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MINI-FOCUS ISSUE: HEART FAILURE

INTERMEDIATE

CASE REPORT: CLINICAL CASE

Incessant Pericarditis With Recurrent Cardiac Tamponade as the Manifestation of Autoimmune Polyglandular Syndrome Type II

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ABSTRACT

A 23-year-old man was admitted for acute pericarditis that evolved to cardiac tamponade and shock with need of emergent pericardiocentesis and inotropic support. Corticosteroid therapy was successful, but despite a gradual tapering, the patient relapsed. Incidentally, the patient developed hyperkalemia with hyponatremia. Subsequent hormonal measurements confirmed autoimmune polyglandular syndrome type-2. (**Level of Difficulty: Intermediate.**)
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A 23-year-old man presented with retrosternal pleuritic chest pain and low-grade fever for 3 days. On presentation, he was apyretic, normotensive, and a pericardial rub was present. The electrocardiogram showed sinus tachycardia and widespread ST elevation associated with PR segment depression (**Figure 1**) and echocardiography showed a mild, circumferential pericardial effusion. The laboratory workup demonstrated normal high sensitivity troponin I (<3.2 ng/l; 99th <34 ng/l), mild leukocytosis (11.9 × 109/l), and very elevated C-reactive protein (27.6 mg/dl, normal: <0.5 mg/dl). The next day, the patient developed cardiac tamponade and an emergent pericardiocentesis was performed. However, after the immediate evacuation of 350 ml of serous fluid, he progressed to profound shock, dependent on high noradrenaline doses. In extreme, a 1-g bolus of methylprednisolone was administered and an immediate, excellent clinical response was verified, allowing the weaning of

LEARNING OBJECTIVES

- To recognize the large spectrum of clinal presentations of Addisonian crisis and prompt diagnosis of this rare but life-threatening situation.
- To emphasize the need of a broader etiological study in incessant pericarditis with cardiac tamponade, particularly in younger age.
- To highlight the role of multidisciplinary and multimodality imaging in management of pericardial diseases.

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noradrenaline the next day and progressive resolution of the effusion.

PAST MEDICAL HISTORY

He had childhood asthma, nonallergic rhinitis, and an idiopathic episcleritis, controlled with topical corticosteroids. One month earlier, he had been admitted to an intensive care unit due to septic shock complicating tonsillitis.

DIFFERENTIAL DIAGNOSIS

A pericardial friction rub in the presence of retrosternal pleuritic chest pain in a young man is highly suggestive of acute pericarditis. However, other diagnoses as myocarditis, pulmonary embolism, pneumoniae, asthma exacerbation, and pneumothorax also should be considered.

INVESTIGATIONS

Streptococcus mitis was isolated in the pericardial fluid and ceftriaxone was initiated. At this point, the echocardiogram showed constrictive-effusive physiology (**Figures 2 to 4**, Videos 1 and 2). Although the autoimmunity workup was pendent, the patient was discharged on colchicine 0.5 mg every day (q.d.),

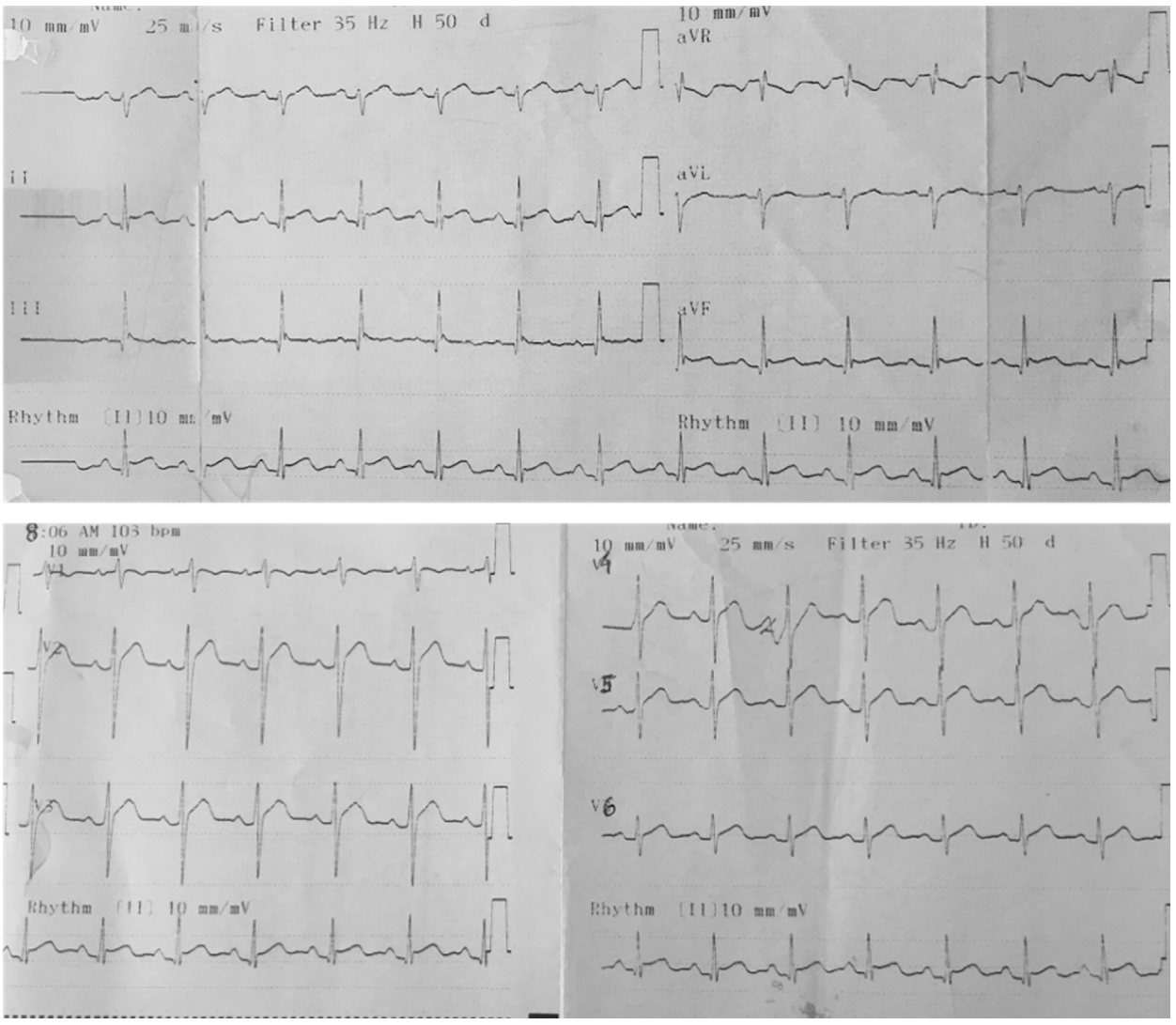
ABBREVIATIONS AND ACRONYMS

Abs = antibodies

AI = adrenal insufficiency

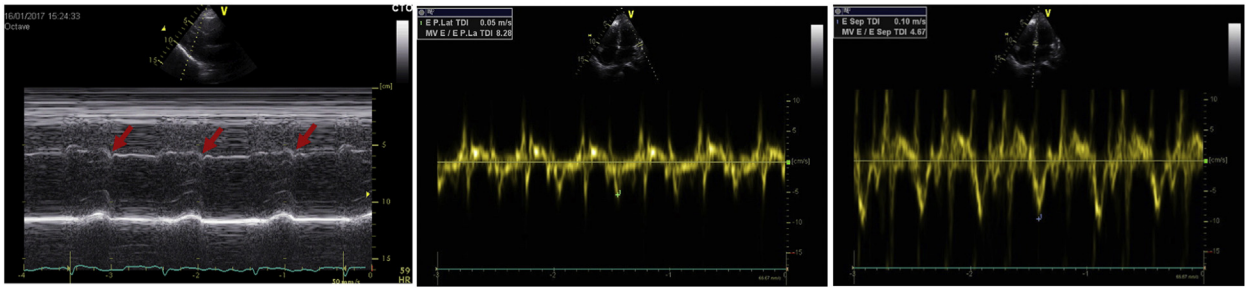
APS = autoimmune polyglandular syndrome

FIGURE 1 Patient Electrocardiogram



Patient electrocardiogram showing widespread ST-segment elevation and PR depression of in inferior and V_2 to V_6 leads.

FIGURE 2 M-Mode and Septal and Lateral Tissue Doppler Measurements



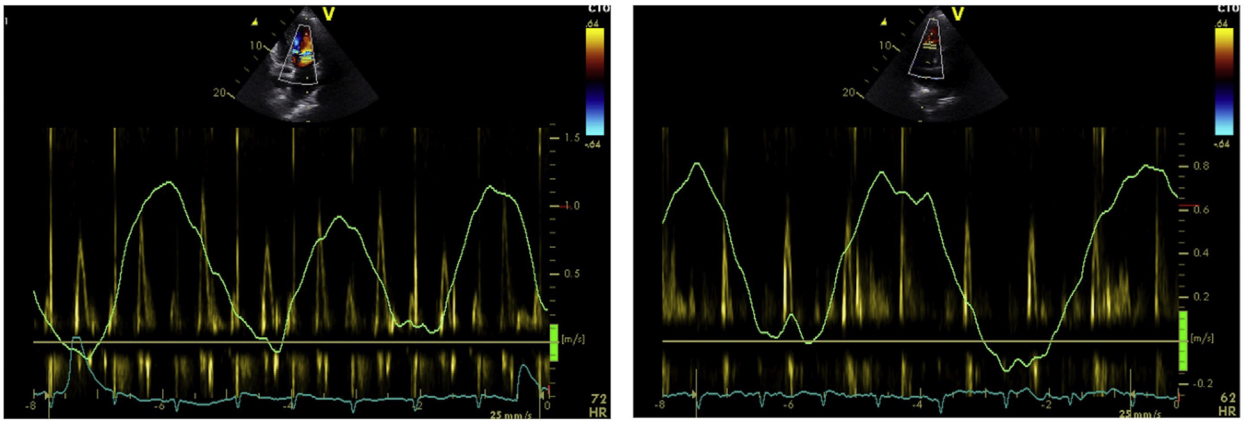
(Left) M mode showing abnormal rapid motion of interventricular septum (notching in early diastole). **(Middle and Right)** Tissue Doppler measurements. A normal septal e' velocity is present and lateral e' velocity is lower than the medial e' velocity, a phenomenon called *annulus reversus*.

ibuprofen 600 mg 3 times a day, and prednisolone 5 mg q.d., with a working diagnosis of idiopathic acute pericarditis. However, he was readmitted 4 weeks later due to incessant pericarditis with cardiac tamponade, needing immediate pericardiocentesis. A pleuro-pericardial window was then performed, and a pericardial biopsy obtained (Figure 5). Cardiac magnetic resonance showed the presence of diastolic paradoxical septal movement, and diffuse pericardial late gadolinium enhancement (Figure 6, Videos 3 and 4).

MANAGEMENT

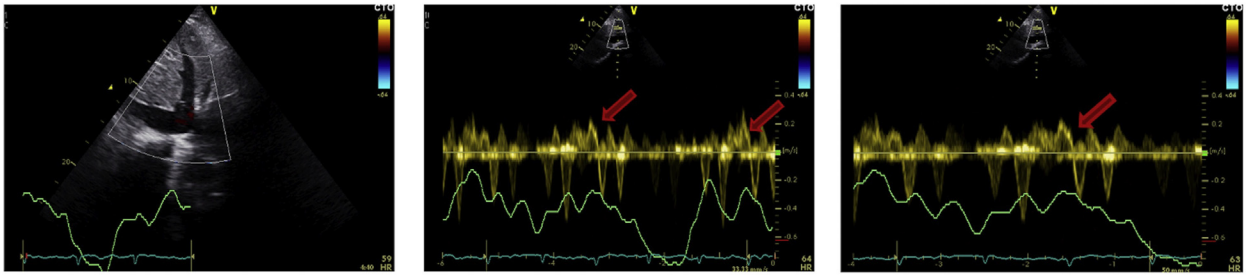
The etiologic study performed so far (Table 1) was inconclusive and the patient was discharged with a higher dose of methylprednisolone (32 mg q.d.). Despite the gradual corticosteroid tapering, symptoms recurred whenever the dose was lowered to <10 mg, leading to several readmissions. Incidentally, during the third rehospitalization, with normal kidney function, a combination of hyperkalemia (5.9 mmol/l) with hyponatremia (129 mmol/l) was found, leading to the suspicion of adrenal insufficiency (AI). Adrenal axis measurements were performed, showing very high levels of adrenocorticotropin (172 pg/ml, normal: 9 to 52 pg/ml) and cortisol under the limit of detection (<1 μg/dl), leading to the diagnosis of Addison's disease. Hormonal replacement therapy with fludrocortisone 0.1 mg q.d. and prednisolone 15 mg q.d. was initiated. Further evaluation for autoimmune diseases showed the presence of anti-intrinsic factor autoantibodies and primary hypogonadism was further found.

FIGURE 3 Mitral and Tricuspid Inflow Velocities at Pulsed Wave Doppler



Exacerbated respiratory variance, a sign of interventricular dependence.

FIGURE 4 2-Dimensional and Spectral Doppler Waveforms of Hepatic Veins



(Left) 2-dimensional echo in subcostal view, showing a plethoric inferior vena cava. **(Middle and Right)** Spectral Doppler waveform of hepatic veins flow. Expiratory reversal of diastolic wave is present, a highly specific sign of the presence of constrictive physiology.

Ultimately, a diagnosis of autoimmune polyglandular syndrome type 2 (APS-2) was established.

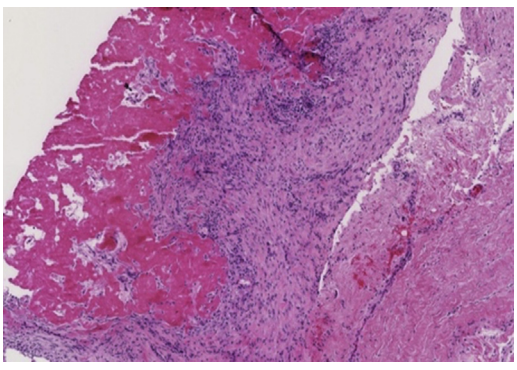
DISCUSSION

We report the case of a young man admitted for acute pericarditis progressing to recurrent cardiac tamponade and shock. Serendipitously, a high-dose bolus of corticosteroid reverted the shock and its maintenance contributed to a progressive and robust clinical response. A few weeks before, he had been admitted for tonsillitis complicated by a septic shock. Retrospectively, both clinical scenarios have in common an impaired response to a stressful event and were probably manifestations of a previously unrecognized adrenal crisis, a life-threatening emergency associated with high mortality unless appropriately recognized and treated (1,2). In our case, it was unknowingly reverted by a bolus of methylprednisolone.

AI is characterized by impaired production or action of glucocorticoids, with or without deficiency in mineralocorticoids and/or adrenal androgens. It can result from disease intrinsic to the adrenal cortex (primary AI or Addison's disease), from pituitary diseases that hamper the release of corticotropin (secondary AI) or from hypothalamic disorders that impair the secretion of the corticotropin-releasing hormone (tertiary AI). The manifestations of primary AI result from deficiency of all adrenocortical hormones, but they can also include signs of other concurrent autoimmune conditions (3). In our patient, the use of methylprednisolone for pericarditis corrected the deficiency of cortisol but not of mineralocorticoids, due to the weak methylprednisolone mineralocorticoid effect. This resulted in hyponatremia and hyperkalemia, manifestations of mineralocorticoid insufficiency.

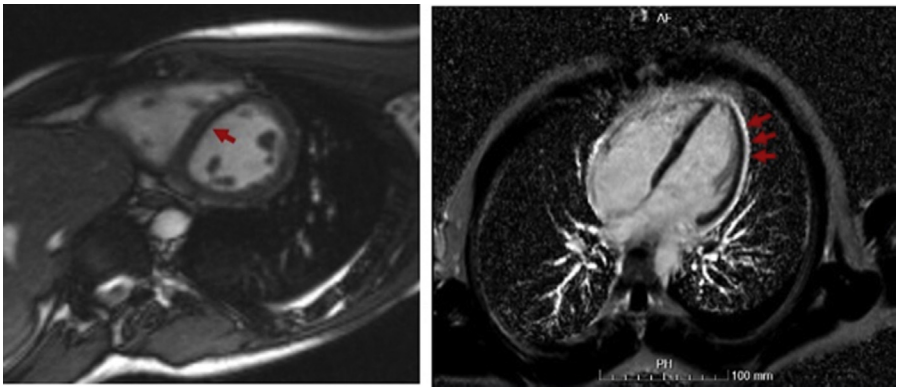
Addison's disease can be associated with other autoimmune conditions. The APS comprise a group of entities characterized by autoimmune activity against more than 1 endocrine organ, can occur in patients of any age, and new components of a given syndrome can appear throughout life. There are rare monogenic forms, as APS-1, and a more common polygenic varieties, APS-2; both have Addison's disease as a prominent component. There are very few reported cases of cardiac tamponade as the first manifestation of APS-2, and most have a prior history of an autoimmune disease. To our knowledge, only 1 case was described (4).

FIGURE 5 Pericardial Biopsy: Presence of Chronic Inflammatory Infiltrate With Angiogenesis



Neutrophil infiltration as well as fibrin deposition are observed, indicating acute inflammatory activity.

FIGURE 6 Cardiac Magnetic Resonance Imaging



(Left) HR SSFP cine sequence showing the presence of "flattening" of septum in the diastole (Videos 3 and 4). **(Right)** Cardiac magnetic resonance late gadolinium enhancement sequence. Presence of diffuse pericardial enhancement **(arrows)**, suggesting active pericardial inflammation.

Currently, there are no specific tests to detect APS-2, but measurement of organ-specific antibodies (Abs) are helpful in assessing disease risk, because these "silent Abs" precede clinical disease and are detectable years before disease onset (5,6). There is no specific treatment for APS-2, only hormonal replacement of associated endocrine disorders (7).

Nonsteroidal anti-inflammatory drugs and colchicine are the mainstay of therapy for recurrent pericarditis, and when a specific cause is identified, treatment should be etiological (8). Corticosteroids provide rapid control of symptoms, but they also favor chronicity and more recurrences. When used, tapering should be particularly slow and if recurrence occurs, every effort should be made to not increase the dose or to reinstate. In cases of corticosteroid dependence, agents such as intravenous immunoglobulin, Anakinra, or azathioprine may be considered (9). If these agents are effective in APS-associated pericarditis is unknown.

TABLE 1 Etiological Study Panel

Free T4/TSH	Normal/Normal
γ Interferon	Negative
Human immunodeficiency virus (HIV) serology	Negative
Cytomegalovirus (IgM/IgG)	–/+
Epstein Barr virus (IgM/IgG)	– /+
Parvovirus (IgM/IgG)	–/+
Herpes virus 1 (IgM/IgG)	–/+
Herpes virus 2 (IgM/IgG)	–/–
Coxiella burnetti	–
Borrelia burgdoferi (IgM/IgG)	– /–
Rickettsia conori (IgG)	+
Treponema pallidum	–
Antinuclear antibodies (ANAS)	+
Anti-dsDNA antibodies	–
Anti-pANCA/c ANCA	– / –
Anti-SSA60, Sm, RNP, Scl70, JO	–
Rheumatoid factor	–

ANCA = antineutrophil cytoplasmic antibodies; dsDNA = double-stranded DNA; Ig = immunoglobulin.

FOLLOW-UP

During the past months, prednisolone was successfully tapered to 5 mg q.d., but unfortunately, he suffered a new recurrence with the for higher doses (currently, 15 mg q.d.).

CONCLUSIONS

The Addisonian crisis is life-threatening situation, because it is rare and has multiple clinical presentations, the diagnosis is very challenging. Pericardial tamponade as the first clinical presentation of pericarditis in a young patient without an evident cause should motivate a broader etiological study.

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KEY WORDS acute pericarditis, Addison crisis, autoimmune polyangular syndrome type 2, cardiac tamponade

APPENDIX For supplemental videos, please see the online version of this paper.