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Pericardial Effusion Complicating Refractory Hypothyroidism Secondary to Autoimmune Atrophic Gastritis: A Case Report

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Abstract Hypothyroidism is characterized by a broad clinical spectrum ranging from asymptomatic or subclinical hypothyroidism to overt myxedema and multisystem failure. Pericardial effusion occurs frequently in myxedema but is rare in other stages of hypothyroidism because of the timeliness in which hypothyroidism is nowadays detected and treated. The author reports a case of progressively worsening pericardial effusion from refractory hypothyroidism secondary to autoimmune atrophic gastritis. The approach to managing pericardial effusion complicating refractory hypothyroidism is discussed.

Keywords: *pericardial effusion, hypothyroidism, refractory hypothyroidism, autoimmune atrophic gastritis*

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1. Introduction

Hypothyroidism is characterized by a broad clinical spectrum ranging from asymptomatic or subclinical hypothyroidism to overt myxedema and multisystem failure. [1] Hypothyroid patients receive supplemental thyroid hormone (levothyroxine) to achieve physiological thyroxine (T4) serum level. [2] The mean daily treatment dosage of supplemental levothyroxine is 1.6 mcg/kg. [2] Hypothyroidism is considered treatment refractory when there is biochemical or clinical evidence of hypothyroidism, despite increasing dosage of levothyroxine beyond 1.9 mcg/kg daily. [3] Common causes for refractory hypothyroidism include poor adherence to levothyroxine, and interactions between thyroxine and medication or food. [4] The author reports a case of progressively worsening pericardial effusion from refractory hypothyroidism secondary to autoimmune atrophic gastritis. Autoimmune atrophic gastritis is an immune mediated chronic progressive inflammation of the gastric body and fundus leading to progressive destruction of parietal cells, leading to hypo-achlorhydria and vitamin B12 deficiency. [5,6] Autoimmune gastritis is diagnosed by the demonstration of autoantibodies against intrinsic factor and parietal cells and by its characteristic histopathological features. [5] To the author's knowledge, this is the first case report of pericardial effusion complicating refractory hypothyroidism secondary to autoimmune atrophic gastritis.

2. Case Report

49-year-old male with underlying hypertension, type 2 diabetes mellitus, hypothyroidism, gout, and history of right sided deep venous thrombosis presents with shortness of breath associated with chills, fatigue, headache, chest tightness, non-productive cough, and petechia on bilateral lower extremities.

In the emergency room, blood pressure was 103/66mmHg, heart rate was 86, respiratory rate was 18, and temperature was 98.3F. Physical examination revealed a morbidly obese patient that was alert and oriented to time, place and person with no other remarkable findings apart from 1+ non-pitting bilateral lower extremity edema.

Patient had pancytopenia with hemoglobin of 6.9g /dl, white blood cell count of 1,400/ml, and platelet of 75,000/ml, with mean corpuscular volume of 105. Vitamin B12 was low (24) while folate level was normal. The thyroid stimulating hormone (TSH) level was elevated (96), T4 level was low (0.51) and Free T3 (1.0) was low despite patient reporting that he has been compliant with his levothyroxine therapy. Anti- thyroid peroxidase (TPO) was elevated at 244. Urinalysis was normal and renal parameters showed acute kidney injury. HIV screening test was non-reactive, and Hepatitis B surface antigen was negative. Rheumatoid Factor and antinuclear antibody (ANA) were negative. Anti-endomysial antibody and Anti-transglutaminase IgA were negative which ruled out celiac disease. Flow

cytometry identified no abnormal B-cell, T-cell or myeloid cell population. Anti-intrinsic factor was elevated at 46.1, and anti-parietal cell was elevated at 51.5 which was consistent with autoimmune atrophic gastritis.

CT chest [Figure 1 and Figure 2] showed moderate pericardial effusion. Echocardiogram showed a left ventricular ejection fraction of 60-65% and moderate to severe pericardial effusion with no right atrial or right ventricular collapse seen. An echocardiogram done five months earlier only showed trivial pericardial effusion. Because patient had thrombocytopenia which makes pericardiocentesis high risk especially considering no signs of any tamponade, conservative management with thyroid replacement was pursued.

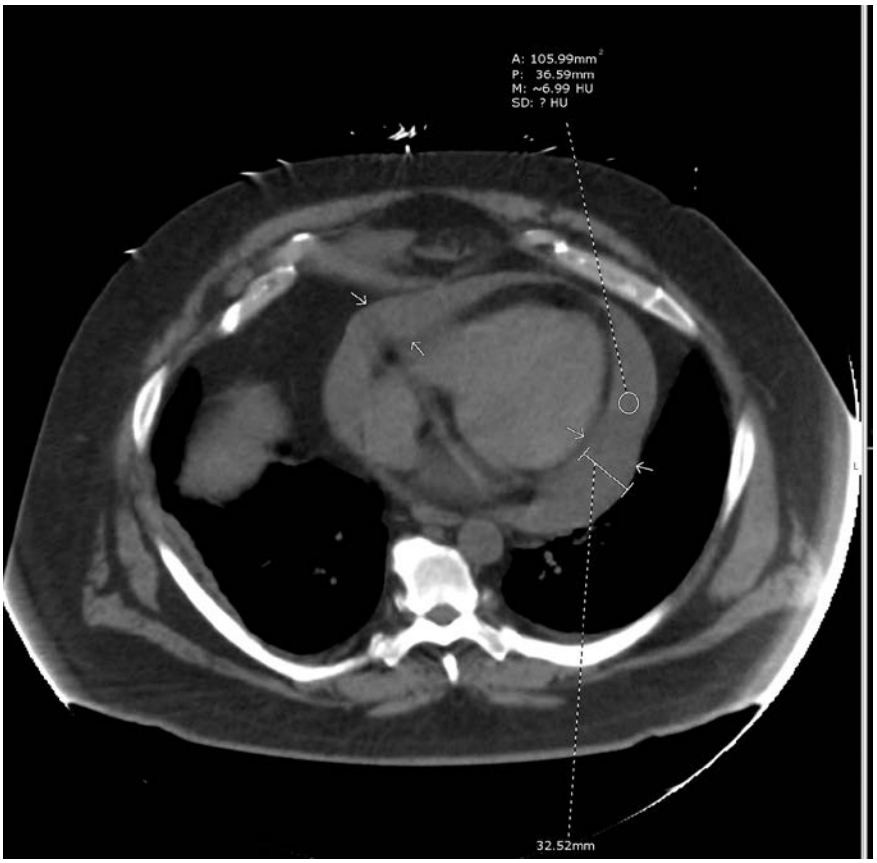

Figure 1. CT chest showing pericardial effusion (transverse plane) (Arrows show pericardial effusion)

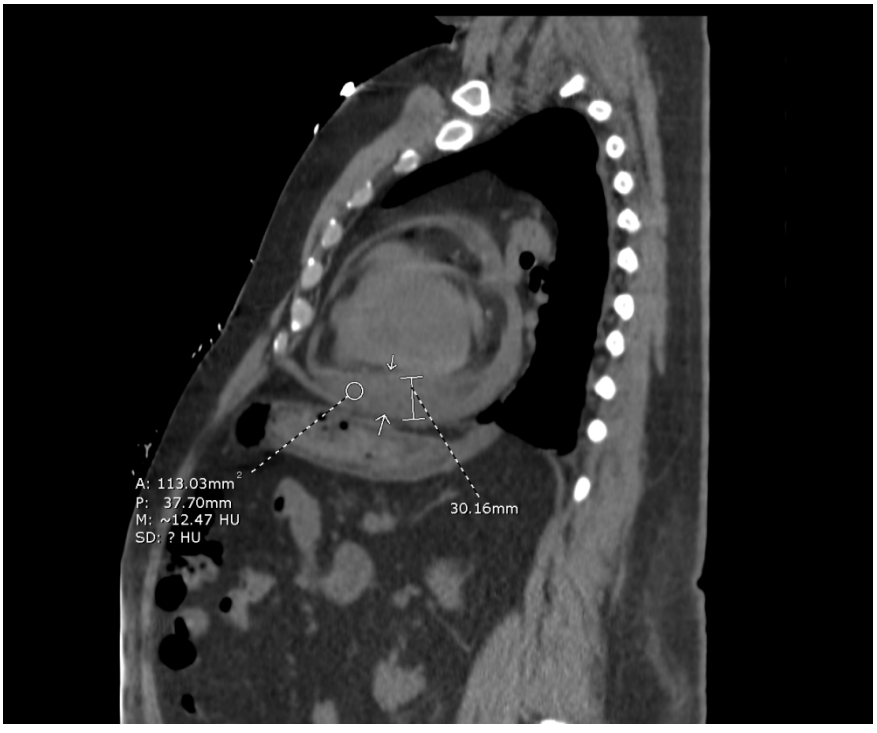

Figure 2. CT chest showing pericardial effusion (sagittal plane) (Arrows show pericardial effusion)

Patient was started on IV levothyroxine and IM Vit B-12. Patient also received three units of packed RBC during his hospital stay. Prior to discharge, patient hemoglobin was 10.5g/dl, WBC was 4,700, platelet was 251,000, TSH was 33 and T4 had normalized. Patient was discharged to follow up with his endocrinologist and cardiologist outpatient.

3. Discussion

The occurrence of pericardial effusion in hypothyroidism has ranged from 3% to 80% in previous studies depending on the duration and severity of the hypothyroidism of the patients in the study, with higher rates in severe and prolonged diseases. [7] Pericardial effusion occur frequently in myxedema, an advanced severe hypothyroidism, but rare in other stages of hypothyroidism because of the timeliness in which hypothyroidism is nowadays detected and treated, especially in high income countries. [7] The pathogenesis of pericardial effusion, like other serous effusions in hypothyroidism, is not fully understood but is likely due to increased capillary permeability, decreased lymphatic drainage of interstitial fluid proteins and derangements in metabolism. [8,9,10]

Cardiac tamponade in hypothyroidism is rare because of the slow accumulation of fluid and the distensibility of the pericardium. [10] While cardiac tamponade will require drainage of the cardiac tamponade using pericardiocentesis or a pericardial window, every hypothyroid patient with pericardial effusion will require the treatment of the hypothyroidism. Pericardial effusion in hypothyroid patient typically resolve with 2-12 months of levothyroxine treatment. [10] For our patient, the pericardial effusion increased over time from trivial to moderate/severe pericardial effusion over a period of five months despite the patient being on levothyroxine treatment. This was because of the refractory hypothyroidism as a result of levothyroxine malabsorption secondary to autoimmune atrophic gastritis.

Hypothyroidism is considered refractory when there is biochemical or clinical evidence of hypothyroidism (serum level of TSH above the upper target level, usually 4.5 mU/L following a six-week interval after the dosage was last increased), despite increasing dosage of levothyroxine beyond 1.9 mcg/kg daily. [3] Apart from autoimmune atrophic gastritis, other causes of refractory hypothyroidism include non-compliance with medication, concurrent use of medication that interfere with levothyroxine absorption, pregnancy and conditions that reduce the absorption of levothyroxine such as celiac disease and helicobacter pylori atrophic gastritis. [3,11] The systematic approach to managing persistently elevated TSH in the presence of levothyroid therapy as outlined by Morris, 2009 and Centanni et al., 2017 include: [3,12]

1. Confirm the diagnosis by measuring both the TSH and the thyroid level hormones (T4 and T3).

2. Ask patient about compliance as medication non-compliance is the most common reason for refractory hypothyroidism. Due to the long half-life of levothyroxine, missing a day could have an effect on thyroid level and TSH that may last for several days.

3. Check patient's medication tablets and bottles to confirm the dose of medication that patient is taking and ensure that there are no pharmacist errors, resulting in tablets inside the bottle that differ from those reported on the label.

4. Review the thyroxine ingestion history to ensure that patient is not taking thyroxine with food or other medications that will interfere with thyroxine absorption. Ideally, thyroxine should be taken on an empty stomach 30-60 minutes before food or other medications.

5. Check for malabsorption syndromes such as celiac disease, short bowel and atrophic gastritis, among others, that will reduce the quantity of thyroxine absorbed.

6. Consider conditions that lead to increased excretion or increased metabolism of thyroid hormone such as nephrotic syndrome, pregnancy and the concurrent use of medications like phenytoin, carbamazepine and rifampin.

7. Treat or correct the identified condition. In many patients, treatment involves increasing the patients' oral levothyroxine dose until the target TSH levels are reached. Softgel and liquid formulations of levothyroxine which are less susceptible to intolerance and malabsorption may be tried. Medication non-compliance can be treated by increasing the size of the tablet or giving the total weekly dose of thyroxine as a once weekly oral dose if lack of compliance persists. Identified cause of malabsorption should be treated and interfering drugs removed when possible.

In summary, the author presents a case of pericardial effusion complicating refractory hypothyroidism secondary to autoimmune atrophic gastritis. The approach to managing refractory hypothyroidism is to find and treat the cause of refractory hypothyroidism. In many patients, treatment involves escalating levothyroxine dose until target TSH is reached. [3,12] Pericardial effusion typically resolves within 2-12 months of levothyroxine treatment while cardiac tamponade will require drainage of the cardiac tamponade using pericardiocentesis or a pericardial window in addition to levothyroxine treatment. [10]

Conflict of Interest

The authors declare that there is no conflict of interest.

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