

Cardiac tamponade in a patient with autoimmune polyglandular syndrome type 2

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Summary

We describe a case of a 40-year-old woman who was admitted to the intensive care unit with a rapid onset of dyspnea and orthopnea. She presented progressive weakness, weight loss and secondary amenorrhea during last year, while intermittent fever was present for the last two months. Initial biochemical evaluation showed anemia, hyponatremia and increased C-reactive protein levels. Clinical and echocardiographic evaluation revealed cardiac tamponade, which was treated with pericardiocentesis. Pleural fluid samples were negative for malignancy, tuberculosis or bacterial infection. Hormonal and serologic evaluation led to the diagnosis of autoimmune polyglandular syndrome (APS) type 2 (including primary adrenal insufficiency and autoimmune thyroiditis), possibly coexisting with systemic lupus erythematosus. After symptomatic rheumatologic treatment followed by replacement therapy with hydrocortisone and fludrocortisone, the patient fully recovered. In patients with the combination of polyserositis, cardiac tamponade and persistent hyponatremia, possible coexistence of rheumatologic and autoimmune endocrine disease, mainly adrenal insufficiency, should be considered. Early diagnosis and non-invasive treatment can be life-saving.

Learning points:

- In patients with the combination of polyserositis, cardiac tamponade and persistent hyponatremia, possible coexistence of rheumatologic and autoimmune endocrine disease, mainly adrenal insufficiency, should be considered.
- Early diagnosis and non-invasive treatment can be life-saving for these patients.
- Primary adrenal insufficiency requires lifelong replacement therapy with oral administration of 15–25 mg hydrocortisone in split doses and 50–200 µg fludrocortisone once daily.

Background

Physicians should be aware of the clinical relationship between cardiac tamponade and adrenal insufficiency, as early diagnosis and non-invasive treatment can be life-saving for these patients.

Case presentation

A 40-year-old woman was admitted to the intensive care unit of our hospital with a rapid onset of dyspnea

and orthopnea. She presented progressive weakness, weight loss (~10 kg) and secondary amenorrhea during last year, while intermittent fever was present for the last two months. No other clinical rheumatologic criteria were present at this time. Autoimmune Hashimoto thyroiditis was diagnosed five years earlier and she was on replacement therapy with levothyroxine.

On physical examination, she was febrile, tachycardic, hypotensive and slightly hyperpigmented. Initial

biochemical evaluation showed anemia (Hemoglobin: 11.3 mg/dL), hyponatremia (Sodium: 131 mEq/L) and increased C-reactive protein levels (CRP: 26.4 mg/L). Echocardiography revealed significant quantity of pericardial fluid (Fig. 1), and cardiac tamponade was diagnosed and treated with pericardiocentesis (performed with pig tail). Pleural fluid samples were sent for investigation and proved to be negative for malignancy or tuberculosis or bacterial infection. Pleural effusions were managed with repeated punctures and placement of discharge drainage pipes.

Investigation

At initial serologic evaluation for polyserositis, apart for low levels of C4 (9 ng/dL (normal range: 16–44)), all other results were negative (extractable nuclear antigens (ENA) autoantibodies, Sjögren's-syndrome-related antigen A and B autoantibodies, antinuclear autoantibodies, Cardiolipin autoantibodies, ribonucleoprotein (RNP) autoantibodies, double-stranded DNA autoantibodies, smooth muscle autoantibodies, beta 2 glycoprotein 1 autoantibodies). The patient continued to present intermittent fever, persistent but improving pleural effusion and persistent hyponatremia.

Hormonal evaluation showed a low morning cortisol with high adrenocorticotrophic hormone (ACTH) levels (Cortisol: 3.5 µg/dL, ACTH: >1400 pg/mL). Primary adrenal insufficiency was then diagnosed. Adrenal computed tomography (CT) was performed (Fig. 2) without any specific findings. Adrenal autoantibodies were positive and the diagnosis of autoimmune primary adrenal insufficiency was set. Because of the presence of autoimmune Hashimoto's thyroiditis too, the diagnosis

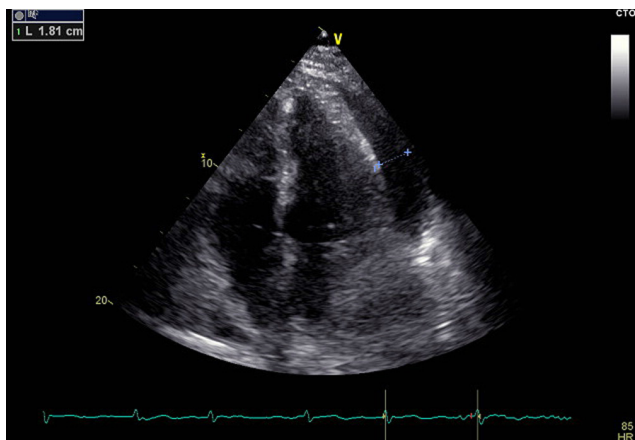


Figure 1
Echocardiography revealing significant quantity of pericardial fluid.



Figure 2
Adrenal CT.

was autoimmune polyglandular syndrome (APS) type 2. Parietal cell autoantibodies were also positive, while ovarian autoantibodies were negative.

A second serologic evaluation revealed positive ENA autoantibodies, assessed with the method of immunoblot. On clinical rheumatologic assessment malar rash, arthritis and polyserositis were present and the diagnosis of systemic lupus erythematosus (SLE) was set.

Treatment

The patient initially received three consecutive pulses with 1 g methylprednisolone switching to orally 32 mg/day. Methotrexate (10 mg/week) and hydroxychloroquine at a dose of 400 mg/day were also added. In one month, tapering of methylprednisolone was started. Patient was doing well, but when she was on 8 mg of methylprednisolone, she presented arthritis of the wrists (metacarpophalangeal and proximal interphalangeal), so methotrexate was increased to a dose of 17.5 mg/week, with gradually complete remission of arthritis. Additionally, isoniazid was administered preventively for 3 months because of a positive Mantoux.

Outcome and follow-up

After three months, the patient had complete remission of symptoms with return of menstruation. Because of regression of polyserositis, methylprednisolone was replaced with hydrocortisone at a replacement dose of 15 mg in the morning and 5 mg in the afternoon



for adrenal insufficiency. Fludrocortisone in a dose of 100 µg per day was also given.

Discussion

This is a very interesting case with coexistence of APS type 2 and SLE, leading to polyserositis and cardiac tamponade.

APS is an infrequent disorder characterized by the presence of a cluster of autoimmune endocrine as well as non-endocrine abnormalities. APS 1 is a rare monogenic disorder resulting from mutations of autoimmune regulator gene. It usually develops in infancy and consists of muco-cutaneous candidiasis along with hypoparathyroidism or Addison's disease (1). APS 2 is a complex polygenic disorder in association with the Human Leucocyte Antigen system class II alleles. It manifests during adulthood and it is more frequent in women. Addison's disease is the prevailing and stable component, in combination with autoimmune thyroid disease or diabetes mellitus type 1 (2, 3). The prevalence of autoimmune Addison's disease is estimated to be 90–140 per million and 21-hydroxylase autoantibodies are detected in 80–90% of the patients (4, 5). Other autoimmune diseases, such as gonadal failure, celiac disease, vitiligo, alopecia, pernicious anemia, myasthenia gravis, rheumatoid arthritis, thrombocytopenia purpura, Sjögren syndrome and serositis, may manifest but less frequently. Each of the APS 2 components can develop apart, from years to decades and this underpins the necessity for lifelong follow-up, as early detection can anticipate serious life-threatening events (4, 5, 6).

SLE is a chronic autoimmune disease that affects mainly women, with a prevalence of 20–150 cases per 100 000 persons. Loss of self-tolerance results in immune complexes and antibodies production that injure multiple organs including kidneys, lungs, heart, brain, skin, joints and serous membrane (7). The disease is characterized by significant heterogeneity in clinical presentation and thus certain clinical and biochemical criteria have been instituted for diagnosis. Various criteria are needed for formal diagnosis, including malar or discoid rash, photosensitivity, oral ulcers, arthritis, serositis and kidney, blood, neurologic or immunologic disorders. Clinical course can be variable with long periods of remission and acute or chronic relapse (7, 8). Mixed connective tissue disease (MCTD) could also be part of the differential diagnosis. MCTD is known to cause effusions and tamponade (9) and it is an overlap syndrome associated with ENA antibodies that incorporates selected clinical

features of SLE, systemic sclerosis (scleroderma) and polymyositis.

The cause of hyponatremia in this patient was primary adrenal insufficiency. Long-standing, persistent hyponatremia associated with weight loss, fatigue and hyperpigmentation should always raise the suspicion of primary adrenal insufficiency. Cortisol deficiency results in increased hypothalamic corticotropin-releasing hormone secretion with consequent elevated vasopressin levels, free water retention, a shift of extracellular sodium into cells and decreased delivery of filtrate to the diluting segments of the nephrons due to decreased glomerular filtration rate. Mineralocorticoid deficiency increases angiotensin II levels and free water retention with parallel sodium loss in urine. Hyponatremia is present in 80–90% of the cases with primary adrenal insufficiency, while hyperkalemia is present in less than 50% of them. It should be noted that hyperkalemia does not develop in secondary adrenal insufficiency because the adrenal zona glomerulosa remains responsive to the renin angiotensin system and aldosterone secretion is intact (4).

Acute pericardial effusion is mainly idiopathic in developed countries, with no identification of any specific cause and presumed to be of viral origin. In 10–20% of the cases, it is associated with autoimmune connective tissue systemic diseases (mostly SLE), or infectious, neoplastic and traumatic situations (10). Pericarditis is a well-recognized feature of SLE with a prevalence of 12–48% (11, 12). It is more common in children than adults with SLE and has a tendency for relapse during disease flares. It may be asymptomatic or clinically significant due to large pericardial effusion. Echocardiography confirms that the diagnosis and fluid removal by pericardiocentesis and corticosteroid administration are needed for management (13). In rare cases, cardiac tamponade occurs and sometimes it can be the presenting symptom (14), while low C4 levels have been found to be predictive of this life-threatening situation in adult patients (15). Likewise, relapsing serositis with pericardial and/or pleural involvement was documented in a series of twenty patients with APS 2 (16). Furthermore, pericarditis with cardiac tamponade and concurrent Addisonian crisis has also been reported in the literature. In ten cases that have been described till now, most of the patients despite compliance to replacement therapy, have experienced recurrent pericarditis and/or pleuritis during follow-up (16, 17, 18, 19). The underlying mechanism for pericardial effusion is possibly the autoimmune inflammation of the pericardium which leads to acute inflammatory reaction and fluid accumulation (20). In accordance, immune complexes



and antibodies were found after fluid sample evaluation (10). Pericardial fluid accumulation can result in increased pericardial pressure, compression of cardiac chambers and cardiac tamponade. In Addison's disease, the existing hypovolemia as a result of aldosterone insufficiency constitutes an aggravating factor as it significantly reduces the filling pressure of the right ventricle.

Regarding the therapeutic approach, lifelong replacement therapy with hydrocortisone and fludrocortisone is recommended. Primary adrenal insufficiency requires lifelong replacement therapy with oral administration of 15–25 mg hydrocortisone in split doses and 50–200 µg fludrocortisone once daily (21). Treatment of the coexisting rheumatologic conditions should be individualized.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Patient consent

Written informed consent has been obtained from the patient for publication of the article and accompanying images.

Author contribution statement

A V, S A P, F P, V T and A K took care of the patient. A V, S A P and P A wrote the article.

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