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Case Report

Thyroid storm in an uncontrolled graves' disease with multiple complications: a case report

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ABSTRACT

Thyroid storm is an acute and life-threatening condition. Graves' disease is the most common cause of thyroid storm. In this case, reported an uncontrolled Graves' disease patient with multiple complications progressing to thyroid storm. A 33-years-old woman was admitted to the emergency department with agitation. Patient had a history of uncontrolled hyperthyroidism four years ago. From physical examination found exophthalmos, bibasilar rales in both lungs, shifting dullness on stomach, swollen feet, and cold extremities. The ECG showed an atrial fibrillation with rapid ventricular response. Thyroid stimulating hormone (TSH) was found very low with 0.02 mIU/L and very high free thyroxine (FT4) with 5.04 ng/dL. The neck USG showed thyroiditis and bilateral neck lymphadenopathy. The patient was hospitalized for 9 days (4 days in ICCU and 5 days in the general ward). A very high thyroid hormone receptor antibody (TRab) of 35.9 signified a diagnosis of Graves' disease. The patient had a total Burch-Wartofsky point scale (BWPS) score of 80 and highly suggestive of a thyroid storm. Multiple complications of Graves' disease are cardiac failure, atrial fibrillation, seizures, vomiting, abdominal cramps, diarrhea, elevated liver enzymes, coma, jaundice, and thromboembolism while in this case the patient had cardiac failure, atrial fibrillation, and elevated liver enzymes. Thyroid storm is diagnosed with clinical features not on laboratory results. It is important to evaluate multiple complications of Graves' disease as an early warning to reduce the mortality of thyroid storm.

Keywords: Case report, Thyroid storm, Graves' disease, Complication

INTRODUCTION

Thyroid storm is an emergency complication of hyperthyroidism. Thyroid storm or thyrotoxic crisis is an acute, life-threatening condition, and involves a multisystem. Graves' disease is the most common cause of thyroid storm that is secondary to thyrotoxicosis.[1] Uncontrolled thyrotoxicosis that progressing to thyroid storm might be precipitated by several factors such as antithyroid discontinuation, nonthyroidal operations, childbirth, severe trauma, infection, iodine exposure through radiocontrast dyes, and amiodarone.[2,3]

Thyroid storm diagnosed with clinical features not on laboratory results. Do not delay patient treatment because of laboratory examination. Clinical presentation includes hypertension, tachycardia, fever, neurological, and gastrointestinal abnormalities.[4] These signs and symptoms are associated with multiple complications of Graves' disease that if uncontrolled would result in thyroid storm. Following complication-cardiac failure, atrial fibrillation, seizures, vomiting, abdominal cramps, diarrhea, elevated liver enzymes, coma, jaundice, and thromboembolism.[4-6]

In this case, reported uncontrolled Graves' disease patient with multiple complications progressing to thyroid storm.

CASE REPORT

A 33-years-old woman was admitted to the emergency department with agitation. Patient agitated around 3 hours before and accompanied by shortness of breath. Patient felt shortness of breath for the past two days and the complaint got worse until the patient had difficulty talking. One day

before, the complaint worsened when lying down in bed and better when sitting in an upright position but at the hospital the complaint persisted even when upright.

Patient also complained of palpitation, fever, cough, nausea, sore throat, hoarse, and swollen feet for 2 days ago. Palpitation was getting worse and persisted at rest. Fever was predominantly in evening until night and slightly better in morning. Patient also coughs accompanied with white phlegm around 3 ml that contain multiple red spots. Nausea was accompanied with abdominal discomfort but history of vomiting was denied. Sore throat and hoarse getting worse since past 2 days. Swollen feet initially appear when in long standing position but persist for 2 days before. Patient also said her stomach has been getting bigger since past 2 years. History of seizure, jaundice, surgery, and trauma was denied.

Patient had a history of hyperthyroidism four years ago. The sign was first discovered when the patient was pregnant four years before. The examination was done at that time and revealed that the patient had hyperthyroidism and was given propylthiouracil (PTU) 100 mg every 8 hours. The patient took the medicine regularly while pregnant but after delivery she didn't take the medication regularly and just took it when didn't feel good. For the past two days, the patient took cold medication and PTU but the symptom didn't get better. The patient also said that her child had a fever and cough since the past week.

The patient was agitated. Pulse rate was 150 times per minute with irregular beat, blood pressure 128/67mmHg, body temperature was 37.2ºC, respiration rate was 25 times per minute, and oxygen saturation of 97% on nasal cannula O_2 four liters per minute. From physical examination found exophthalmos as seen in figure 1, bibasilar rales in both lungs, shifting dullness on stomach, swollen feet, and cold extremities. The thyroid gland size was normal but there were enlarged lymph nodes on both sides of the neck (Figure 2).

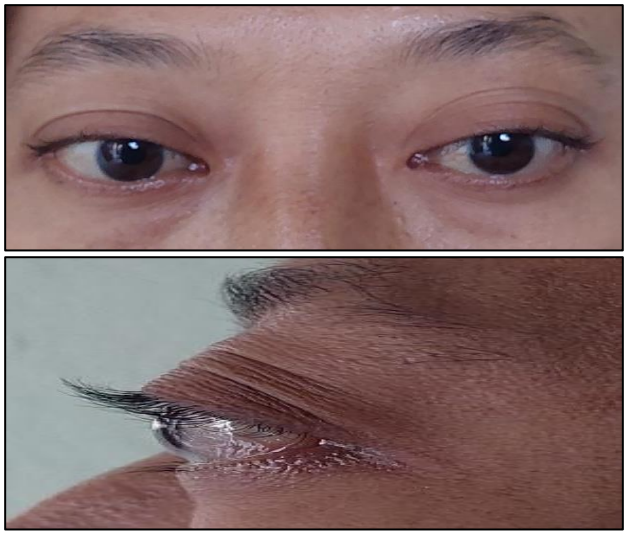


Figure 1: Sign of exophthalmos.

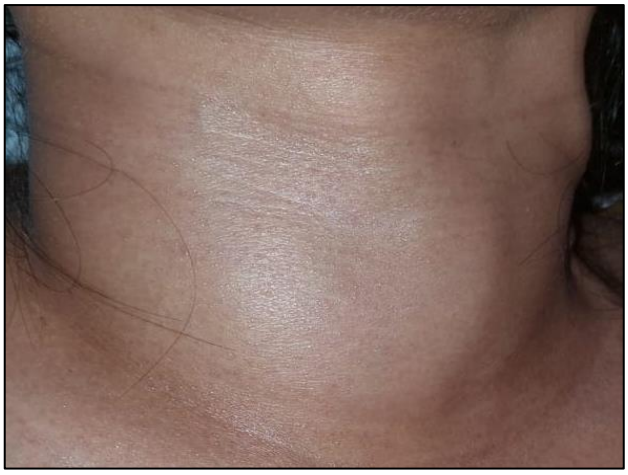


Figure 2: Enlarged lymph nodes on both side of the patient's neck.

The ECG showed an atrial fibrillation with rapid ventricular response (Figure 3). The laboratory result found leukocyte $5.27\times10^3/\mu L$ with increased neutrophil to lymphocyte ratio of 6.04, hemoglobin 11.2 g/dL, hematocrit 34.8%, thrombocytopenia with $85\times10^3/\mu L$, SGPT 33 U/L, increased SGOT 63 U/L, ureum 15 mg/dL, serum creatinine 0.4 mg/dL, sodium 136 mmol/L, hypokalemia with 3.1 mmol/L, chloride 97 mmol/L, and troponin I<0.01ng/ml. Blood gas analysis showed normal pH of 7.45, decreased PCO2 of 31 mmHg, decreased PO_2 of 52 mmHg, decreased cHCO3 of 21 mmol/L, decreased ABE of -3, and decreased oxygen saturation of 86%.

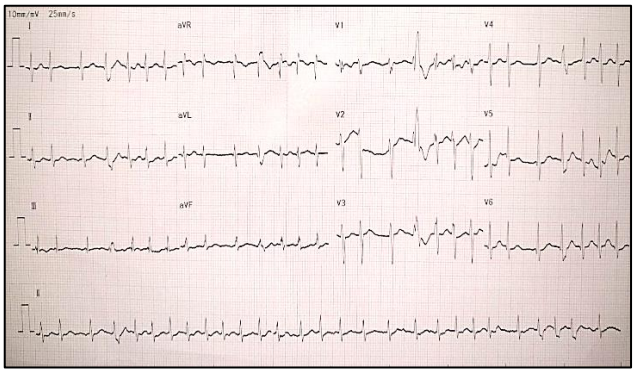


Figure 3: Atrial fibrillation with rapid ventricular response in patient ECG.

TSH found very low with 0.02 mIU/L and very high free thyroxine (FT4) with 5.04 ng/dL. Patient also tested with negative HbsAg and negative anti HCV. The C-reactive protein of the patient showed very high with 51 mg/L. From chest X-ray (Figure 4) revealed pneumonia with left pleural effusion. Echocardiography showed normal cardiac dimension with ejection fraction of 76.32% and mild tricuspid regurgitation as shown in Figure 5. Neck ultrasonography (USG) as shown in Figure 6 revealed that increased vascularisation in thyroid parenchyma without enlargement of thyroid and enlarged lymph nodes on both side of neck (1.34×0.37 cm on right and 1.19×0.32 cm on

left). From the neck USG concluded that there was thyroiditis and bilateral neck lymphadenopathy.

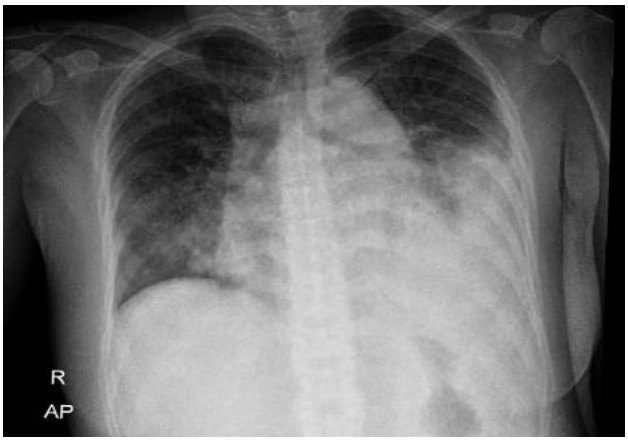


Figure 4: Pneumonia and left pleural effusion from patient's chest x-ray.

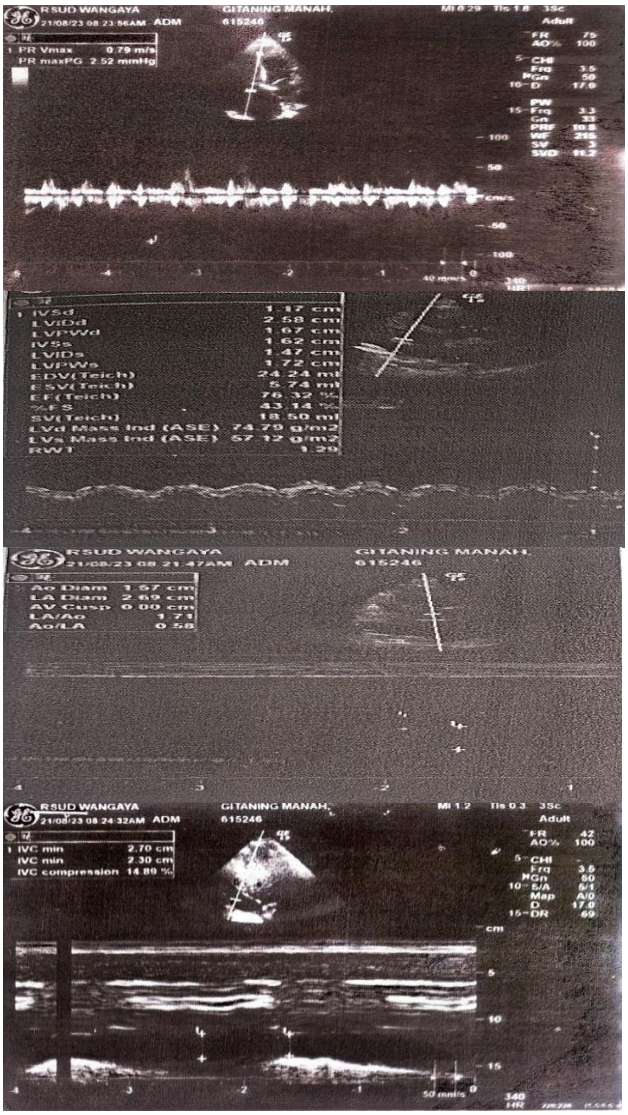


Figure 5: Echocardiography showed normal cardiac dimension with mild tricuspid regurgitation.

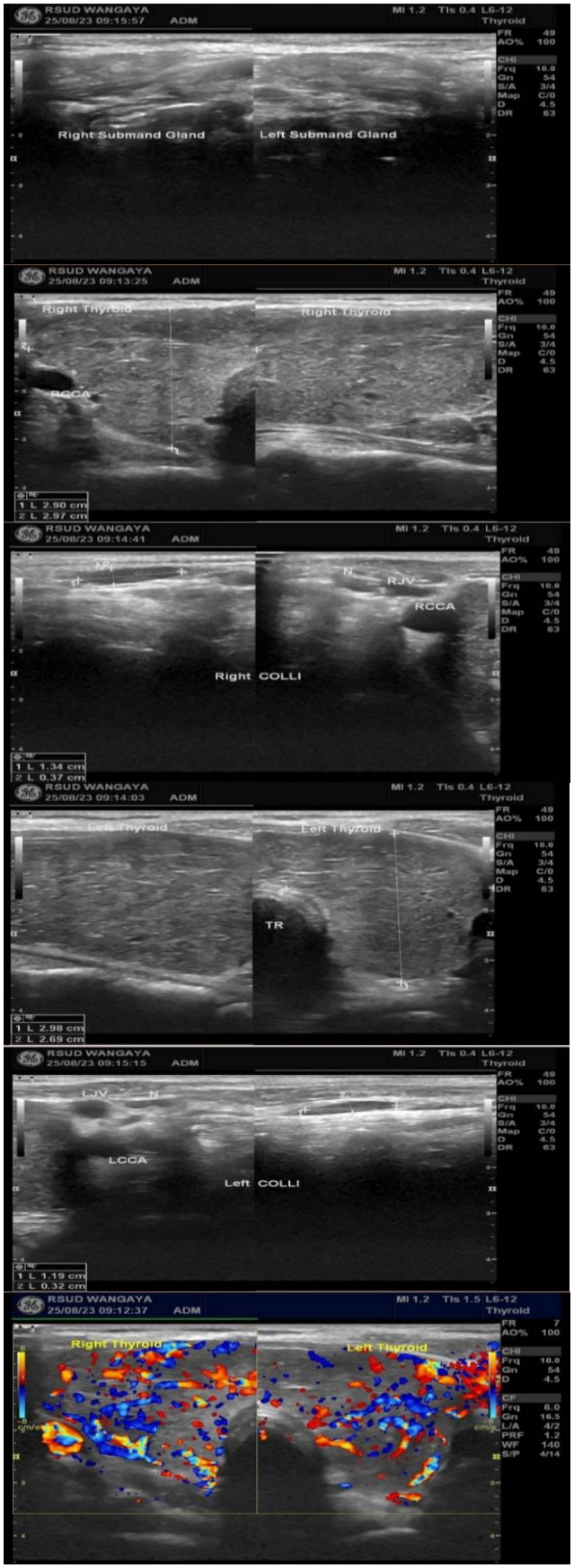


Figure 6: Neck USG shown thyroiditis and bilateral neck lymphadenopathy

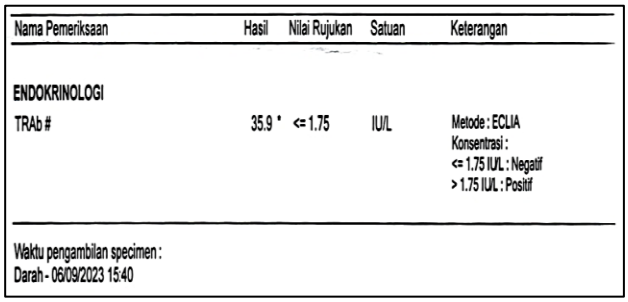
Patient admitted to ICCU with diagnoses of thyroid storm, acute heart failure, atrial fibrillation with rapid ventricular response, pneumonia, left pleural effusion, hypokalemia, and thrombocytopenia. The patient had the total BWPS score of the 80 that was highly suggestive of the thyroid storm.

The patient was treated with collaboration of three specialist doctors that consist of cardiologist, endocrinologist, and pulmonologist. Initially patient given nasal cannula O_2 four liters per minutes, drip of furosemide 5mg/hour, digoxin 0.5 mg diluted in 20 ml of sterilized water every 12 hours, drip of potassium chloride (KCl) 25 Meq in NaCL 0.9% 12 drops per minutes, PTU 200mg/4 hours orally, hydrocortisone 100 mg/12 hours, ceftazidime 1gr/8 hours, tranexamic acid 500mg/8 hours, omeprazole injection 40 mg/12 hours, and codeine 10mg/8 hours orally. Lugol was not administered because unavailable at the hospital.

After the first day, the patient's condition was slightly better and the patient had a better response. The potassium became 3.8 after drip of KCl then the drip of KCl discontinued. In ICCU, the patient's condition was getting better after four days of treatment. The agitation had diminished. The symptoms like shortness of breath, palpitation, fever, cough, nausea, sore throat, hoarse, and swollen feet subsided then the patient moved to the general ward (GW). The treatment in general ward was furosemide injection 20 mg/8 hours, digoxin 0.25 mg/24 hours orally, propranolol 10 mg/24 hours orally, PTU 300 mg/6 hours orally, hydrocortisone injection 100 mg/24 hours, ceftazidime injection 1gr/8 hours, omeprazole injection 40 mg/12 hours, and codeine 10 mg/8 hours orally.

Table 1: Patient progression during hospitalization.

Variables	21/8	22/8	23/8	24/8	25/8	26/8	27/8	28/8	29/8
General condition	Weak	Weak	Weak	Moderate	Moderate	Moderate	Moderate	Good	Good
Blood pressure (mmHg)	128/67	120/59	130/50	117/68	103/57	96/68	103/77	105/73	112/75
Heart rate (bpm)	150	112	78	75	64	85	76	70	71
Respiration rate (x/mnt)	25	22	18	18	20	20	20	20	20
Temp (ºC)	37.2	37.0	36.4	36.5	36.3	36.3	36.5	36.7	36.9
Visual analog scale (1-10)	5	3	3	2	2	2	1	0	0
Room	ICCU	ICCU	ICCU	ICCU	GW	GW	GW	GW	GW



Nama Pemeriksaan	Hasil	Nilai Rujukan	Satuan	Keterangan
ENDOKRINOLOGI				
TRAb #	35.9 *	<=1.75	IU/L	Metode : ECLIA Konsentrasi : <= 1.75 IU/L : Negatif > 1.75 IU/L : Positif

Waktu pengambilan specimen :
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Figure 7: TRab level of the patient showed a diagnosis of Graves' disease.

At the general ward, because of the improved condition of the patient, the dose of PTU decreased to 200 mg/8 hours and injection of hydrocortisone stopped. The patient progression during hospitalization shown in Table 1. After the ninth day of therapy (four days in ICCU and five days in the general ward), there was an improvement of the patient's condition and discharged from the hospital. The take-home oral medications were furosemide 1×40 mg, digoxin 1×0.125 mg, propranolol 1×10 mg, PTU 3×200 mg, and codeine 3×10 mg. The patient then continued to be treated as an outpatient. At the first control, the patient's condition was good with no complaints. Thyroid hormone receptor antibody (TRab) tested after the first control with a very high result of 35.9 (Figure 7) that signified a diagnosis of Graves' disease.

DISCUSSION

Graves' disease is the most common etiology of thyroid storm. Graves' disease is auto-immune disease that results in high levels of thyroid hormone/also called hyperthyroidism. Hyperthyroidism in this case caused by increased production of thyroid hormone due to thyroid-stimulating immunoglobulins (TSIs)/ commonly called TSH receptor antibodies (TRAb) binding with TSH receptors. This bind then activates receptor causing growth of thyroid gland and increase thyroid hormone synthesis by thyroid follicles.[7] Moreover, TSH receptor and MHC (Major histocompatibility complex) class II variants were found to be strongly associated with persistently TRAb-positive Graves' disease.[8] In this case, patient had very high TRAb with result of 35.9 while reference is lower than 1.75. This indicated patient had positive Graves' disease.

Anyone can be affected with Graves' disease but women may be more susceptible than men. The prevalence of Graves' disease is 3% in women and 0.5% in men. The

incidence is 20 to 40 new cases in every one thousand populations every year.[9,10] It is more common in the population with age between 30 and 60 years.[11] In this case, presented a 33-years-old woman with uncontrolled Graves' disease. The age and gender of the patient in accordance with the highest prevalence of Graves' disease (women with age between 30 and 60 years).

Pathophysiology of thyroid storm is not definitive, but there are several precipitating factors that superimpose the incidence of thyroid storm. The triggers or precipitating factors are infection, thyroid surgery, major trauma, parturition, or iodine exposure from radiocontrast dyes or amiodarone.[12] The most common trigger of thyroid storm is infection.[13] These factors may causing enhanced binding to thyroid receptors, increasing tissue response, decreasing affinity of thyroid binding proteins for thyroid hormone, and sudden increase of free thyroid hormone that resulted in thyroid storm.[14] Other than that, patients with incomplete or interrupted treatment of hyperthyroidism increased risk of thyroid storm.[12] In this case, the patient had pneumonia and also uncontrolled Graves' disease that increased risk and precipitating the thyroid storm.

Thyroid storm has an abrupt onset as the most frequent clinical manifestation. The others are fever, exophthalmos, goiter, profuse diaphoresis, flushing, warm skin, nausea, vomiting, diarrhea, abdominal pain, tachycardia with more than 140 beats/minutes, agitation, delirium, coma, psychosis, atrial fibrillation, and unexplained jaundice. The symptoms in thyroid storm progressively increase to lethal levels within 24-48 hours.[12] In this case, the patient was agitated for 3 hours before being admitted to hospital as the sign of sudden onset of thyroid storm. The other clinical manifestations of thyroid storm from the patient were fever, exophthalmos, tachycardia with 150 beats/minutes, atrial fibrillation, nausea, and abdominal discomfort that worsened for 2 days before admitted.

The complications of Graves's disease are cardiac failure, atrial fibrillation, seizures, vomiting, abdominal cramps, diarrhea, elevated liver enzymes, coma, jaundice, and thromboembolism.[15] In the heart, triiodothyronine (T3) as an active of thyroxine (T4) binds to thyroid hormone receptors (THR) regulates the expression of cardiac genes that have contractile function positively and negatively regulates genes that have a role in relaxation of cardiac muscle. Thyrotoxicosis positively regulates genes and decreases the others thus causing high output heart failure. Thyrotoxicosis also shortens myocyte's refractory period that increased atrial sensitivity to thyroid hormones and would result in atrial fibrillation.[16] Thyrotoxicosis also causing free-radical damage to hepatocytes that resulted in anoxia of the hepatocyte induced by hypermetabolic state. The accelerated decomposition of liver glycogen and protein causing degeneration of liver cells and increased liver enzymes as the sign of liver dysfunction.[17] In this case, the patient had cardiac failure, atrial fibrillation, and elevated liver enzymes as complication of Graves' disease.

Thyroid storm diagnosed with clinical features not on laboratory results. In 1993, Burch and Wartofsky made a scale consisting of multiple clinical signs and symptoms to diagnose thyroid storm as shown in Table 2. The score higher than 45 is suggestive of a thyroid storm, score of 25-44 shown impending storm, and unlikely a thyroid storm when the score is below than 25.[18] In this case, the patient had total BWPS score of 80. The temperature was 37.2ºC 5-point, tachycardia more than 140 beats per minutes 25 point, atrial fibrillation present 10 point, bibasilar rales 10 point, nausea 10 point, agitation 10 point, and sign of infection as precipitating event 10 point. Score 80 was highly suggestive for diagnosis of the thyroid storm.

Table 2: The BWPS.[18]

Criteria	Point	Patient's score
Temperature (ºC)		
37.2-37.7	5	5
37.8-38.3	10	
38.4-38.8	15	
38.9-39.3	20	
39.4-39.9	25	
≥40.0	30	
Central nervous system effects		
Absent	0	10
Mild (agitation)	10	
Moderate (delirium, psychosis, extreme lethargy)	20	
Severe (seizures, coma)	30	
Gastrointestinal-hepatic dysfunction		
Absent	0	10
Moderate (diarrhea, nausea/ vomiting, abdominal pain)	10	
Severe (unexplained jaundice)	20	
Tachycardia (bpm)		
90-109	5	25
110-119	10	
120-129	15	
130-139	20	
≥140	25	
Congestive heart failure		
Absent	0	10
Mild (pedal edema)	5	
Moderate (bibasilar rales)	10	
Severe (pulmonary edema)	15	
Atrial fibrillation		
Absent	0	10
Present	10	
Precipitating event		
Absent	0	10
Present	10	
Total patient's score		80

The therapy of thyroid storm aimed to 1) ameliorating hyperadrenergic effects of thyroid hormone with the use of beta-blocker, 2) Antithyroid medication to decrease

further synthesis of thyroid hormones, 3) Using iodides to decrease hormonal release from the thyroid glands, and 4) Glucocorticoids or iodinated radiocontrast dyes to prevent excessive secretion of thyroid hormones and prevent conversion T4 to T3 peripherally.[15] In this case, propranolol was used as beta-blocker to ameliorating hyperadrenergic effects of thyroid hormone, PTU was administered to decreased synthesis of thyroid hormone, and hydrocortisone was used to prevent conversion of T4 to T3 peripherally and also inhibit excessive release of thyroid hormone. Iodides or Lugol to decrease hormonal release from the thyroids glands was not administered because the medication was unavailable at the hospital.

CONCLUSION

This case report was to remind and highlight multiple complications of Graves' disease that would help in early diagnosis and treatment of thyroid storm. The diagnosis of thyroid storm does not depend on laboratory results but on clinical features. The BWPS score can be used to diagnose the possibility of thyroid storm. Do not delay patient treatment because of laboratory examination and immediately treat as soon as possible. It is also important to evaluate multiple complications of Graves' disease such as cardiac failure, atrial fibrillation, seizures, vomiting, abdominal cramps, diarrhea, elevated liver enzymes, coma, jaundice, and thromboembolism as an early warning to reduce the mortality of thyroid storm. The main therapy of thyroid storm is beta-blocker, antithyroid medication, iodide, glucocorticoids or iodinated radiocontrast dyes.

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