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Case Report

A case of severe hypothyroidism causing cardiac tamponade associated with lithium intoxication

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ABSTRACT

A 70-year-old man was referred to our emergency department for shortness of breath on exertion and systemic edema. He had been taking lithium carbonate for 2 years (500 mg/day over previous 3 months) for bipolar disorder diagnosed at age 60. He was diagnosed with hypothyroidism accompanied by Hashimoto's disease 2 weeks before hospitalization. Massive pericardial effusion and bilateral pleural effusions were demonstrated by transthoracic echocardiography and computed tomography. Cardiac tamponade occurred on the 3rd day. Pericardiocentesis and thoracentesis were performed once and three times, respectively, because of the acute deterioration of hemodynamic status due to pleural and pericardial effusion. Lithium carbonate is a widely used and effective treatment for bipolar disorder. However, lithium has a narrow therapeutic range and many side effects. An important aspect of this case was the rapid development of severe hypothyroidism, although serum lithium concentration was measured regularly and was maintained within the therapeutic range. It is important to note that lithium can cause serious complications, as in this patient, even if serum lithium concentration is measured regularly and maintained within the therapeutic range. We report the first case of cardiac tamponade caused by hypothyroidism associated with administration of lithium.

<**Learning objective:** Lithium carbonate is a widely used and effective treatment for bipolar disorder. Goiter and hypothyroidism are common clinical side effects of lithium, but the complication of cardiac tamponade has not been reported. An important aspect of this case was the rapid development of severe hypothyroidism, although serum lithium concentration was measured regularly and was maintained within the therapeutic range. Therefore, timely diagnosis and treatment of hypothyroidism by routine assessment of thyroid function should be performed.>

Introduction

Lithium carbonate is a widely used and effective treatment for bipolar disorder. However, lithium has a narrow therapeutic range and many side effects [1]. Pericardial effusion caused by hypothyroidism is demonstrated by echocardiogram in almost 30% of patients; however, complications involving cardiac tamponade are very rare and usually occur in prolonged untreated hypothyroidism [2,3]. Goiter and hypothyroidism are common clinical side effects of lithium [1,4,5], but the complication of cardiac tamponade has not been reported, to our knowledge. We report the first case of cardiac tamponade caused by hypothyroidism associated with administration of lithium.

Case report

A 70-year-old man was referred to our emergency department for shortness of breath on exertion and systemic edema. He had been taking lithium carbonate for 2 years (500 mg/day over previous 3 months) for bipolar disorder diagnosed at age 60. Serum lithium had been maintained in the range of effective blood concentration from 0.4 to 1.4 mEq/L under monthly monitoring (therapeutic range; 0.6–1.2 mEq/L, toxic level > 1.5 mEq/L). The examination of anemia [hemoglobin (Hb) 9.2 g/dL] revealed hypothyroidism 3 weeks before hospitalization, although thyroid function was normal in 2006. He was diagnosed with hypothyroidism accompanied by Hashimoto's disease, because free-T4

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level was below measurable levels (less than 0.3 ng/dL) and thyroid autoantibodies were positive [anti-thyroglobulin antibody 25,000 U/mL, anti-thyroperoxidase antibody (TPO-Ab) 219 U/mL]. Lithium was discontinued and levothyroxine sodium 25 μg/day was started under the administration of hydrocortisone 10 mg/day one week before hospitalization. On admission, the vital signs of the patient were as follows: height, 153 cm; weight, 62 kg; body temperature, 36.8 °C; blood pressure, 121/81 mmHg without paradoxical pulse; heart rate, 78 beats/min with regular rhythm; respiratory rate, 14 breaths/min; SpO2, 94% (on room air). Physical examination showed face edema and pitting edema in both legs. He had diffuse enlargement of the thyroid gland, faint heart sound without murmurs, and decreased breath sounds in both lower lung fields. A blood examination revealed normocytic normochromic anemia (Hb 9.5 g/dL), slightly low levels of serum albumin (3.4 g/dL), elevation of creatine phospholinase (1634 IU/L), normal accessory thyroid function, and normal adrenal function. Serum lithium level on admission was below measurable levels (<0.1 mEq/L). The chest X-ray revealed massive cardiomegaly (Fig. 1A). Electrocardiogram showed normal sinus rhythm and low voltage in the limb leads. Computed tomography (CT) chest scan showed massive bilateral pleural effusions and pericardial effusion (Fig. 1B), and echocardiography revealed considerable pericardial fluids. Although levothyroxine was reduced from 25 μg/day to 12.5 μg/day and hydrocortisone (300 mg/day i.v.) was administered for 2 days, dyspnea was gradually aggravated. On the 3rd day, re-examination of echocardiography revealed cardiac tamponade (Fig. 2A and B). Five hundred and fifty mL of pericardial fluids was removed by pericardiocentesis. The cardiac function after pericardiocentesis was normal with an ejection fraction of 67%. The removed fluids did not reveal inflammatory cells or malignant cells. In addition, thoracentesis was performed three times on the right side and once on the left within 1 week of hospitalization. Levothyroxine was continued at 12.5 μg/day, and prednisolone was started at 30 mg/day on day 5 and gradually decreased to 7.5 mg on the 94th day. Serum free-T4 level and thyroid-stimulating hormone (TSH) levels were normalized on days 17 and 62, respectively. Cardiothoracic ratio improved from 69% to 50% (Fig. 3A) and follow-up echocardiographic images showed absence of pericardial fluids as presented in Fig. 3B on the 62nd day.

He was transferred to a nearby psychiatric hospital on the 35th day and has been treated as an outpatient at our hospital.

Discussion

Lithium can cause goiter and hypothyroidism, which occur in approximately 40–50% and 20–30% of patients, respectively [1,4]. In the present patient, thyroid function was examined and found to be normal in 2006. As no further examination was conducted, it is unclear whether his thyroid function had already decreased and thyroid antibody titer was elevated at the start of the treatment in 2010. Previous clinical studies have shown that lithium exacerbates pre-existing autoimmune thyroid disease by accelerating the increase in thyroid antibody titer, but was not able to produce thyroid antibodies *de novo* in humans [4]. Therefore, because of the high incidence of thyroid dysfunction during lithium treatment, physical thyroid examination and serum TSH and TPO-Ab titers are necessary before lithium treatment begins [4,5]. In addition, Bocchetta et al. have shown that the annual rate of development of hypothyroidism was 1.5% in patients on long-term lithium therapy, and that patients with thyroid antibodies had a 6.4% chance of requiring levothyroxine therapy compared to 0.8% for antibody-negative patients (relative risk 8.4%) [6]. Considering this increased prevalence, it was assumed that our patient had a predisposition for chronic thyroiditis or subclinical hypothyroidism.

In most cases, the symptoms of cardiac tamponade are vague and not acute because the pericardial effusion forms slowly and the pericardial sac is able to distend without causing sudden deterioration of cardiac function. The diagnosis is made by detecting cardiomegaly on chest radiography and is verified by echocardiography. However, in this patient, a chest X-ray was taken for the first time on the day of hospital transport and the pleural effusion and cardiac enlargement were noticed for the first time.

The Pharmaceuticals and Medical Devices Agency (PMDA) of Japan published "A request for proper use of lithium carbonate and measurement of the serum lithium level" on April 9, 2012 [7]. From April 2006 to November 2011, 98 cases of serious lithium poisoning were reported to the PMDA.

In our patient, although serum lithium level was maintained within the therapeutic range, the patient developed severe hypothyroidism due to lithium poisoning.

The mechanisms by which lithium causes hypothyroidism and goiter are considered to be increase of lithium in intrathyroidal iodine content, inhibition of the coupling of iodotyrosine, and inhibition of thyroxine release [1]. In our patient, thyroid ultrasound showed enlargement of both lobes and a marked increase

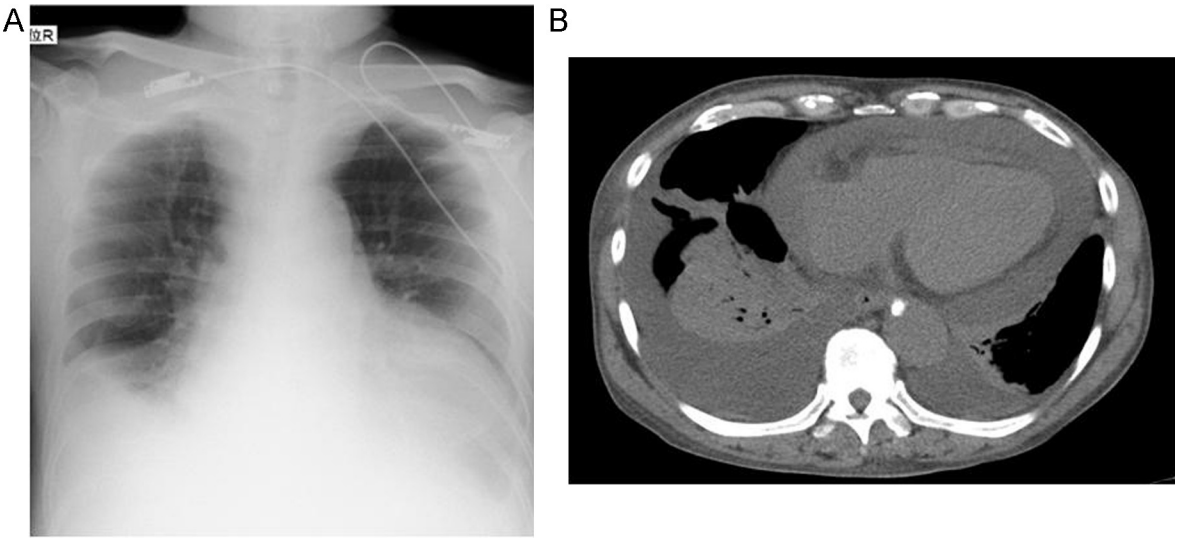

Fig. 1. (A) Chest X-ray on admission showed prominent cardiomegaly and blunting of bilateral costophrenic angles. (B) Chest computed tomography scan revealed a large quantity of pericardial effusion and bilateral pleural effusions.