Atypical and severe presentation of autoimmune polyglandular syndrome type 2

Presentación grave y atípica de un síndrome autoinmune poliglandular tipo 2

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ABSTRACT

Background: Recurrent pericarditis has been described as an unusual manifestation of autoimmune polyglandular syndrome type 2 (APS 2). Case report: We describe a case of a 44-year-old woman who was admitted to hospital due to 5 pericarditis, 3 of them with cardiac tamponade, and in the etiological study of this pathology she was diagnosed with an APS 2. Conclusion: The association of serositis with APS 2 is exceptional with less than 10 cases reported in the literature. The presence of recurrent pericarditis of unknown cause should make us consider APS 2 in the differential diagnosis.

Keywords: autoimmune polyglandular syndrome, pericarditis, cardiac tamponade, recurrent polyserositis, case report.

RESUMEN

Introducción: La pericarditis recidivante se ha descrito como una manifestación poco frecuente del síndrome poliglandular autoinmune tipo 2 (APS 2). Caso clínico: Presentamos el caso de una mujer de 44 años que ingresa en el hospital debido a 5 pericarditis, 3 de ellas con taponamiento cardiaco, y en el estudio etiológico de dicha patología se diagnostica un APS 2. Conclusión: La asociación de serositis con el APS 2 es excepcional, con menos de 10 casos publicados en la literatura. La presencia de pericarditis de casusa desconocida debe hacernos considerar el APS 2 en el diagnóstico diferencial.

Palabras clave: syndrome poliglandular autoimmune, pericarditis, taponamiento cardiac, poliserositis recidivante, caso clínico

INTRODUCTION

Autoimmune Polyglandular Syndrome type 2 (APS 2) is characterized by the combination of Addison's disease (the defining component), type 1 diabetes mellitus, and/or autoimmune primary hypothyroidism. A variety of organ-specific autoimmune associated conditions, such as vitiligo, hypogonadotropic hypogonadism, autoimmune hepatitis, alopecia, pernicious anemia, seronegative arthritis, or myasthenia, have also been described[1]. Since the association of serositis with APS 2 is exceptional, we consider that the following clinical case report is of special interest.

CASE REPORT

A 44-year-old woman, with no relevant medical history, presented to the emergency room with fever of several days of evolution, associating pleuritic chest pain and bilious vomiting. She also referred frequent vomiting in the last month, and one-year history of asthenia and a 15 kg weight loss. On physical examination, she had a blood pressure of 88/66 mmHg, generalized skin hyperpigmentation and an axillary temperature of 38ºC were observed. Blood test were performed, showing 13.3 x 10^9 leucocytes, which 45% neutrophils, C-reactive protein (CRP) of 12 mg /dl, creatinine level of 3.9 mg / dl, a Glomerular Filtration Rate (MDRD4) of 13 ml / min, a sodium level of 125 mmol /L and a potassium level of 4.5 mmol / L. The electrocardiogram showed no alterations except for low voltages, and the chest X-ray evidenced an enlarged cardiac silhouette and minimal bilateral pleural effusion.

She was admitted with the diagnosis of acute pericarditis, suspicion of adrenal insufficiency and probable prerenal renal failure in the setting of volume depletion from continuous vomiting. Treatment with fluid therapy, corticosteroids, acetylsalicylic acid (ASA) and colchicine was initiated. During hospital admission, she was diagnosed with autoimmune hypothyroidism, with high serum thyroid-stimulating hormone (TSH) values (13 µU/ml) and both anti-thyroid peroxidase antibodies and anti-thyroglobulin antibodies positive. An autoimmune adrenal insufficiency was diagnosed too, with a morning serum cortisol of 2 µg/dl, a serum corticotropin (ACTH) of 352 pg/ml and positive anti-adrenal antibodies. With these data, the presumptive diagnosis of APS 2 was made, and hormone replacement therapy with levothyroxine 75 µg and hydrocortisone 30 mg daily was initiated, with favorable evolution. Serum antinuclear antibodies, cardiotrope virus serologies and Mantoux test were performed to establish the cause of pericarditis but were negative. Finally, the patient was discharged, with chronic hormone replacement therapy.

After 9 months, the patient presented again to the emergency department with a cardiac tamponade due to a new episode of acute pericarditis, with bilateral pleural effusion and hemodynamic instability, although without requiring pericardiocentesis. She clinically improved with treatment with corticosteroid, ASA and colchicine, and finally she was discharged again.

One month later, she came back to the emergency department with a new episode of cardiac tamponade due to another episode of acute pericarditis, with hemodynamic instability. A positron emission tomography-computed tomography (PET-CT) was made, with no significant findings. The determination of antibodies against several viruses (Coxsackie B, Epstein Barr, cytomegalovirus, herpes simplex 1 and 2, adenovirus, influenza), as well as against *Chlamydia pneumoniae, Borrelia burgdorferi, Brucella Spp., Salmonella Spp. and Mycoplasma pneumoniae*, was negative. Antinuclear anti-deoxyribonucleic acid (DNA) and anti-extractable nuclear antigens (ENAs) antibodies were also negative. Prednisone

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60mg daily was prescribed in a tapering regimen.
After 4 months, the patient was admitted again for cardiac tamponade, coinciding with a decrease in prednisone daily dose from 10 mg to 5 mg. Pericardiocentesis and pericardial fluid analysis were performed, obtaining exudative material with nonspecific inflammatory cytology. To complete the aetiological study of recidivant pericardial effusion a genetic study was performed to rule out autoinflammatory syndromes, with no findings.
Due to development of corticosteroid dependence, immunosuppressive therapy with azathioprine 200 mg and prednisone 7.5 mg daily was initiated. Twelve months after treatment with azathioprine the patient has not had any new pericarditis.

DISCUSSION

APS 2 is the most frequent endocrine autoimmune syndrome, although it continues to be a rare disease, approximately 1:20.000[1]. Addison's disease (AD) is present in 100% of the cases, autoimmune thyroid diseases (AITD) in 69–82% and type 1 diabetes mellitus (T1DM) in 30–52% of the patients[2]. Dual combinations are more common than the classical triad of AD, AITDs and T1DM, which appears only for 7.5% of cases, according to a meta-analysis published in 2020[3]. The mean age at the time of diagnosis is 34.7 years[3]. It has a polygenic inheritance pattern,and has been found to be strongly associated with HLA haplotypes with DR3/DQ2 and DR4/DQ8 and with DRB1*0404[4]. A series of minor clinical manifestations have been described that have also been associated with APS 2, such as: vitiligo, hypogonadotropic hypogonadism, autoimmune hepatitis, alopecia, pernicious anemia, seronegative arthritis, myasthenia, multiple sclerosis or coeliac disease.

Recurrent polyserositis has been described as an unusual manifestation of APS 2. To the best of our knowledge, less than 10 cases have been reported in the literature[5-10] (table 1). Although theoretically it is more frequent in women , half of the published cases are men. Endocrinopathy can be diagnosed before serositis, coincidental, or later; as in the present case, among the reported cases, the most common presentation is the sinchronic diagnosis of adrenal crisis together with acute pericarditis. Pericardial involvement has been found more common than pleural[5-10].

CONCLUSION

The presence of recurrent pericarditis of unknown cause should make us consider APS 2 in the differential diagnosis. In addition, we must be aware of the clinical manifestations suggestive of polyserositis in patients with APS 2. Effusive-constrictive pericarditis in the setting of autoimmune diseases and endocrine dysregulation can produce profound hemodynamic instability and cardiac tamponade. In fact, early recognition can prevent cardiac tamponade and be life-saving.

Table 1. Published cases of serositis and autoimmune polyglandular syndrome type 2

	Medical History	Clinical presentation	Physical exploration	Blood tests	Positive antibodies at diagnosis	Complications
Torfoss et al. [5], 1997, Case 1	Man, 42 years. No relevant pain medical history.	Pleuritic chest pain	Hyperpigmentation, hypotension	MSC <1µg/dl, hypertransa minasemia	TPO, AA	Recurrent pericarditis with tapering corticosteroids therapy
Torfoss et al. [5], 1997, Case 2	Man 36 years. No relevant medical history.	Pleuritic chest pain	Man 36 years. No relevant medical history.	MSC <1 µg/dl	TPO, AA	Cardiac tamponade and pericarditis
Fernández et al. [6], 2006, Case 1	Man 43 years. Graves disease	Chest pain and dyspnea	Hyperpigmentation, hypotension	MSC <1 µg/dl	AA	2 pericarditis
Alkaabi et al. [7], 2008, Case 1	Woman, 34 years. Autoinmune hypothyroidism	Chest pain and dyspnea	Hyperpigmentation, hypotension	MSC <1 µg/dl	TPO y AA	7 pericarditis
Alkaabi et al. [7], 1997, Case 2	Woman, 35 years. Autoinmune hypothyroidism	Dyspnea	Hyperpigmentation, hypotension	MSC 2 µg/dl	TPO, TGA, EA	2 hospitalizations for pleural effusion, celiac disease
Alkaabi et al. [7], 1997, Case 3	Man, 58 y.ears No relevant medical history.	Chest pain and dyspnea	Hyperpigmentation	MSC <1µg/dl	TPO	Autoinmune Hypogonadism, 1 pleuritis, 5 pericarditis
Palmer et al. [8], 2014, Case 1	Man 54 years. APS 2 (stop Prednisone 6 months before)	Chest pain	Hyperpigmentation, hypotension, weak peripheral pulses	MSC <1 µg/dl	No	Recurrent pericarditis in the same admission
Khalid et al [9], 2015, Case 1	Woman 48 years. APS 2.	Pleuritic chest pain and dyspnea	Hypotension, tachycardia	-	-	Cardiac tamponade and adrenal crisis
Mcnamara et al [10], 2017, Case 1	Man 29 years. Hypothyroidism	Chest pain	Hypotension, tachycardia	MSC <1 µg/dl	TPO y AA	Cardiac tamponade and pericarditis
Current case	Woman 44 years. No relevant medical history.	Chest pain and dyspnea	Hyperpigmentation, fever, vomiting	MSC 2 µg/dl	TPO, AA, TgAB	5 pericarditis, adrenal crisis

MSC: Morning Serum Cortisol. TPO: anti-thyroid peroxidase antibodies; TgAB: antithyroglobulin antibodies; AA: anti-adrenal antibodies; TGA: Anti-tissue transglutaminase antibodies; EA: antibodies against endomysium

LIST OF ABBREVIATIONS

APS 2: autoimmune polyglandular syndrome type 2
AD: Addison disease
AITD: Autoinmune thyroid disease
T1DM: Type 1 Diabetes mellitus
MSC: Morning serum cortisol.
TPO: anti-thyroid peroxidase antibodies;
TgAB: antithyroglobulin antibodies;
AA: anti-adrenal antibodies;
TGA: Anti-tissue transglutaminase antibodies;
EA: antibodies against endomysium

CONFLICT OF INTEREST

None

FUNDING

None

ETHICAL APPROVAL

Ethical approval is not required at our institution for publishing a case report in a medical journal.

CONSENT FOR PUBLICATION

Informed consent was obtained from the patients to publish this case.

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