CLINICAL VIGNETTE

Unique Presentation and Treatment of Chronic Recurrent Pericarditis

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Case

A 71-year-old female with hyperlipidemia and obesity presents with one year of progressively worsening fatigue and intermittent dizziness. Her initial assessment revealed normal blood pressure and resting sinus bradycardia of 52 beats per minute (bpm). Her exam revealed was normal, without murmurs. Labs revealed mild pre-diabetes, normal cholesterol on statin therapy, and normal hemoglobin and thyroid studies. She had normal recent stress test and echocardiogram. She underwent heart rate monitoring which found symptomatic bradycardia to heart rate of 35-40 bpm. She subsequently underwent placement of dual-chamber permanent pacemaker.

During pacemaker placement, the patient experienced the acute onset of sharp bilateral chest pain and she reported "the most severe headache of her life". Her electrocardiogram (ECG) showed diffuse ST segment changes and the patient became acutely hypotensive. A stat echocardiogram showed a new large pericardial effusion with echocardiographic evidence of tamponade. She was successfully treated with urgent pericardiocentesis. Post-procedure, the patient continued to report bilateral pleuritic chest pain that was worse in the supine position, with shortness of breath, and ongoing severe headaches. Head CT revealed no intracranial hemorrhage or other neurologic issues. Repeat ECG showed persistent diffuse ST segment elevations and the patient was started on high dose ibuprofen and colchicine 0.6 mg twice daily for clinical pericarditis. She was discharged and was still symptomatic after 2 weeks of therapy. She switched to indomethacin with subsequent resolution of her chest pain and ST elevations, although her headaches continued to persist.

After completing 4 weeks of therapy, the patient discontinued her medications due to resolution of chest pain. Shortly after stopping medication chest pain recurred and her headaches worsened. Repeat echo showed no pericardial effusion. She was restarted on colchicine and indomethacin as well as oral steroids with resolution of both her headache and chest pain. Unfortunately, attempts to wean her steroids resulted in recurrent symptoms requiring reescalation of steroid dose. A proton pump inhibitor was added to treat potential gastritis component, with minimally improved chest pain. At this point the patient reported onset of blurred vision, weight gain, frequent infections, poor sleep, along with increasing frustration with her chest pain and headache. She started acupuncture therapy and was able to very slowly reduce and eventually discontinue prednisone. She remains on colchicine and indomethacin and her inflammatory markers have normalized.

Unfortunately, she had another recurrence of her pleuritic chest pain and headache despite ongoing therapy. Her inflammatory markers were again found to be markedly elevated, with erythrocyte sedimentation rate (ESR) 70 and C-reactive protein (CRP) 112. Ischemic, neurologic, and rheumatologic testing revealed no alternative etiologies for her chest pain and headaches. Prednisone was restarted and interleukin-1 inhibition with rilonacept was started. After a loading dose and initiation of weekly subcutaneous infusions, the patient reported complete resolution of chest pain and headache after two weeks and was able to rapidly titrate off colchicine, indomethacin, and steroids within 6 weeks. Inflammatory markers significantly improved with ESR 35 and CRP 5.3, with full normalization after 3 months of therapy. She was continued on weekly rilonacept with no further relapses.

Discussion

Acute pericarditis is an inflammatory process affecting the pericardium. It is most commonly caused by an infection, often viral illnesses. However, non-infectious causes such as autoimmune conditions, trauma and iatrogenic triggers, metabolic conditions such as myxedema coma and uremia, as well as medication side effects can also cause pericarditis.[1] Our patient, had iatrogenic perforation of her right ventricle during pacemaker placement that led to cardiac tamponade. The pericardial blood acted as a local irritant to cause a Dressler-like syndrome.

Pericarditis most often presents as a sudden onset sharp chest pain. It can be uni- or bi-lateral and is described as pleuritic, worse with a deep breath. The pain typically is exacerbated with lying back and improved with sitting up and/or leaning forward. Our patient instantly experienced sharp bilateral chest pain and a headache as soon as the right ventricle was perforated. While she had the classical chest pain that is associated with pericarditis, her symptoms of headache were atypical. A literature search did not reveal any case reports of headaches associated with pericarditis. The two were likely associated since extensive neurologic testing was negative, and the onset of symptom was at the time of perforation and because exacerbation and alleviation of her chest pain was always associated with exacerbation and alleviation of her headache.

In order to establish a diagnosis of acute pericarditis patients must meet at least 2 of 4 criteria. These are: classic pericarditis chest pain; pericardial friction rub, suggestive ECG changes of pericarditis which are diffuse ST elevation; and/or new or worsening pericardial effusion. Our patient had met 3 or 4 criteria. She did not have a friction rub.[2] If the patient's chest pain resolves and reoccurs after 4-6 weeks without symptoms, or the above diagnostic criteria (ECG changes, pericardial effusion, elevation of inflammatory markers), it is considered recurrent pericarditis. This differs from chronic or incessant pericarditis symptoms that do not resolve for 4-6 weeks or wax and wane for short periods of time. Chronic pericarditis is reserved for chest pain that persists longer than 3 months, such as in our patient.

Treatment

Medical therapy aims to resolve symptoms by reducing local and systemic inflammation, normalizing serum inflammatory markers, and preventing recurrent episodes and chronic complications like constrictive pericarditis. Non-steroidal anti-inflammatory drugs (NSAIDs) are the first line therapy with high initial dosing (ibuprofen 600 to 800 mg 3 times a day or indomethacin 25 to 50 mg 3 times a day) followed by a slow taper.[1] Aspirin 650 to 1000 mg 3 times a day can also be used and is preferred in pericarditis after acute myocardial infarction or cardiac surgery since NSAIDS are contraindicated. Gastro-intestinal protection with proton pump inhibitors may be required while on this treatment especially in those at increased risk of complications.

The open-label COPE trial[2] and the double-blinded ICAP trial[3] established the addition of colchicine to NSAIDs as first-line therapy with a class IA recommendation in European Society of Cardiology guidelines.[4] Colchicine needs to be adjusted for weight and renal function (ranging from 0.3 to 1.2 mg per day) for a duration of at least 3 months. This significantly reduced the risk of recurrent pericarditis with a number needed to treat (NNT) of only 4. Use was further investigated in recurrent disease in the CORP trial showing benefit with similar dosing, extended for 6 months.[5] Colchicine is also generally safe, with gastrointestinal symptoms being the most common side effects.

Glucocorticoids are reserved for patients with refractory symptoms or multiple recurrences despite standard therapy, those with comorbidities that require steroid treatment, or who have contraindications to standard therapy. Steroid use has been associated with increased rates of recurrent pericarditis, especially when used at high doses or with rapid tapers. Instead, low to moderate dose prednisone (0.2 to 0.5 mg/kg/day) with a slow taper over 2-3 months while monitoring symptoms and CRP levels is recommended.[6]

In patients who develop incessant or chronic pericarditis, even the treatment options above may not be enough to resolve symptoms. Because of the role of interleukin-1 (IL-1) in the innate inflammatory cascade at the pericardium, it has been studied as a treatment target for resistant pericarditis. Rilonacept, anakinra, and goflikicept are targeted IL-1 alpha and beta receptor blockers. In three respective trials comparing this drug to placebo, IL-1 receptor inhibition was superior to placebo in preventing pericarditis reoccurrence.[7] In the RHAPSODY trial, use of rilonacept allowed for rapid discontinuation of NSAIDS, colchicine, and steroids in treatment of chronic/recurrent pericarditis. Furthermore, the side effect profile of IL-1 inhibitors are more favorable compared to the current standard therapy and include primarily injection site reaction and mild increase in cholesterol.[8] The trial using goflikicept also included patients with a non-inflammatory phenotype. These patients had clinical signs and symptoms of pericarditis but had normal CRP and normal cardiac magnetic resonance imaging, which is different from the prior two trials which required elevated CRP. Even patients with a non-inflammatory phenotype had decreased recurrence of pericarditis with IL-1 inhibition suggesting that CRP may not be the correct marker of disease activity.[7] Trials of IL-1 inhibition are still in early stages and questions about duration of therapy have not been answered.

Conclusion

In summary, pericarditis has an incidence of about 28 cases per 100,000 subject per year, of which 15-30% of patients have a first reoccurrence. The SARS-CoV-2 virus and less commonly the vaccine are newly viral identified causative agents of pericarditis that have put highlights on this condition.[9] The diagnosis is clinical, based on meeting 2 of 4 criteria: pleuritic chest pain, pericardial rub, diffuse ST segment elevations with reciprocal PR depressions on ECG, and/or new pericardial effusion. If these symptoms recur 4-6 weeks after a symptom free period, the condition is considered recurrent or chronic if lasting for 3 months without a period of remission. Currently the hallmark of therapy includes NSAIDS, colchicine, and glucocorticoids. Novel agents such as IL1 receptor inhibitors are proving to be effective in treating pericarditis.

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