CASE REPORT

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Severe Pericardial Effusion Due to Autoimmune Hypothyroidism With Levothyroxine Withdrawal and Systemic Lupus Erythematosus

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Abstract

The presence of autoantibodies is a common link between autoimmune hypothyroidism (AH) and Systemic Lupus Erythematosus (SLE). The coexistence of AH (Hashimoto's Thyroiditis) and SLE is common; however, massive pericardial effusion (PEEF) with signs of tamponade is extremely rare and only a few cases have been reported in literature. We present a case of a 54-year-old female who came in with progressive dyspnea who was found out to have massive PEEF from overt AH and concurrent SLE, which was successfully managed medically. This gave us valuable insight that massive pericardial effusion occurring in overt hypothyroidism may be secondarily caused by other co-existing disease entities such as SLE. The importance of the correct diagnosis cannot be overemphasized, as this largely contributed to the successful management of this case.

Key words: pericardial effusion, pericardial tamponade, autoimmune hypothyroidism, systemic lupus erythematosus, case report

INTRODUCTION

Autoimmunity is a common link between autoimmune hypothyroidism (AH) and Systemic Lupus Erythematosus (SLE) and appears to explain the increase in prevalence of one condition in the presence of the other. Pericardial effusion as a manifestation of each disease is common, but massive pericardial effusion with cardiac tamponade is rare. SLE pericardial effusion has an incidence of 1-2.5%,[1] while there are only about 20 reported cases of AH causing cardiac tamponade in the literature.[2] Pericardial effusion caused by hypothyroidism due to AH (also known as Hashimoto's thyroiditis) can lead to massive pericardial effusion if left untreated. It can be more difficult and challenging to treat. The management of massive pericardial effusion ranges from medical management to life saving surgical procedures. The usual indication for pericardiocentesis, pericardiostomy or creation of a pericardial window is the presence of cardiac tamponade with signs of hemodynamic compromise.[3] Here, we present a rare case of massive pericardial effusion with signs of tamponade caused by both AH and SLE which was successfully managed medically (Figure 1).

CASE

A 54-year-old, hypertensive, Filipino female, non-smoker, was admitted due to difficulty of breathing. Three years prior to admission, she developed hoarseness, cold intolerance and easy fatigability. She consulted an ENT and was assessed with left vocal cord paralysis. No thyroid enlargement was noted both on physical examination and on ultrasound, but thyroid function test showed elevated TSH and levothyroxine 50 mcg 1 tablet once a day was started. Her symptoms improved but she was lost to follow up.

One year prior to admission, she stopped taking levothyroxine because she was in denial about her illness and did not understand the need for levothyroxine maintenance therapy. She then started to have easy fatigability and cold intolerance. Six months prior to admission, she developed increased sleepiness, slowed responses, forgetfulness, blurring of vision, dry skin, weight gain, myalgia and knee arthralgia. No rashes, alopecia and photosensitivity were noted. A week prior to admission, patient had constipation, two pillow orthopnea, and exertional dyspnea when climbing one

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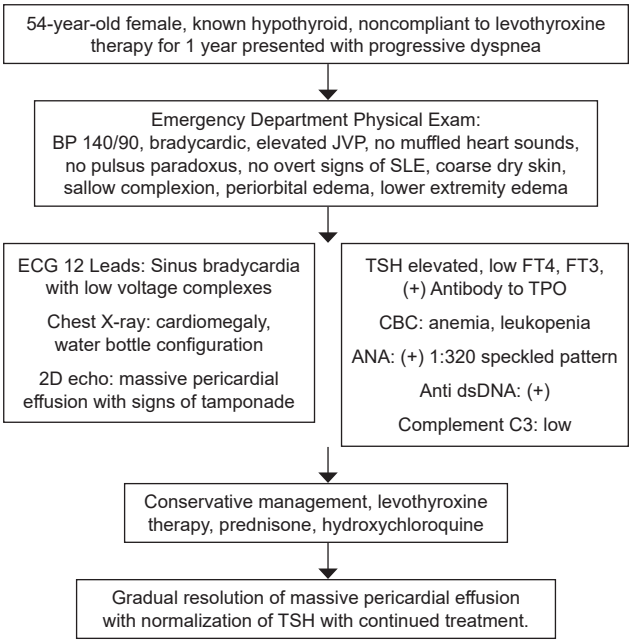


Figure 1. Timeline of pertinent information in the care of this patient.

flight of stairs. A day prior to admission, she experienced difficulty of breathing and consulted at a local hospital. Electrocardiogram revealed sinus bradycardia and 2D-echocardiography showed a large pericardial effusion with signs of tamponade. She was given furosemide 40 mg intravenously and was advised to undergo pericardiostomy. She was referred to our institution and was admitted under the Cardiology service, and co-managed by the Endocrinology service. Pertinent family history includes presence of goiter in the maternal side and sibling (sister).

On physical examination, she was conscious, coherent, in distress. Her blood pressure was 140/90 mm Hg, bradycardic at 57 beats per minute with a regular rate, tachypneic at 22 cycles per minute, afebrile and with body mass index of 28 kg/m^2. She had cold, coarse, dry skin, sallow complexion, no moon facies, no facial plethora, no rashes, no pigmentation. Examination of the eyes revealed pink palpebral conjunctivae, anicteric sclerae, periorbital edema, lid lag, retraction with Queen Anne's sign (thinning of the lateral third of eyebrows) but no exophthalmos. She also had dry lips, macroglossia, distended neck veins, elevated JVP at 5 cm H20 at 30°C. Physical examination of the thyroid showed diffusely enlarged, firm, 4 x 2 x 1 cm right and left thyroid lobes but with no thyroid bruit. She had normal breath sounds with adynamic precordium, apex beat at 5th left intercostal space, no heaves, lifts or thrills. Heart sounds were not muffled. She had full pulses on all extremities with non-pitting edema grade 2 on both lower extremities. No pulsus paradoxus was noted. Her deep tendon reflexes were blunted on all extremities. Neurological examination revealed delayed responses to questions and delayed short term recall, however, long term memory was intact.

At the Emergency Department, 12L ECG showed sinus bradycardia, low voltage limb leads and non-specific ST-T wave changes (Figure 2A). Chest radiograph showed an enlarged heart with water bottle configuration (Figure 2B). There were no pulmonary infiltrates. Thyroid panel was consistent with primary AH: elevated TSH = 95.66 uIU/mL (NV = 0.35-4.94), low FT3 = <1 pg/mL (NV = 1.71-3.71), low FT4 = <0.4 ng/dL (NV = 0.7-1.48) and elevated anti-TPO = 770.9 IU/mL (NV = <9.0). Ultrasound of the thyroid showed non-uniform echo pattern without thyroid enlargement. A 2-dimensional echocardiogram confirmed the presence of massive PEEF with doppler evidence of tamponade (Figure 3). The patient was referred to a cardiothoracic surgeon for possible pericardiostomy.

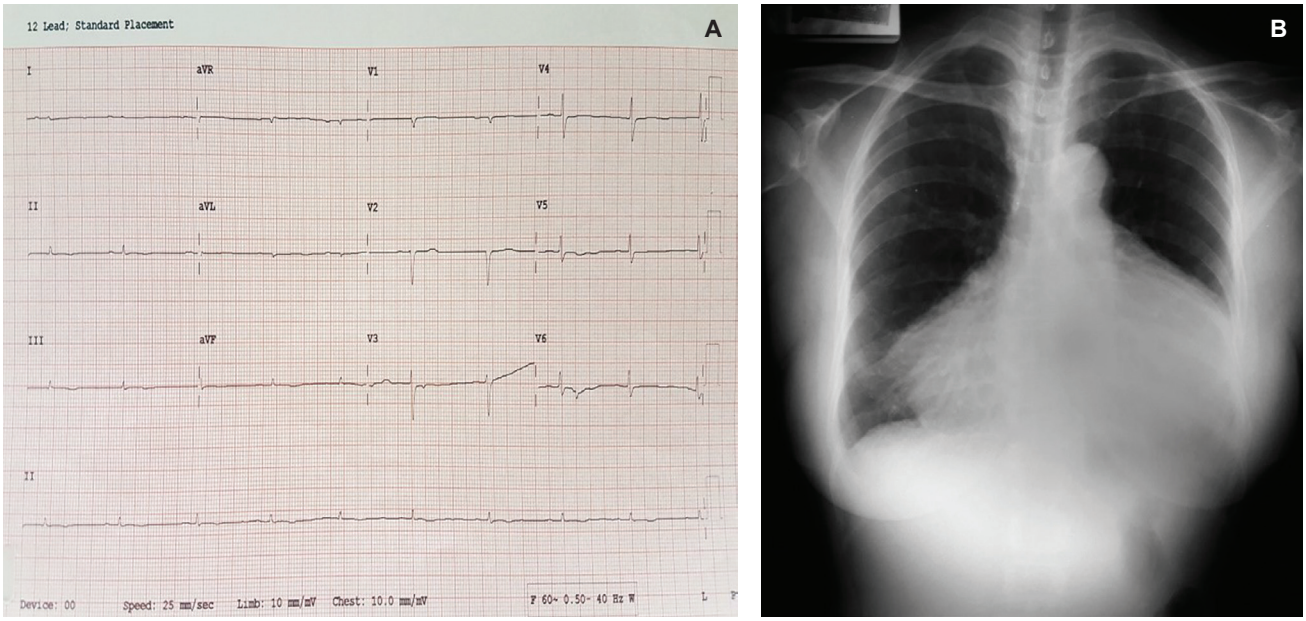
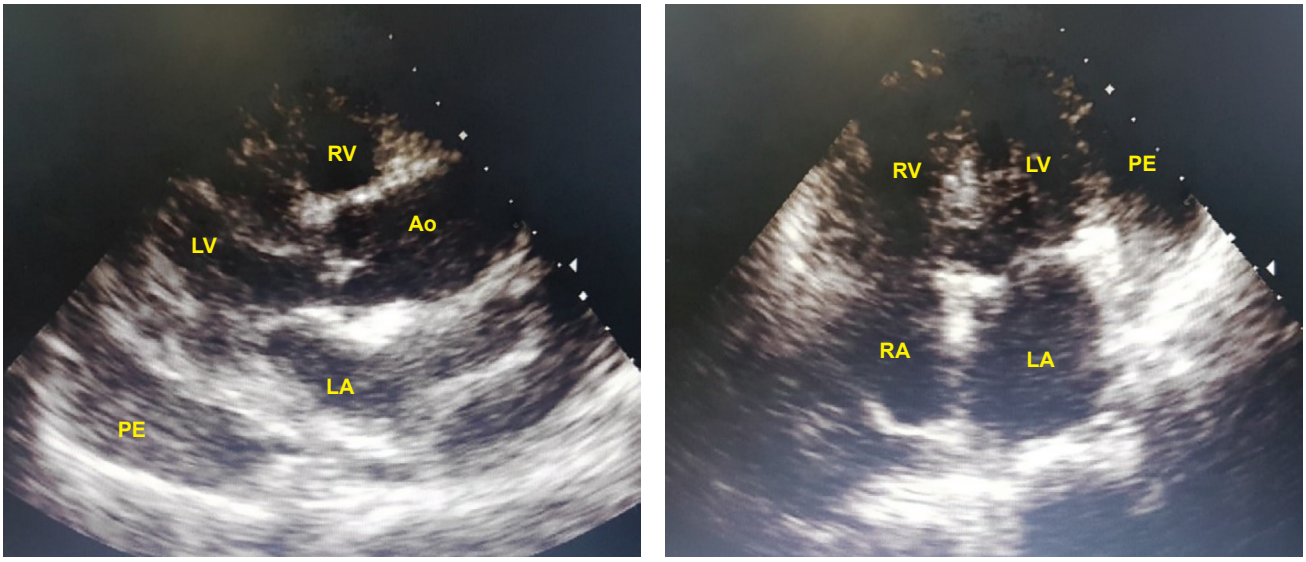


Figure 2. (A) ECG showing sinus bradycardia and low voltage limb leads. **(B)** Chest X-ray showing water bottle configuration.



RV, right ventricle; LV, left ventricle; LA, left atrium; LV, left ventricle; Ao, Aorta; PE, pericardial effusion

Figure 3. 2D echocardiogram with Doppler studies done on admission showed an echo free space posterior to the left ventricle, anterior to the right ventricle and superior to the right atrium with widest diameter of 4.0 cm suggestive of large pericardial effusion. There was an exaggerated respiratory variation of 19.6% at peak mitral inflow and 37.8% at peak tricuspid inflow suggestive of Doppler evidence of tamponade.

A multidisciplinary meeting was held to ensure the best management. As the patient was assessed as having high risk for surgical intervention due to the severe hypothyroidism, the team consensus was to maximize medical management. Since BP continued to be stable, conservative management was continued and patient was monitored closely for worsening cardiac condition.

Patient was started on levothyroxine therapy by the Endocrine service, initially at 50 mcg daily and slowly titrated up to 100 mcg daily. Other laboratory findings were anemia with Hgb of 92 g/L (NV = 11-15), leukopenia of 2.7 x10^9/L (NV = 4-10), albuminuria (+1) and elevated creatinine level of 1.21 mg/dL (NV = 0.51-0.91). With these laboratory results, SLE as a secondary cause of PEEF was entertained, she was referred to rheumatology service and subsequent work up was done. Her ANA was positive at 1:320 dilution with speckled pattern, likewise, her anti-dsDNA was positive at 516.25 IU/ml (NV = <0-200). Her Complement factor 3 (C3) level was low at 0.89 g/L (NV = 0.9-1.8). Summing up both clinical and laboratory results, patient fulfilled six criteria in the Systemic Lupus International Collaborating Clinics (SLICC) criteria for SLE. She was then started on prednisone 30 mg once daily and hydroxychloroquine 200 mg once daily.

She was closely monitored. Her vital signs remained stable during the course of hospitalization. Her dyspnea was relieved by diuretics, on top of the levothyroxine and prednisone therapy. Repeat 2D echocardiography after several days of medical management showed a decrease in the pericardial effusion (Figure 4) and patient was subsequently discharged. Outpatient followup showed further resolution of effusion (Figure 5). After a month on levothyroxine 100 mcg daily, her thyroid function test also normalized with TSH of 1.6 uIU/mL (NV = 0.35-4.94), FT4 of 1.7 ng/dL (NV = 0.7-1.48) and FT3 of 2.9 pg/mL (NV = 1.71-3.71). Repeat 2D echocardiography done 9 after months showed further decrease in the pericardial effusion now measuring 0.7 cm widest diameter. Patient continued to take levothyroxine, prednisone and hydroxychloroquine with frequent follow up with cardiology, rheumatology and endocrinology services. A summary of the biochemical parameters and echocardiographic findings from illness to recovery of this patient is shown (Table 1).

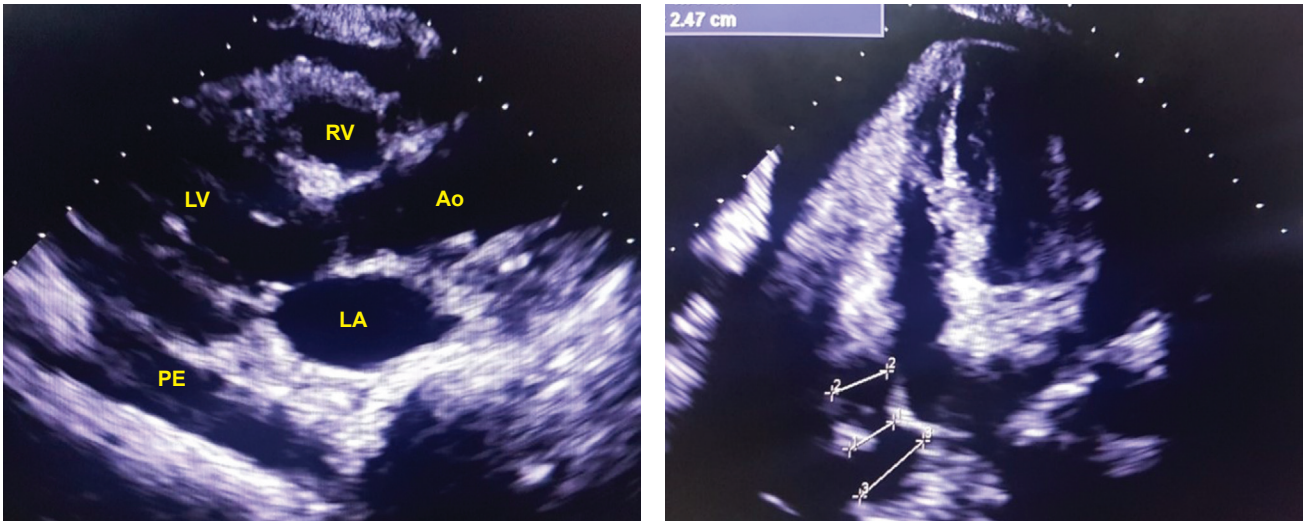
Table 1. Biochemical parameters and echocardiographic findings from illness to recovery

Day	0	4	16	30	270
Biochemical Parameters					
Serum TSH (uIU/mL) NV: 0.35-4.94	95.66			1.6	
Serum FT4 (ng/dL) NV: 0.7-1.48	<0.4			1.7	
Serum FT3 (pg/mL) NV: 1.71-3.71	<1			2.9	
Echocardiographic Findings					
Pericardial Effusion widest diameter on 2D echo (cm)	4	2.1	1.49		0.7
Signs of Tamponade	+	+	+		-

TSH, Thyroid Stimulating Hormone; FT4, free thyroxine; FT3, free triiodothyronine; NV, normal value; 2D echo, 2 dimensional echocardiogram

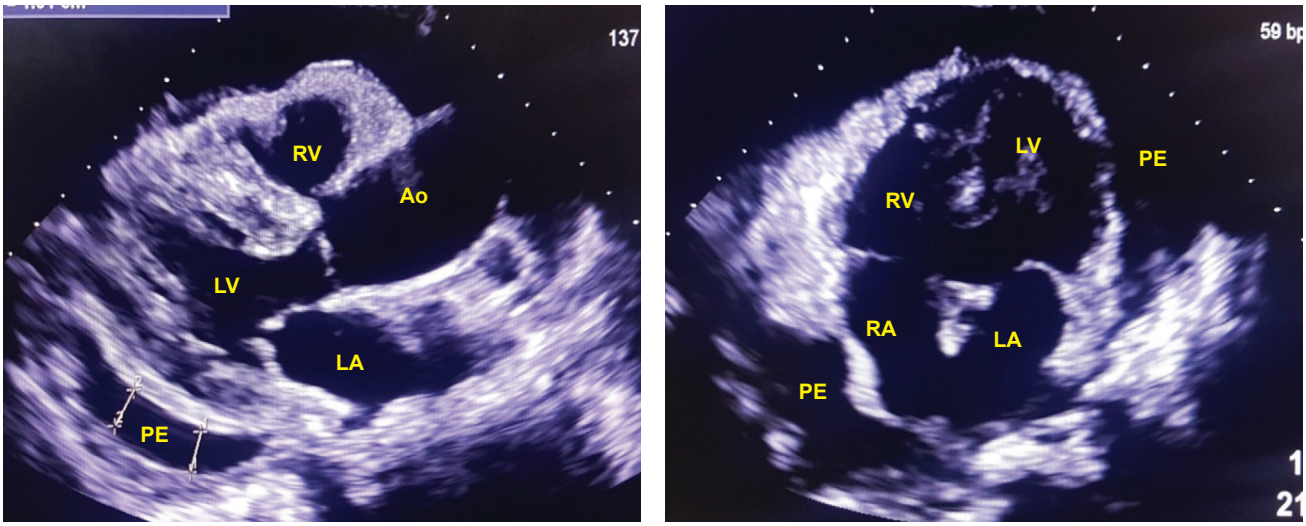
DISCUSSION

Autoimmunity is a common ground for both autoimmune hypothyroidism (AH) and Systemic Lupus Erythematosus (SLE) and appears to explain the increase in prevalence of one condition in the presence of the other. The prevalence of AH reported in the literature among patient with SLE is between 3.9%-21.4%[4] while SLE is observed to



RV, right ventricle; LV, left ventricle; LA, left atrium; LV, left ventricle; Ao, Aorta; PE, pericardial effusion

Figure 4. Follow up plain 2D echocardiogram done 4 days later showed a decrease in amount of pericardial effusion with widest diameter now measuring 2.1 cm from previous 4.0 cm, with noted RA collapse during systole and RV collapse during diastole suggestive of echocardiographic evidence of tamponade.



RV, right ventricle; LV, left ventricle; LA, left atrium; LV, left ventricle; Ao, Aorta; PE, pericardial effusion

Figure 5. 2D echocardiogram with Doppler studies done 16 days after the first study showed a further decrease in amount of pericardial effusion with widest diameter now measuring 1.49 cm from previous 2.1 cm, consistent with moderate pericardial effusion, with echocardiographic evidence of tamponade.

occur in 5.9% of patients with AH.[5] Around one fifth to one half of patients with SLE have positive thyroid autoantibodies[4] while 16% of patients with autoimmune hypothyroidism may present with positive Anti-dsDNA.[5] A potential genetic connection between these two entities is said to involve the human leukocyte antigen (HLA) DR 3,4,5 of the major histocompatibility complex proteins but a complete explanation is still unknown.[6]

Our case presented with signs and symptoms consistent with hypothyroidism and with history of non-compliance to levothyroxine therapy, so autoimmune hypothyroidism as the cause of the effusion was one of the initial considerations. Pericardial effusion in mild AH occurs in 3-6% of cases but can be as high as 30%-80% in severe cases.[7] Although pericardial effusion is a common manifestation, massive PEEF with tamponade is rare. There are roughly 20 cases reported in the literature.[2]

The underlying mechanism of pericardial effusion in AH is said to be caused by the accumulation of glycosaminoglycans and increase capillary permeability leading to protein leakage to interstitial space resulting to water retention causing edema and serous effusion.[8] It is rare to develop massive pericardial effusion in AH, as pericardial fluid accumulates at a slow rate, allowing the pericardial sac to compensate for the increase in volume and intrapericardial pressure.[9] In cases of massive pericardial effusion in AH, other entities should be ruled out including a possible infection, malignancy, systemic diseases and

other metabolic causes. For this case, there were no significant clinical clues that would point to an infection, malignancy, uremia but some findings pointed to a possible concurrent SLE, thus this was further worked up.

Other cardiovascular changes in hypothyroidism would include decrease in cardiac output caused by a decrease in stroke volume and heart rate reflecting the loss of inotropic and chronotropic effects of thyroid hormones[10] which could explain the patient's bradycardia even in the presence of large effusion. It should be noted that bradycardia with low voltage complexes is more consistent with hypothyroidism as opposed to the tachycardia encountered in other conditions.[10] This atypical ECG finding can suggest or enhance the suspicion of hypothyroidism in patients with pericardial effusion.

More than 50% of patients with SLE present with pericardial effusion on echocardiography.[11] However, massive pericardial effusion as an initial presentation is rare and occurs only in 1-2.5% of cases.[1] The underlying mechanism is an immune-mediated inflammation which could be in the form of pericarditis or vasculitis and seen in active SLE.[12] This is more associated with lupus nephritis, Libman-sacks endocarditis and myocardial dysfunction.[13] Our patient manifested signs of lupus nephritis. The rarity of cardiac tamponade in SLE seems to be explained by the same mechanism in AH. Our patient fulfilled six of the Systemic Lupus International Collaborating Clinics criteria (clinical criteria: leukopenia, renal manifestations, serositis; laboratory criteria: (+) ANA speckled pattern, (+) anti-dsDNA and low complement level) and was diagnosed with SLE.

Levothyroxine therapy is the cornerstone for the treatment of pericardial effusion in AH. Different dosing regimens were observed in the different cases reported.[9-18] Average dose was between 50 mcg to 125 mcg daily and delivered through intravenous or oral route. Some started at a small dose with gradual up-titration, while others started with full doses. All of the reports showed resolution of effusion after a few months of levothyroxine therapy. In conjunction with levothyroxine therapy, most of the cases performed surgery for signs of cardiac tamponade (pericardiocentesis or pericardial window) while a few cases showed resolution with only medical management.[9-18] Our case was started with lower levothyroxine dose at 50 mcg considering the patient's age. The dose was gradually titrated up to 100 mcg daily which was well tolerated.

High dose steroid and anti-inflammatory agents are given for SLE pericarditis and pericardial effusion. For life or organ threatening conditions, the administration of IV pulse steroid is even indicated.[19] Although rare, pericardiocentesis is also indicated for cases of massive pericardial effusion with tamponade. Our case was started on prednisone 30 mg once a day and slowly tapered down for months with gradual resolution of pericardial effusion.

We found one similar case where massive pericardial effusion in tamponade was complicated with both AH and SLE. A case report by Chaudhari et al., entitled "SLE or hypothyroidism: Who can triumph in cardiac tamponade?" described a 36-year-old Hispanic female with a history of SLE in remission who presented with progressive dyspnea and massive pericardial effusion in tamponade and subsequently diagnosed with SLE in activity with concommitant autoimmune hypothyroidism. The patient was treated with urgent pericardiocentesis and was given levothyroxine and steroid therapy which resolved the condition.[20] Another case described both AH and SLE causing instead a massive peritoneal effusion (ascites).[21] This case was diagnosed first with AH and later fulfilled criteria for SLE. Patient was treated with levothyroxine replacement and steroid therapy with noted improvement of her condition.

Surgery in pericardial effusion is not indicated unless there is hemodynamic compromise. Pericardiocentesis offers both diagnostic and therapeutic advantages. SLE effusion is usually exudative and filled with fibrinous products, active and/or chronic infiltrates, while AH effusion is more transudative. It effects drainage of the effusion, termination of tamponade and relief of symptoms. This was not done in this case, as the patient's blood pressure remained stable, even in the presence of tamponade physiology on echocardiogram. This may be considered as one of the limitations as we were not able to establish the definite cause of the effusion and remains a diagnostic uncertainty. However, as medical management with levothyroxine and steroid proved to be effective for this case, as manifested by resolution of the large pericardial effusion, it may be concluded that management was appropriate, and that pursuing diagnostic certainty would be a purely academic exercise.

CONCLUSION

In conclusion, this was a rare case of a combination of AH and SLE causing massive pericardial effusion with signs of tamponade which was managed medically. This gave us valuable insight that massive pericardial effusion occurring in overt hypothyroidism may be secondarily caused by other co-existing disease entities such as SLE. It is prudent to always keep the possibility in your differential diagnosis, as the correct consideration largely contributed to the successful management of this case.

Ethical Consideration
Patient consent was obtained prior to submission of the manuscript.

Statement of Authorship
The authors certified fulfillment of ICMJE authorship criteria.

Author Contribution Statement
SI, KAT, MFCG, FRG, JUH conceived the study; developed the methodology, applied statistical techniques; provided study materials; reviewed and edited the manuscript; managed the research activity planning. SI, MFCG, FRG, JUH validated the data;

SI and KAT conducted the research, JUH supervised the research activity planning. SI programmed the software; curated the data and acquired financial support for the study.

Author Disclosure
The authors declared no conflict of interest.

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