CLINICAL VIGNETTE

An Unusual Cause of Pericardial Effusion

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Case

An 84-year-old woman with a history of heart failure, permanent atrial fibrillation and anoxic brain injury from out-of-hospital cardiac arrest resulting in dementia presented with her daughter for evaluation. The patient had an implantable cardiac defibrillator placed after her arrest 3 years ago and had undergone atrioventricular (AV) nodal catheter ablation 6 months ago. During the visit, the patient reported nonspecific complaints, including increased fatigue, mild dyspnea and malaise which had been present for several weeks. An echocardiogram 9 months earlier was significant for mild to moderate mitral valve regurgitation, restricted movement of a posterior mitral valve leaflet and a mildly reduced left ventricular ejection fraction of 45%. Recent interrogation of the patient's pacemaker had shown normal function. Medications included rivaroxaban 15 mg daily.

The patient's vital signs included a normal temperature, a blood pressure of 120/71 mmHg, a heart rate of 80 bpm and an oxygen saturation of 97%. Physical exam revealed a frail appearing woman with cognitive impairment. Her cardiac exam was significant for a regular rhythm with a grade 2 holosystolic murmur. She had mild bilateral pitting edema in her lower extremities and unremarkable pulmonary exam. Electrocardiogram showed no discernable atrial rhythm, ventricular pacing and premature ventricular beats.

Urgent repeat echocardiography was significant for interval development of a moderate sized pericardial effusion without evidence of tamponade. Labs were significant for elevated C-Reactive protein (CRP) of 2.1 mg/dL and an elevated B-type natriuretic peptide (BNP) of 265 pg/mL. Complete blood count, comprehensive metabolic panel, thyroid panel and erythrocyte sedimentation rates were normal. An upper respiratory SARS-CoV-2 RT-PCR test was negative. CT scan of the chest verified correct placement of the patient's cardiac device leads. This also showed small bilateral pleural effusions and incidental hepatic capsular nodularity. The patient was given a trial of gentle diuresis and empiric treatment for pericarditis with colchicine and a nonsteroidal anti-inflammatory medication. She was instructed to hold her rivaroxaban in anticipation of a possible invasive procedure.

Subsequent echocardiography showed that her pericardial effusion had increased in size and was now large (Figure 1). It was still without signs of tamponade. Her CRP was 20.1 mg/dL and her BNP was 738 pg/mL. She was also noted to have low albumin of 3.4 g/dL and alanine transaminase, 6 U/L, as well as an elevated international normalized ratio (1.6). Interval history was significant only for the progression of her fatigue. Vital signs were not significantly changed and her exam was stable aside from the development of jugular venous distention. The patient was referred to the hospital for pericardiocentesis. This was uncomplicated and yielded 635 mL of brownish red fluid. The red blood cell count was 414,000 /uL and the white blood count was 2,950 /uL with a lymphocyte predominance. Based on a protein level of 4.7 g/dL and an LDH of 1,998 U/L, the fluid was classified as exudative according to Light's criteria. Adenosine deaminase and acid fast bacteria stains were normal. The patient's Gram stain was negative for organisms. The patient was discharged after an observation period. Follow up of the patient's pericardial fluid labs showed a positive cytomegalovirus (CMV) PCR. Cultures showed no growth and cytology was negative for malignant cells.

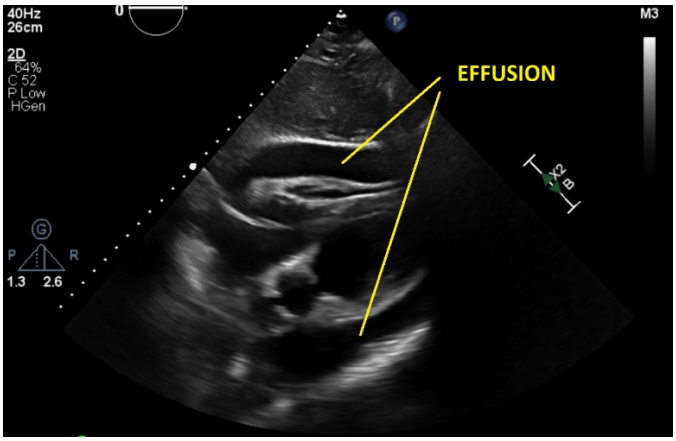

Figure 1

Discussion

The pericardium is a sac that contains the heart and portions of the great vessels. It is divided into inner visceral and outer parietal layers, the latter of which contains fibrous connective tissue, which is not highly distensible.[1] Pathology involving the pericardium includes pericarditis, pericardial effusion, constrictive pericarditis, pericardial masses and congenital conditions.[2] Clinical presentation of pericardial disease ranges from asymptomatic to hypotension and death.

Pericardial effusion is the accumulation of fluid in the pericardial space beyond the physiologic normal amount of 10-50 mL. Pericardial effusion may be classified, by the diameter of fluid, as small (< 10 mm), moderate (10-20 mm) or large (>20 mm).[3] Approximately 25-30% of large effusions are complicated by pericardial tamponade.[4] In this condition, after enough pericardial content has accumulated to fill a pericardial reserve volume, there is significant compression of the heart.[5] This compression causes impaired venous return and cardiac filling, which may lead to hypotension and death if untreated.[4]

Patients with pericardial effusion are generally asymptomatic or only symptomatic from their underlying etiology until early tamponade is present. Although physical examination maneuvers for the detection of pericardial effusion in the absence of tamponade have been described,[6] they are not reliable and are not generally used in current practice. Once tamponade has developed, a number of nonspecific physical exam findings may be present.[6] These include tachycardia, hypotension, elevated jugular venous pressure with diminished y descent and pericardial rub.

Pulsus paradoxus, with abnormally large decrease in systolic blood pressure with inspiration, is the best-known physical exam finding in tamponade.

Outside of tamponade, diagnosis of pericardial effusion typically requires diagnostic testing. The most common electrocardiographic findings in pericardial effusion are sinus tachycardia, low QRS voltage and electrical alternans (periodic variation in QRS amplitude).[7] In patients with cardiac comorbidities, such as AV block and pacemaker implantation as in our patient, some of these findings may not be discernable. Chest x-ray is not sufficiently specific to detect all but the largest effusions. Transthoracic echocardiography is considered the first-line imaging modality for assessing pericardial effusion and has the advantage of providing physiologic criteria to support or reject a diagnosis of tamponade. Cardiac magnetic resonance and computed tomography have a growing role.[8]

Evaluation and management of pericardial effusion is focused on determining an etiology of the effusion and treating or preventing tamponade. Although specific numbers vary, approximately one-third of pericardial effusions are due to malignancy. Uremia, collagen vascular disease, iatrogenic, post-myocardial infarction and infectious causes make up the majority of the remaining diagnoses while no etiology is established in about one-fourth of cases.[9]

Pericardiocentesis is typically performed when tamponade is present or developing as well as when the etiology is unclear. This often includes cases of suspected malignancy or infection. Pericardiotomy and pericardiectomy are sometimes required when effusions are refractory, inaccessible percutaneously or require tissue for a diagnosis.

CMV has long been associated with pericardial effusion, though effusions are not a common manifestation of this infection. Due to CMVs ubiquitous nature, it should be diagnosed with culture or PCR rather than serology alone. When tested, CMV has been shown to be present in a significant number of cases of pericardial effusion.[10] There is speculation that some of these cases may represent latent CMV infections that reactivate when the immune system is compromised.

Case Course

The patient was discharged home in stable condition. Due to her pre-existing status of endstage dementia, she and her family decided to pursue comfort-only hospice care and declined additional treatments and consultations. Due to a brief change in her goals of care 4 months later, an echocardiogram was done and showed no effusion.

Conclusion

Pericardial effusion is a condition that often remains subclinical until the development of life-threatening tamponade. Pericardiocentesis or other intervention is indicated when tamponade is developing or when the etiology remains unclear. A considerable number of cases are still classified as idiopathic. CMV infection should be suspected, and tested for, in cases of idiopathic pericardial effusion, particularly in the elderly and immunosuppressed.

REFERENCES

1. **Rodriguez ER, Tan CD**. Structure and Anatomy of the Human Pericardium. *Prog Cardiovasc Dis*. 2017 Jan-Feb;59(4):327-340. doi: 10.1016/j.pcad.2016.12.010. Epub 2017 Jan 4. PMID: 28062264.
2. **Klein AL, Abbara S, Agler DA, Appleton CP, Asher CR, Hoit B, Hung J, Garcia MJ, Kronzon I, Oh JK, Rodriguez ER, Schaff HV, Schoenhagen P, Tan CD, White RD**. American Society of Echocardiography clinical recommendations for multimodality cardiovascular imaging of patients with pericardial disease: endorsed by the Society for Cardiovascular Magnetic Resonance and Society of Cardiovascular Computed Tomography. *J Am Soc Echocardiogr*. 2013 Sep;26(9):965-1012.e15. doi: 10.1016/j.echo.2013.06.023. PMID: 23998693.
3. **Adler Y, Charron P, Imazio M, Badano L, Barón-Esquivias G, Bogaert J, Brucato A, Gueret P, Klingel K, Lionis C, Maisch B, Mayosi B, Pavie A, Ristic AD, Sabaté Tenas M, Seferovic P, Swedberg K, Tomkowski W; ESC Scientific Document Group**. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases: The Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC)Endorsed by: The European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J*. 2015 Nov 7;36(42):2921-2964. doi: 10.1093/eurheartj/ehv318. Epub 2015 Aug 29. PMID: 26320112; PMCID: PMC7539677.

4. **Ariyarajah V, Spodick DH**. Cardiac tamponade revisited: a postmortem look at a cautionary case. *Tex Heart Inst J*. 2007;34(3):347-51. PMID: 17948086; PMCID: PMC1995065.
5. **Spodick DH**. Pathophysiology of cardiac tamponade. *Chest*. 1998 May;113(5):1372-8. doi: 10.1378/chest.113.5.1372. Erratum in: *Chest* 1998 Aug;114(2):662. PMID: 9596321.
6. **Ewart W**. Practical Aids in the Diagnosis of Pericardial Effusion, in Connection with the Question as to Surgical Treatment. *Br Med J*. 1896 Mar 21;1(1838):717-21. doi: 10.1136/bmj.1.1838.717. PMID: 20756103; PMCID: PMC2406464.
7. **Bruch C, Schmermund A, Dagres N, Bartel T, Caspari G, Sack S, Erbel R**. Changes in QRS voltage in cardiac tamponade and pericardial effusion: reversibility after pericardiocentesis and after anti-inflammatory drug treatment. *J Am Coll Cardiol*. 2001 Jul;38(1):219-26. doi: 10.1016/s0735-1097(01)01313-4. PMID: 11451278.
8. **Cosyns B, Plein S, Nihoyanopoulos P, Smiseth O, Achenbach S, Andrade MJ, Pepi M, Ristic A, Imazio M, Paelinck B, Lancellotti P; European Association of Cardiovascular Imaging (EACVI); European Society of Cardiology Working Group (ESC WG) on Myocardial and Pericardial diseases**. European Association of Cardiovascular Imaging (EACVI) position paper: Multimodality imaging in pericardial disease. *Eur Heart J Cardiovasc Imaging*. 2015 Jan;16(1):12-31. doi: 10.1093/ehjci/jeu128. Epub 2014 Sep 23. PMID: 25248336.
9. **Sagristà-Sauleda J, Mercé AS, Soler-Soler J**. Diagnosis and management of pericardial effusion. *World J Cardiol*. 2011 May 26;3(5):135-43. doi: 10.4330/wjc.v3.i5.135. PMID: 21666814; PMCID: PMC3110902.
10. **Campbell PT, Li JS, Wall TC, O'Connor CM, Van Trigt P, Kenney RT, Melhus O, Corey GR**. Cytomegalovirus pericarditis: a case series and review of the literature. *Am J Med Sci*. 1995 Apr;309(4):229-34. doi: 10.1097/00000441-199504000-00009. PMID: 7900747.