Cardiac tamponade under thyroid hormone replacement therapy in a patient with empty sella syndrome

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Pericardial effusion is a common manifestation of hypothyroidism, observed in approximately 1/3 of patients without replacement therapy.[1] In hypopituitarism, pericardial effusion is usually due to hypothyroidism, however, cardiac tamponade is a very rare complication of both hypothyroidism and adrenal insufficiency.[2-4] Herein, we report a case of hypopituitarism with myxedema and pericardial effusion, in which cardiac tamponade developed under thyroid hormone replacement therapy. After 11 days of replacement therapy, cardiac tamponade was unexpected, and concomitant adrenal insufficiency was thought to be the cause. Interestingly, adrenocortical hormones were being closely monitored and cardiac tamponade was the first manifestation of adrenal failure.

A 62-year-old male, with no history of previous disease was admitted to the hospital with a symptom of slow movements, malaise, and edema in extremities. His vital signs were normal. On physical examination, coarse hair, dry skin, nonpitting edema in lower extremities, and distant heart sounds were prominent. The thyroid gland was firm but not enlarged. Electrocardiogram showed low voltage in all derivations and chest x-ray (CXR) revealed cardiomegaly. The finding of the laboratory examinations were free: T3 (fT3 0.1 pg/ml [1.5-4.7 pg/ml]), and T4 (fT4 0.4 ng/dl [0.7-1.9 ng/dl]) were very low; surprisingly, thyroid stimulating hormone (TSH) was increased mildly (24.2 IU/ml [0.35-5 IU/ml]). Anti-M [4000 IU/ml (0-115)] and anti-thyroid peroxidase [2329 IU/ml (0-34)] antibody levels were positive in high titers. Cortisol levels were measured by chemiluminescence assay method using bio-Diagnostic Products Corporation (Llanderis, UK), Immulite 2000 immunoassay analyzer. The adrenocorticotropic hormone (ACTH) level was 29.36 pg/ml (6-57 pg/ml) and cortisol level was normal. Follicle stimulating hormone, luteinizing hormone, and testosterone levels were also low. Oral T3 and T4 and intramuscular testosterone replacement treatments were started immediately. Simultaneous echocardiography showed a massive pericardial effusion without the signs of cardiac tamponade (**Figure 1**). The tumor markers were within normal levels, antiviral IgM antibodies were negative, and rheumatological markers were normal. Purified protein derivative test was negative. He responded well to the therapy and on serial echocardiographic examinations, pericardial effusion was regressed.

Meanwhile, due to the gonadal hormonal deficiency with the suspicion of hypopituitarism, hypophyseal magnetic resonance imaging was performed and an empty sella syndrome was diagnosed. Autoantibodies to the thyroid gland were positive in high titers indicating Hashimoto's disease. Therefore, he had both hypopituitarism and primary hypothyroidism. The cortisol levels were normal at the fourth and eighth day of treatment [19 and 24 mcg/dl (6-24 mcg/dl) consecutively)]. On the thirteenth day of replacement therapy, suddenly hypotension (70/40 mm Hg) and tachycardia (107 beats/minute) developed. On physical examination, mild jugular venous distension and pulsus paradoxus were found. The diagnosis of cardiac tamponade was confirmed with echocardiography, which showed an increase in pericardial fluid with an early diastolic collapse of right ventricle, and pericardiocentesis was performed immediately. Approximately 820 ml of a clear yellow fluid with a protein content of 5.2 gr/dl was drained. Approximately 500 cc of residual fluid was found at the control echocardiography in the same day. After the procedure, his blood pressure and heart rate returned to normal levels. Due to cardiac tamponade, the hormonal status was re-analyzed. Free T3 (1.87 pg/ml [1.57-4.71]), free T4 (0.92 pg/ml [0.7-1.9]), and TSH levels (4.5 IU/ml [0.5-5]) were normal; however, cortisol (1.17 mcg/dl [6-24]), and ACTH (4.11 pg/ml [6-57]) levels were found to

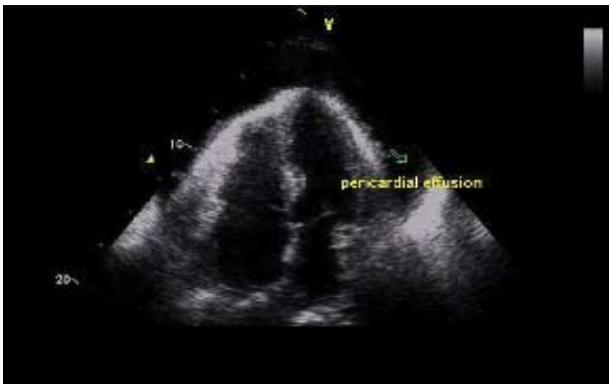

Figure 1 - Echocardiogram showing massive pericardial effusion surrounding the anterior and lateral wall.

be low. Steroid replacement therapy was started immediately. During hospitalization, he had no fever and infections, his white blood cell count and C-reactive protein levels were normal. The bacterial and tuberculosis cultures of the pericardial fluid were negative. Cytologic examination was normal. One month later, under thyroxine and cortisol replacement therapy, he was asymptomatic with no sign of pericardial effusion confirmed with CXR and echocardiography.

Pericardial effusion is a common manifestation of hypothyroidism, however, cardiac tamponade rarely occurs during this disease. Few case reports were found in the literature demonstrating cardiac tamponade due to hypothyroidism, and in these reports cardiac tamponade was the initial manifestation.[3,5] We could not find any case reports in the literature, thus, this is the first case, in which cardiac tamponade developed under thyroid replacement therapy.

One interesting feature of this case was the existence of both primary and secondary hypothyroidism due to Hashimoto's thyroiditis and hypopituitarism as a result of empty sella syndrome. Gonadal and thyroid hormone deficiency can be seen in both diseases. This coincidence is also very rare. Another interesting point was the development of cardiac tamponade due to adrenal failure. There were only 2 patients reported in the literature who developed cardiac tamponade due to adrenal insufficiency.[4] In these cases, cardiac tamponade occurred in the setting of both hypothyroidism and adrenal insufficiency as a result of polyendocrine deficiency syndrome. Our patient was investigated for other causes of pericardial fluid such as malignant, rheumatological, and infectious diseases especially tuberculosis. All these conditions were ruled out in our patient. We thought that adrenal failure was the etiological factor of cardiac tamponade by decreasing intravascular volume, thereby, limiting right ventricular filling in the setting of pericardial effusion. The thyroid and gonadal hormones were low at admission, so hypopituitarism was suspected. Unexpectedly, the cortisol and ACTH levels were normal, nevertheless, we closely followed the cortisol levels during thyroid replacement therapy. However, despite close follow-up, cardiac tamponade due to adrenal failure developed suddenly. Replacement of thyroid hormones easily regresses the pericardial effusion, so pericardiocentesis should be reserved in the case of cardiac tamponade. Pericardiocentesis may be necessary if the pericardial effusion does not resolve with hormone replacement therapy and if other etiological factors are thought.

In conclusion, pericardial effusion is a common, however, cardiac tamponade is a very rare manifestation of hypothyroidism. Pericardiocentesis is necessary, only when cardiac tamponade develops and if the effusion does not resolve with hormone replacement therapy. We reported a very rare case, which combined both primary and secondary hypothyroidism, and secondary adrenal insufficiency causing cardiac tamponade.

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