follow-up, she had had no recurrences of heart failure or pericarditis.

Discussion

Cholesterol pericarditis is a rare etiology of pericarditis that can be idiopathic or associated with RA, hypothyroidism, or tuberculosis.^{1,2} This condition was first reported in 1919 when Dr J.S. Alexander described the aspirate of a pericardial effusion to have a "scintillating gold paint appearance."³

Figure 1. (A) Echocardiography showed minimal pericardial effusion, <10 mm (blue arrow) and a thickened pericardium (red arrow). (B) Computed tomography of the heart showed a thickened pericardium measuring up to 3 mm (red arrow), but no calcification. (C) Hemodynamics tracing showed equalization of left ventricular end-diastolic pressure and right ventricular end-diastolic pressure (red arrow), square-root sign (blue arrow), ventricular interdependence (green arrow indicating inspiration), and high right ventricular end-diastolic pressure.

Figure 2. (A) Intraoperatively, a very thick pericardium (**white arrow**) was discovered around the myocardium (**blue arrow**). (B) Histopathology testing showed dense fibrosis in the pericardium, focal chronic inflammation, and variably sized collections of cholesterol material (**blue arrow**). (C) Histopathology testing showed cholesterol clefts within the pericardial tissue. The empty spindle-shaped spaces are cholesterol crystals (**blue arrow**).

Since then, cholesterol pericarditis has remained a relatively rare disease.² The pathogenesis of cholesterol pericarditis is poorly understood, but it is characterized by inflammatory cholesterol deposits within the pericardium. These cholesterol crystals precipitate and provoke a granulomatous foreign body reaction, leading to aggressive inflammation.² Pericardial fluid has a concentration of cholesterol equal to or exceeding the serum concentration, but serum cholesterol levels do not correlate with disease.⁴

RA likely predisposed our patient to developing this condition.¹ In hindsight, her multiple previous wrist surgeries were likely due to undiagnosed RA, which was also an important cardiac risk factor for her myocardial infarction. RA itself is a chronic inflammatory disease of unknown etiology that can result in pericardial inflammation and thickening over time,⁴ so we naturally treated for that first. Clues that her condition was not due to RA were the normalization of the C-reactive protein level, resolution of joint swelling, and persistence of symptoms despite escalating immunosuppression.

This case illustrates several important points. First, cholesterol pericarditis can present with minimal pericardial effusion. To our knowledge, this case of cholesterol pericarditis is the first reported in the literature to have occurred with minimal effusion. Previous reports describe moderate-to-large volumes of gold-coloured pericardial fluid.⁵ Second, cholesterol pericarditis does not respond to typical immunosuppression, suggesting that the pathophysiology is distinct from RA. Third, pericardiectomy led to sustained remission. The decision for pericardiectomy was made after multidisciplinary discussion, and based on the evidence we had of pericardial constriction from multimodality imaging and invasive hemodynamics. Lastly, further research is needed on how to diagnose this condition earlier and in a noninvasive manner, especially in cases without pericardial fluid available for analysis. The rarity of this condition makes larger studies challenging, but advancements in imaging may help us better characterize pericardial composition in the future.

Cholesterol pericarditis is likely an underdiagnosed condition, and clinicians must keep a low threshold for considering it in cases of refractory pericarditis. In our patient, multidisciplinary collaboration and pericardiectomy led to a successful outcome and sustained remission.

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Disclosures

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at <https://www.cjcopen.ca/> and at <https://doi.org/10.1016/j.cjco.2021.09.018>.