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Case Report: Pneumonia Provocates Thyroid Storm in Graves Disease

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ABSTRACT

Introduction: A thyroid crisis is an endocrine emergency involving many organ systems and can be fatal to the patient's survival. Although cases of thyroid crisis are rare, the mortality rate is significant which reaches 20–50%. The presence of comorbidities such as pneumonia infection increases the risk of death dramatically. Infection is a factor that can trigger thyroid crisis and exacerbate thyrotoxicosis. This condition of thyroid crisis most often occurs in people with hyperthyroidism caused by Graves' disease. We present the case of a patient with Graves' disease, aged 22 years, who developed a thyroid crisis due to community-acquired pneumonia infection. This study aims to provide a case report regarding the thyroid crisis due to pneumonia.
Results: We carried out a physical and some appropriate supporting examinations to confirm the diagnosis. Wayne's index was 26, indicating hyperthyroidism. Assessment with Burch-Wartofsky obtained a score of 45, indicating suspicion of a thyroid storm. Then supportive care was provided to the patient. The community-acquired pneumonia as a triggering factor was treated with antibiotics. Thyrotoxicosis conditions were treated with antithyroid, beta-blocker, and glucocorticoid drugs. The patient's condition improved after treatment.
Conclusion: It is crucial to detect and treat thyroid storm as quickly as possible since it has a high mortality rate. Wayne's score is useful for identifying hyperthyroidism based on clinical symptoms. The Burch-Wartofsky Point Scale scores are used to diagnose thyroid storms. Thyroid storm should be managed according to PERKENI (Perkumpulan Endokrinologi Indonesia) and ATA (American Thyroid Association) recommendations. This case serves as an example of how to make a proper diagnosis and treatment to prevent morbidity and death due to thyroid crisis.

Keywords: community-acquired pneumonia; Graves disease; thyroid storm; thyrotoxicosis

INTRODUCTION

A thyroid storm is a potentially fatal hyperthyroidism syndrome characterized by multi-system dysfunction[1] . It is most typically found in patients with underlying Graves' hyperthyroidism, but it can

occur in any kind of thyrotoxicosis[2]. Other causes of thyroid storm include infections, various kinds of trauma, a sudden withdrawal of antithyroid medication, hyperglycemic crisis, and exogen iodine in large quantities[3]. Community-acquired pneumonia is one of the infections that cause thyroid storms. In both the developed and developing countries, community-acquired pneumonia is one of the deadliest diseases. Developing countries are also the hardest hit by a slew of other factors, such as limited financial access to healthcare and a lack of preparedness for environmental changes[4]. Similar case reports previously also mentioned that pneumonia induced thyroid storm[5-7].Thyroid storm still has a high death rate in the modern period, and early recognition of this disease, along with specialized treatments, can make the better outcome[3].

We have a case to report of a 22-year-old woman with Graves disease experiencing a thyroid storm with the triggering factor being community-acquired pneumonia infection. The purpose of this study is to describe a case of pneumonia-induced thyroid storm.

CASE PRESENTATION

A 22-year-old woman with a history of Graves' illness emitted to the Universitas Sebelas Maret Hospital's Emergency Department on 15th October 2021 with a major complaint of palpitation for the past two weeks. The palpitation was getting worse for the last 4 days before being admitted to the hospital. The palpitation was persistent at rest and was not associated with anxiety. She also had difficulty on sleep. She complained of watery stools 3 times per day and nausea for the last 2 days. She also felt of headache and neck stiffness getting worse since 4 days before admission. She had a cough with yellowish phlegm since a week ago. The patient's medical record revealed that she had been undergoing treatment for hyperthyroidism for the past 11 months at a hospital in Ngawi city, East Java. However, due to her busy schedule of working in a new place in Boyolali, Central Java, she didn't take her medicine (propranolol 10mg/8hours and methimazole 20mg/day orally) regularly, and in the last 4 days, she has stopped taking medicine herself.

She was determined to be a febrile, with a blood pressure of 185/104 mmHg, a pulse rate of 145 beats per minute, a respiratory rate of 22 per minute, and a room air oxygen saturation of 97%.

INVESTIGATION

Physical examination revealed exophthalmos, hyperreflexia, warm, moist, and smooth skin, and coarse crackles in both lung fields. The thyroid gland is not enlarged in the neck and is the same color as the surrounding skin, JVP R+2 cm H_2O. On auscultation, there was a positive bruit.

Wayne's index was 26, indicating hyperthyroidism. Burch-Wartofsky Point Scale (BWPS) score was 45. We also calculated the covid-19 early warning score (COVID-19 EWS), which came out at 1 (highly suspected patient if the score $\geq$ 10). We did antigen swab for COVID and the result was negative.

From a complete blood count, the leukocyte count was 5.77 x 10^3/µL, hemoglobin 13.4 gram/dl, hematocrit 42%, platelets 261 x 10^3/µL. SGOT 18 U/L, SGPT 14 U/L, creatinine 0.34 mg/dl, ureum 36 mg/dl, sodium 141, potassium 4, chloride 103, and calcium 1.00 mmol/L on blood chemistry examination.

TSHs were found to be 0.050 mIU/ml (normal range 0.550-4.780 mIU/ml) and FT4 >100.00 qmol/L (normal range 10.60-19.40 qmol/L) in early laboratory results. The initial chest X-ray (Figure 1) revealed inhomogeneous perihilar opacity in both lungs, as well as an air bronchogram. With a heart rate of 145 beats per minute, an ECG revealed sinus tachycardia (Figure 2). Anti TPO was also tested, and the result was 863.61 IU/mL (normal range: 5.61 IU/mL) (Figure 3). Urinalysis was normal.

A prior thyroid ultrasound at the hospital in Ngawi city revealed a widespread goitre but no bilateral thyroid nodules.

Figure 1. The initial chest radiograph, which was taken on 15th October 2021, showed inhomogeneous perihilar opacity in both lungs, as well as an air bronchogram.

Figure 2. Sinus tachycardia of 145 bpm was detected on the electrocardiogram, which was examined on 15th October 2021.

ENDOKRINOLOGI				
Anti-TPO #	863.61 *	< 5.61	IU/mL	Metode : CMIA Konsentrasi : <5.61 IU/mL : Negatif >= 5.61 IU/mL : Positif

Waktu pengambilan specimen :
Darah Beku - 18/10/2021 16:41

Figure 3. Anti-TPO, which was examined on 18th October 2021, the result was 863.61 IU/mL (normal range: 5.61 IU/mL)

This patient was treated for a thyroid storm as well as a secondary infection from community-acquired pneumonia. Antibiotics, anti-thyroid (methimazole), steroid (hydrocortisone), beta-blockers (propranolol), and anti-hypertensive drugs were among the treatments. We gave the oxygen therapy as needed, ringer lactate infusion 20 drops per minute, ceftriaxone injection 2 gram/24 hours, omeprazole injection 40mg/12 hours, hydrocortisone injection 100mg/ 8 hours, methimazole 60mg/24 hours orally, propranolol 80mg/ 6 hours orally, ivabradine 5mg/ 12 hours orally, amlodipine 10 mg/ 24 hours orally, and NAC (N-acetylcysteine) 200mg/ 8 hours orally.

The patient's symptoms, which included heart palpitations and diarrhea, had diminished after three days of treatment. Within four days of treatment, the headache, neck stiffness, and cough subsided. She might be able to get enough rest and eat properly. The results of the sputum culture performed when she first arrived at the hospital on October 15th, 2021, revealed that *Streptococcus pneumoniae* was the type of bacterium that caused pneumonia. The antibiotic sensitivity test shown that the organism was sensitive to the ceftriaxone that had been administered a few days before. After receiving therapies for 5 days, the patient's clinical condition improved with < 25 scoring of *Burch-Wartofsky.* She was omitted from the hospital in good-health overall condition, and was given oral medication consisting of cefixime 2x200 mg, NAC 3x200 mg, methimazole 1x40 mg, propranolol 3x40 mg, ivabradine 2x5 mg, and amlodipine 1x10 mg. She was then continue treated as an outpatient.

Table 1. General condition, GCS and Vital Signs during Hospitalization

Time	General Condition	GCS (Glasgow Coma Scale)	Vital Signs				
			BP (Blood Pressure) mmHg	HR (Heart Rate) bpm	RR (Respiration Rate) per minute	T (Temp) ºCelcius	VAS (Visual Analog Scale)
15th Oct 2021	Looks sick, weak	E4V5M6	185/104	145	22	36.7	4 on the chest
16th Oct 2021	Look sick, weak	E4V5M6	157/89	127	22	36.7	3 on the chest
17th Oct 2021	Look sick, weak	E4V5M6	144/79	102	20	36.5	1-2 on the chest
18th Oct 2021	Good	E4V5M6	125/88	97	18	36.5	0 on the chest
19th Oct 2021	Good	E4V5M6	120/85	91	18	36.5	0 on the chest

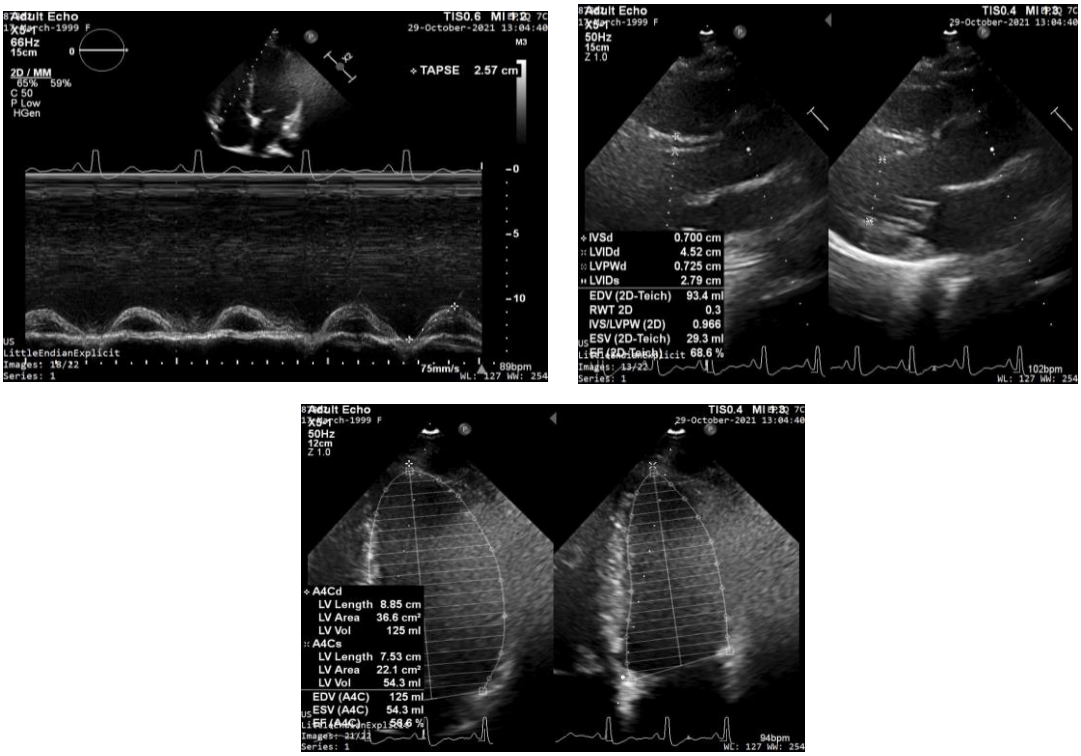

Figure 4. Echocardiography which was examined on 29th October 2021, showed normal cardiac dimension, good LV and RV function, normal diastolic function, and pulmonary and tricuspid regurgitation.

We plan recheck TSHs and FT4 after 4-6 weeks of theraphy. We conducted an echocardiographic test on the patient while she was receiving outpatient care. Echocardiography showed normal cardiac dimension. Good LV and RV function. Normal diastolic function. Mild pulmonary and tricuspid regurgitation (Figure 4).

DISCUSSION

A thyroid storm, often referred to as a thyroid crisis, a thyrotoxic storm, and a thyrotoxic crisis is an uncommon but lethal endocrine emergency. It is a presenting symptom of a thyrotoxic disease that is markedly exaggerated[8]. Frank Howard Lahey coined the phrase "the crisis of exophthalmic goiter" in 1926[9]. It is an uncommon form of hyperthyroidism. Thyroid storm results in between 1% and 2% of hyperthyroidism hospitalizations. According to a US study, the normal population's storm incidence varied from 0.57 to 0.76 occurrences per 100,000 per year, whereas hospitalized patients' incidence ranged from 4.8 to 5.6 cases per 100,000 per year[10]. The incidence of thyroid storm was 0.2% of all thyrotoxicosis patients and 5.4% of inpatient thyrotoxicosis patients, according to the Japanese National Survey. Comparable to those with thyrotoxicosis but without thyroid storm, the average age of individuals experiencing from thyroid storm was 42 to 43 years old. Comparable to thyrotoxicosis without storm, the male-to-female ratio for the incidence of thyroid storm was around 1:3[11].

Thyroid storm is an uncommon clinical episode of hyperthyroidism that can lead to serious problems. This should be monitored because thyroid storm alone has a death rate of 20–50%, and complications such as infections, such as pneumonia, enhance the risk even more. Because thyroid storm has a high mortality rate, it is critical to diagnose and treat it as soon as possible[12].

Untreated thyrotoxicosis may be precipitated by nonthyroidal operations, childbirth, severe trauma, infection, or iodine exposure through radiocontrast dyes or amiodarone[13]. Table 2 lists both common and uncommon triggers. In hospitalized patients, the most prevalent cause of thyroid storm is infection [3,13,14]. About 25-43% of storm patients have no clear triggering cause[15].

Table 2. Thyroid Storm Triggers [16]

Prevalent	Unusual
Infectious disease	A strong palpation of the thyroid gland
Acute medical condition	Thyroiditis subacute
Episodes of acute psychosis	Overdosage of thyroxine
Procedures for nonthyroidal surgery	Intoxication from aspirin
Parturition	Mole hydatidiform
Trauma	Opioid toxicity
Antithyroid medication withdrawal	Neurotoxins
Following radioactive iodine treatment	Chemotheraphy for cytotoxic cells
Post-thyroidectomy	
Following the administration of a large quantity of iodine	
Iodine-based contrast agents for radiography	

The presence of co-morbidities, especially infections such as pneumonia, can trigger thyroid storm. Thyroid storm is most usually linked with Graves' disease, although it may also occur in individuals with toxic nodular goiter or other forms of thyrotoxicosis[17]. The involvement of hyperthyroidism in infection risk is mostly related to the body's hypermetabolic effect. Downregulation of the neutrophil response to sites of inflammation and/or infection is caused by changes to the

sympathetic nervous system. As a result, the risk of infection complications, such as bacterial pneumonia, is significantly increased.

We diagnosed the patient with *community-acquired pneumonia* based on her coughing up yellow mucus for a week before admission. During the physical examination, a respiratory rate of 22 per minute, both lung fields had coarse crackles. Initial chest radiographs revealed heterogeneous perihilar opacity and an air bronchogram in both lungs. The sputum culture revealed *Streptococcus pneumoniae* to be the causative bacteria causing pneumonia.

After a study of the patient's medical history, physical examination, radiological examination, and immunological research, Graves disease was identified in this case. Graves' disease will cause hyperthyroidism, which may be measured using the Wayne index. The most common complications are vision impairment, chemosis, proptosis, diplopia, corneal ulcers, dermopathy (0.5-4%), and acropathy (1%)[18]. In addition to clinical criteria, this patient's test results validated the diagnosis of hyperthyroidism: a TSH level of 0.050 mIU/ml (normal range: 0.550-4.770 mIU/ml) and an increased fT4 level of >100.00 pmol/L (normal range: 10.60-19.40 pmol/L)[19].

The thyroid looks normal or slightly enlarged in Graves' disease. Colour flow imaging demonstrated a modest to a significant increase in parenchymal blood flow[20]. Ultrasonography of this patient's thyroid showed a diffuse goitre and a lack of bilateral thyroid nodules. Thus, the ultrasound images of the patient's thyroid are consistent with Graves' illness. Thyroid Peroxidase (anti-TPO) antibodies will be increased on immunological testing; in this case, the titer will be 863.61 IU/mL (normal range: 5.61 IU/mL).

Graves' disease is an organ-specific autoimmune disorder distinguished by anti-TPO (thyroid peroxidase antibody) and anti-TG antibodies (anti-thyroglobulin antibodies). The three principal thyroid antigens are anti-thyroglobulin antibodies, thyroid peroxidase, and anti-TSH antibodies. Receptors Anti-TPO was chosen since it is less costly and more practical than other choices[20-22].

Table 3.Wayne's Index[23]

Symptoms	Score	Signs	Present	Absent
Dyspnea on exertion	+1	Palpable thyroid	+3	-3
Palpitation	+2	Bruit	+2	-2
Tiredness	+2	Exophthalmos	+2	-
Preference for heat	-5	Lid retraction	+2	-
Preference for cold	+5	Lid lag	+1	-
Excessive sweating	+3	Hyperkinesis	+4	-2
Nervousness	+2	Hands hot	+2	-2
Increased appetite	+3	Hands moist	+1	-1
Decreased appetite	-3	Pulse rate >80/m	-	-3
Decreased weight	+3	Pulse rate >90/m	+3	-
Increased weight	-3	Atrial fibrillation	+4	-
Total score interpretation >19 = toxic 11-19 = equivocal <11 = euthyroid				

To diagnose a thyroid storm, we must first determine the hyperthyroidism state of the patient. Wayne's score is still useful for identifying hyperthyroidism based on clinical symptoms since test confirmation is often delayed. The diagnostic index assigns a score to the presence or absence of several hyperthyroidism signs and symptoms (Table 3)[23,24]. A thyroid function test should then be ordered to confirm the diagnosis. In this patient, dyspnea on exertion scored +1, palpitation scored +2, fatigue

scored +2, preference for cold scored +5, excessive sweating scored +3, nervousness scored +2, bruit scored +2, exophthalmos scored +2, hands hot scored +2, hands moist scored +1, and pulse rate >90 beats per minute scored +4. Total index for Wayne's index was 26, which indicates hyperthyroidism.

In fatal thyrotoxic patients who can cause death with indications of systemic decompensation, the diagnosis of thyroid storm should be determined clinically. The patient was diagnosed using the Burch Wartofsky Point Scale (BWPS) > 45 criteria or the Japanese Thyroid Association (JTA) category of thyroid storm 1 (TS1) or thyroid storm 2 (TS2) and systemic decompensation required immediate treatment. Clinical judgment needs to be made immediately to start therapy whether or not aggressive therapy is needed in patients with BWPS 25-44. Patients with thyroid storm should be treated using a comprehensive and multi-linear approach to treatment[25].

Table 4. The Burch-Wartofsky Point Scale (BWPS)[14,18]

Criteria	Point
Dysfunction of thermoregulation	
Temperature (ºC)	
37.2-37.7	5
37.8-38.3	10
38.4-38.8	15
38.9-39.3	20
39.4-39.9	25
≥40.0	30
Cardiovascular	
Tachycardia (beats per minute)	
90-109	5
110-119	10
120-129	15
130-139	20
≥140	25
Atrial fibrillation	
Absent	0
Present	10
Congestive heart failure	
Absent	0
Mild	5
Moderate	10
Severe	15
Dysfunction of the gastrointestinal and liver	
Manifestation	0
Absent	10
Moderate (diarrhea, abdominal pain, nausea/vomiting)	15
Severe (jaundice)	
Central nervous system disruption	
Manifestation	0
Absent	10
Mild (agitation)	20
Moderate (delirium, pyshosis, extreme lethargy)	30
Severe (seizure, come)	
Causative occurrence	
Status	
Absent	0
Present	10
Total Score	
>45	Thyroid storm
25-44	Impending storm
<25	Storm unlikely

The Burch-Wartofsky Point Scale (BWPS) score was 45, with tachycardia at 145 bpm scoring 25, diarrhea and nausea scoring 10, and precipitant history scoring 10. Below is the Burch-Wartofsky Point Scale (BWPS) table for diagnosing a thyroid storm.

In this instance, the report of a 22-year-old woman with Graves disease experiencing a thyroid storm was precipitated by an infection of community-acquired pneumonia. Relevant case reports by Dookhan *et al*. have previously identified pneumonia as a precipitant of a thyroid storm. *Streptococcus pneumoniae* was detected in a 34-year-old Caucasian female with hyperthyroidism using urine antigen testing since sputum gram stain was inconclusive owing to a lack of samples collected from patient [5]. Prabawa *et al.* published a case report of a thyroid crisis in a 28-year-old woman at 36 weeks and 2 days of pregnancy, which was caused by community-acquired pneumonia [6]. A 58-year-old lady with a multinodusa struma and an impending thyroid storm due to a community-acquired pneumonia infection was seen by Permana IGKA [7].

We treated the patient for thyroid storm using PERKENI (Perkumpulan Endokrinologi Indonesia) and ATA (*American Thyroid Association*) guidelines, which included appropriate intravenous fluid resuscitation and nutritional support, anti-thyroid (methimazole), antibiotics, steroid (hydrocortisone), beta-blockers (propranolol), and anti-hypertensive drug[25,26]. Lugol was not administered in this case because it was unavailable at the hospital.

Table 5 below describes thyroid crisis drugs along with their dosages and the mechanism of action of these drugs [14,25,26].

Table 5. Thyroid Storm : Drugs and Doses [14,25,26]

Drug	Dosing	Comment
Propylthiouracil	500-1000 mg load, then 250 mg every 4 hours	Prevent the synthesis of new hormones Prevent the conversion of T4 to T3
Methimazole	60-80 mg/d	Prevent the synthesis of new hormones
Propranolol	60-80 mg every 4 hours	Considering invasive monitoring in individuals with congestive heart failure High dosages of T4 inhibit T3 conversion. Alternative drug: esmolol infusion
Iodine (saturated solution of potassium iodine)	5 drops (0.25 mL or 250 mg) orally every 6 hours	Do not begin until 1 hour after taking antithyroids Inhibit hormone synthesis Prevent thyroid hormone releasing The alternative medication is Lugol's solution.
Hydrocortisone	300 mg intravenous load, then 100 mg every 8 hours	Could prevent T4-to-T3 conversion Prevention of relative adrenal insufficiency Dexamethasone is a substitute medication.

Since five days of therapy, the patient's clinical manifestations improved, her Burch-Wartsky score fell below 25, and she was revealed for outpatient settings.

One of the limitations of this case report is the absence of a repeat thyroid function test (FT4) after 4-6 weeks of medication and continued TSH monitoring if the FT4 is normal. Due to Boyolali's proximity to her place of residence and place of employment, the patient elected to continue treatment there after her first outpatient evaluation and sense of stability.

CONCLUSION

A thyroid storm is an uncommon and potentially fatal endocrinologic emergency that can be triggered by infections, including community - acquired pneumonia. We report a case of a 22-year-old woman with Graves disease experiencing a thyroid storm with a triggering factor was community-acquired pneumonia infection.

To diagnose a thyroid storm, we must first determine the hyperthyroidism state of the patient. Wayne's score is still useful for identifying hyperthyroidism based on clinical symptoms since test confirmation is often delayed. The Burch-Wartofsky Point Scale (BWPS) scores are used to diagnose thyroid storms.

Thyroid storm should be managed according to PERKENI (Perkumpulan Endokrinologi Indonesia) and ATA (*American Thyroid Association*). Broad-spectrum antibiotics can be used to treat community-acquired pneumonia. The patient's condition improved after treatment. To reduce the concomitant morbidity and mortality associated with this illness, early detection and treatment are critical.

The patient must be educated on the significance of medication adherence in Graves' disease, and she should not stop taking her medicine alone. Both the patient and the physician must be aware of the triggers of a thyroid crisis that might threaten the patient's health.

CONFLICT OF INTEREST

The authors reported no potential competing interests.

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