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Co-Incidence of Diabetic Ketoacidosis and Thyroid Crisis at Klungkung Regional General Hospital

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Abstract: Diabetic ketoacidosis (DKA) is a complication of diabetes mellitus characterized by uncontrolled of hyperglycemia, metabolic acidosis and increased ketone concentrations in the body. Thyroid crisis is one of the acute and life-threatening complications of hyperthyroidism where the symptoms involve multi-organ systems. The coincidence of DKA with Thyroid Crisis is rare and the pathophysiology of this coincidence is not well known and is still widely debated. Early recognizing and managing both emergencies will improve the success of patient management. In these case report there is a coincident of DKA and thyroid crisis at Klungkung Regional General Hospital. **Case Report:** KS, female, 57 years old came to the emergency room of RSUD Klungkung with the main complaint of nausea and vomiting accompanied by shortness of breath, cough with yellow phlegm and fever since 5 days ago. Other complaints were weakness, dizziness, and palpitations. The patient has a history of DM since 3 years ago and is routinely treated using basal and prandial insulin. Thyroid disease was known since 6 months ago and routinely took Tiamazol, but since 5 days ago the patient stopped the medication because he felt weak and ate little because of complaints of nausea and vomiting with concerns that blood sugar was falling. On examination of vital signs the patient appeared very ill, consciousness E3V4M6 appeared agitated. Blood pressure 130/80 mmHg, pulse 102x/min. Respiratory rate 28x/min seemed fast and deep breaths, axillary temperature 390C with oxygen saturation 89% room temperature and 98% with oxygen 4 liters per minute nasal cannul. On auscultation of the lungs, coarse rhonki sound in the right and left paracardial confirms the clinical pneumonia. On laboratory examination, hyperglycemia was found, with blood glucose (BS) 456mg/dL, urinalysis results obtained ketones +3 and glucose +3. The results of blood gas and electrolyte analysis showed metabolic acidosis at pH 7.17, PCO2 19.0mmHg, HCO3- 7.0 mmol/L, BE (B) -22mmol/L and Potassium 5.4mmol/L. FT4 was 29.87 pmol/L and TSH <0.10 uIU/mL with a Burch Wartofsky score of 55 supporting the diagnosis of thyroid crisis. The patient was admitted to the intensive

care unit with the management of hydration to overcome fluid and electrolyte balance disorders, blood glucose regulation with rapid insulin drip, administration of thyroid hormone activity antagonists and management of pneumonia with adequate antibiotics. **Discussion:** DKA and thyroid crisis are two separate events and their co-occurrence is rare. Both are life-threatening conditions that if not treated promptly will lead to death. The pathophysiology of the coincidence of DKA and thyroid crisis is unknown and debated. One theory states that thyrotoxicosis will change carbohydrate metabolism and increase insulin resistance by increasing glycogen breakdown in the liver, while uncontrolled glucose production will increase metabolic damage. Management of this coincidence requires tight regulation of the patient's glucose levels as the administration of corticosteroids in the management of thyroid crisis runs the risk of increasing glucose levels and thus aggravating the patient's DKA condition. **Conclusion:** A case of DKA coincidence with thyroid crisis triggered by pneumonia in a 57-year-old woman at RSUD Klungkung has been reported. By correcting fluid and electrolyte balance disturbances, tight blood glucose regulation, administration of antithyroid and corticosteroids at optimal doses and handling pneumonia with adequate antibiotics gave good results to the patient.

Keywords: DKA, Thyroid crisis, Coincidence

INTRODUCTION

Diabetic ketoacidosis (DKA) is a complication of diabetes mellitus characterized by uncontrolled hyperglycemia, metabolic acidosis and increased ketone concentrations in the body. This condition is a life-threatening emergency. The triggers include infection, newly diagnosed diabetes, or discontinuation of treatment that results in uncontrolled glucose levels. This condition is generally more common in Type 1 DM (T1DM) but is not uncommon in Type 2 DM (T2DM). The incidence of T2DM in Indonesia is estimated between 6-8% of total population while the incidence of DKA ranges from 0 to 56 per 1000 people per year. Based on gender and race, the incidence of DKA is higher in women and non-whites with a mortality rate of more than 5% has been reported in elderly patients and those with comorbid diseases.

Thyroid crisis is one of the acute and life-threatening complications of hyperthyroidism caused or triggered by uncontrolled hyperthyroidism, discontinuation of antithyroid drugs, surgery, infection, trauma or metabolic disturbances which symptoms involve multi-organ systems and if not treated properly will cause irreversible damage to the cardiovascular system and cause death with a mortality rate ranging from 8-25%.

Thyroid crisis is a rare hyperthyroid event. It is found in 1-2% of hospitalized hyperthyroid patients. The incidence in the United States ranges from 0.57-0.76 cases per 100,000 people per year.

DKA and thyroid crisis are two life-threatening emergencies. DKA can be caused by thyroid storm and vice versa. Although this coincidence is rare, these conditions are potentially life-threatening if not recognized and treated as quickly as possible. So early recognizing and managing these two emergencies will improve patient outcomes.

Case Report

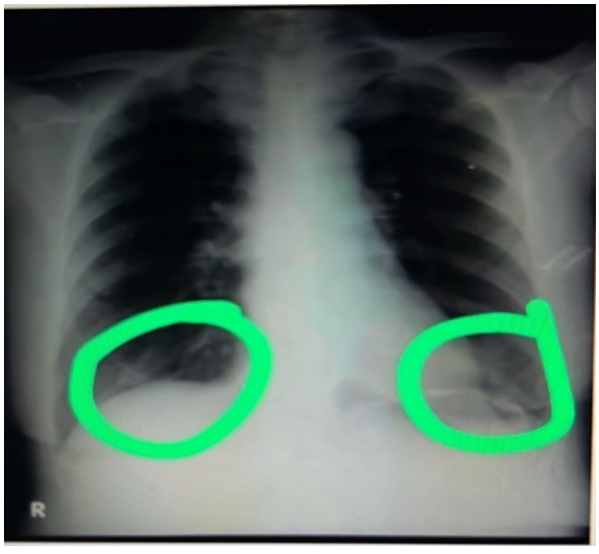
KS, a 57-year-old female, came to the emergency room of Klungkung General Hospital with complaints of nausea accompanied by vomiting since 5 days and worsened one day before admitted. Frequency of vomiting >10 times per day, containing food consumed, no blood or

blackness, black stools denied abdominal pain was also denied. The patient also complained of eating and drinking very little. Shortness of breath began to be felt since 1 day before admitted, did not improve with a change in position and was accompanied by a cough with yellowish phlegm. The patient also complained of fever since 5 days up and down accompanied by complaints of weakness, dizziness and palpitations without complaints of chest pain. Defecation and urination are within normal limits.

The patient has a history of DM since 3 years earlier and thyroid disease since 6 months ago and routine control at the Internal Medicine Polyclinic of Klungkung Hospital. With treatment is basal insulin injection of 18 IU every night and prandial insulin 6 IU every morning, afternoon and evening meal but since 5 days ago both insulins have not been injected because the patient's eating and drinking is greatly reduced with concerns about hypoglycemia. For hyperthyroid medication history, the patient routinely takes tiamazol 10 mg once a day and propranolol 10 mg twice a day. These two hyperthyroid medications were also not taken by the patient because since 5 days the patient felt weak. On vital signs examination, the patient appeared to be very ill, appeared agitated with consciousness E3V4M6. Blood pressure 130/80 mmHg, with a pulse rate of 102x/min regular and strong lift. The patient's respiratory rate was 28x/min seemed fast and deep breaths, axillary temperature 39^0C with oxygen saturation 89% at room temperature and 98% with oxygen 4 liters per minute nasal cannul. The patient is 162cm tall and weighs 60kg with a BMI of 22.86kg/m2 and normal nutritional status. On lung auscultation, coarse rhonki sound was found on the right and left paracardial.

Routine blood tests obtained Hb 15.0g / dL (N: 10.8-16.5 g / dL), WBC 8.32 thousand / µL (N: 3.5-10 thousand / µL) hematocrit 47.1% (N: 35-55%) platelets 168 thousand / µL (N: 145-450 thousand / µL). Liver function examination showed SGOT 19U/L (N: 8-37 U/L) SGPT 23 U/L (N: 13-42 U/L). The renal function examination showed ureum 25mg/dL (N: 10-50mg/dL) creatinine 0.5mg/dL (N: 0.6-1.2mg/dL).

The electrolyte examination showed Na 136 mmol/L (N: 135-145mmol/L) K 5.4mmol/L (N: 3.5-4.5mmol/L) and Cl 94mmol/L (N: 95-105mmol/L). GDS test results were 456mg/dL (N: 80-200mf/dL). routine urine showed ketones +3 and glucose +3. Blood gas analysis showed pH 7.17 (N: 7.35-7.5) PCO2 19.0mmHg (N: 35-45mmHg) HCO3- 7.0 mmol/L (N: 22-26 mmol/L) BE (B) -22mmol/L (N: (-2)-(+2)mmol/L) suggesting metabolic acidosis. FT4 examination was 29.87 pmol/L (N: 9-22pmol/L) and TSH <0.10 uIU/mL. The ECG showed sinus tachycardia with a rate of 102x/min. The thorax photograph showed 50% CTR and infiltrates on the right and left basal and paracardial areas suggestive of pneumonia.



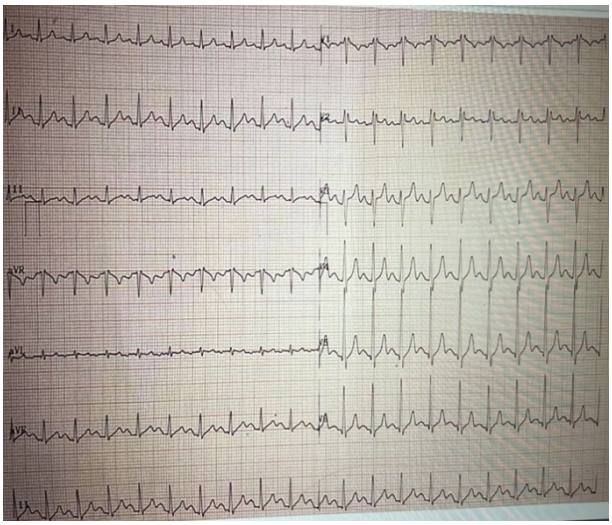


Figure 1. Thorax photo dan patient ECG

From the history, physical examination and support, the patient was diagnosed with diabetic ketoacidosis (DKA) with thyroid crisis pneumonia and mild hyperkalemia.

The patient was treated in the Intensive Care Unit (ICU) room by providing oxygenation therapy with a target oxygen saturation of >95%, hydration by loading 0.9% NaCl fluid 2L in 2 hours followed by 30 drops per minute. Because the patient's potassium level was 5.4, blood glucose regulation was immediately continued with rapid insulin drip according to the protocol and the patient was fasting during rapid insulin drip. Other therapy was given proton pump inhibitor (PPI) Esomeprazole 40mg every 12 hours IV, antiemetic ondancetron 4mg every 8 hours IV. For the management of pneumonia, antibiotics levofloxacin 750mg every 24 hours IV and ceftriaxon 1 gram intravenously every 12 hours, antipyretic paracetamol 500mg every 8 hours PO, mucolytic N-acetyl cystein 200mg every 8 hours PO. While for the management of thyroid crisis, PTU 100 mg every 4 hours, lugol iodine solution was not available so it could not be given, hydrocortisone 100mg IV every 6 hours and propranolol 40 mg every 6 hours PO. The patient was planned for a repeat electrolyte AGD after 6 hours of the first AGD. After 12 hours of rapid insulin drip, blood sugar reached 124mg/dL and ketone negative so rapid insulin drip was stopped. One hour before the drip was stopped, 10 IU basal insulin was given and continued with 4 IU prandial insulin every 8 hours.

The patient was treated for 3 days in the ICU and 2 days in the regular ward. On the first day of treatment in the ICU, the patient still complained of nausea vomiting palpitations and fever. The results of repeated AGD obtained metabolic acidosis improved with pH has increased to 7.26. On the second day of follow-up in the ICU room, complaints of nausea began to decrease and there were no complaints of palpitations. Shortness of breath was reduced and there was no fever. On the second day, AGD re-examination was obtained normal results. Fasting blood sugar 250 mg/dL and 330 in post prandial, ketone urine is negative so that the basal insulin dose is increased to 12 IU every 24 hours and prandial insulin 8 IU with 35kcal/kgBB DM diet nutrition.

On the third day of treatment, complaints of nausea and vomiting were reduced, shortness of breath was also reduced and fever was absent. Fasting blood sugar results 240 mg/dL and post prandial 295, basal insulin dose was increased to 18 IU SC every 24 hours and prandial insulin 12 IU. On the fourth day the patient was transferred to the regular room. Complaints of nausea and vomiting were reduced, there were no more complaints of palpitations, tightness, and fever. Fasting sugar was 195 mg/dL and post prandial 260 mg/dL and hydrocortisone therapy was stopped on day four while PTU dose was reduced to 100 mg every 8 hours and propranolol 20 mg every 6 hours.

RESULT AND DISCUSSION

DKA and thyroid crisis are two separate events, but both are life-threatening conditions that if left untreated will lead to death. The pathophysiology of the coincidence of DKA and thyroid crisis is unknown and debated. One theory is that thyrotoxicosis will alter carbohydrate metabolism and increase insulin resistance by increasing glycogen breakdown in the liver, while uncontrolled glucose production will increase metabolic damage.[9]

DKA is one of the complications of diabetes mellitus which the American Diabetes Association (ADA) defines as a triad condition consisting of ketonemia, hyperglycemia and acidosis.[3]

There are several etiologies or precipitating factors in DKA, namely catabolic stress due to acute illness or injury such as trauma, surgery, or infection, medication non-compliance, and new

diabetics. In this patient there was a history of discontinuation of T2DM medications for 5 days and the patient also had pneumonia. Both of these were triggers in this patient where it is stated that the most common infections found as causes of DKA are pneumonia and urinary tract infections which account for between 30% to 50% of cases.

In this patient, insulin withdrawal also triggered DKA. Insulin plays a role in lowering plasma glucagon levels and also decreases hepatic glucose production by inhibiting glycogenolysis and gluconeogenesis. Glucose uptake by skeletal muscle and adipose tissue may be enhanced by insulin. Both of these mechanisms result in a decrease in blood glucose. In diabetic ketoacidosis, insulin deficiency and increased counter-regulatory hormones can lead to increased gluconeogenesis, accelerated glycogenolysis, and impaired glucose utilization. This will eventually lead to increasingly severe hyperglycemia. Insulin deficiency and increased counter-regulatory hormones also lead to the release of free fatty acids into the circulation from adipose tissue (lipolysis), which undergo hepatic oxidation of fatty acids to ketone bodies (beta-hydroxybutyrate and acetoacetate), resulting in ketonemia and metabolic acidosis.

Pneumonia infection accompanied by DKA and discontinuation of thyroid therapy are likely to be the triggers for Thyroid Crisis to occur in this patient. There was an increase in thyroid hormone levels of FT4 29.87 pmol/L (N: 9-22pmol/L) and TSH <0.10 uIU/mL. In the study, there are several conditions or factors that trigger a thyroid crisis, which is sudden discontinuation of antithyroid drugs, surgery either on the thyroid gland or other organs, trauma, infection, DKA, and cardiovascular disease.

Criteria	Points
Thermoregulatory dysfunction	
Temperature (°C)	
37.2–37.7	5
37.8–38.3	10
38.4–38.8	15
38.9–39.4	20
39.4–39.9	25
≥ 40.0	30
Cardiovascular	
Tachycardia (beats per minute)	
100–109	5
110–119	10
120–129	15
13–139	20
≥ 140	25
Atrial fibrillation	
Absent	0
Present	10
Congestive heart failure	
Absent	0
Mild	5
Moderate	10
Severe	20
Gastrointestinal-hepatic dysfunction	
Manifestation	
Absent	0
Moderate (diarrhea, abdominal pain, nausea/vomiting)	10
Severe (jaundice)	15
Central nervous system disturbance	
Manifestation	
Absent	0
Mild (agitation)	10
Moderate (delirium, psychosis, extreme lethargy)	20
Severe (seizure, come)	30
Precipitating event	
Status	
Absent	0
Present	10
Total score	
> 45	Thyroid storm
25–45	Impending storm
< 25	Storm unlikely

Figure 2. Pathogenesis of DKA

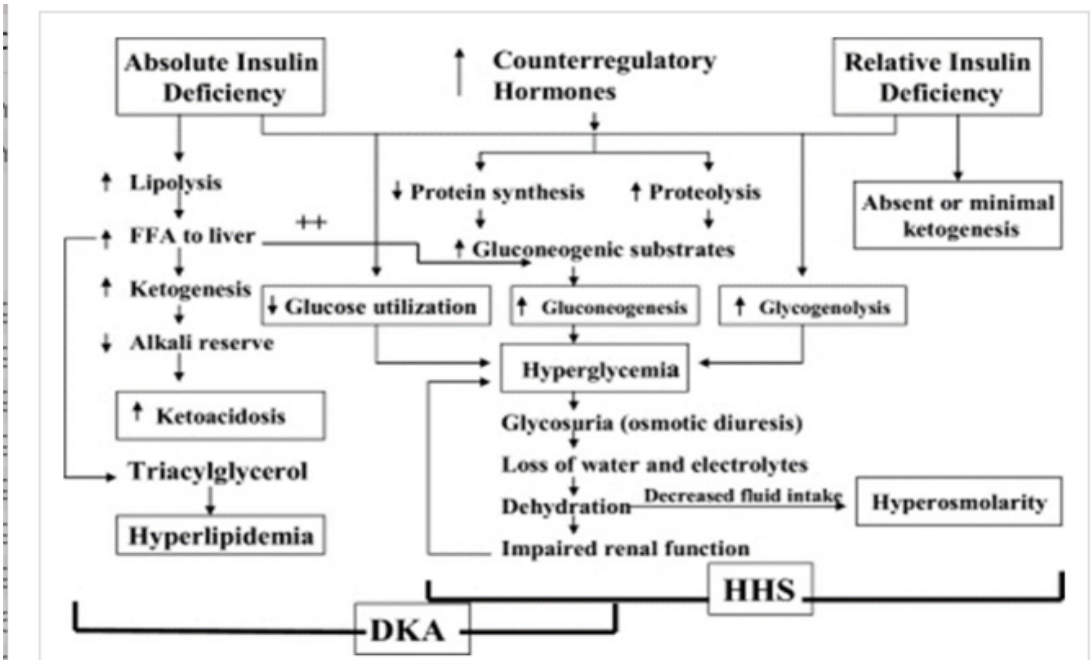


Figure 3. Burch-Wartofsky scale

The clinical symptoms in this patient were due to overexpression of thyroid hormones, namely increased metabolic activity and increased oxygen demand, causing tachycardia, shortness of breath and altered mental status. These conditions are consistent with those experienced in the patient, namely tachycardia with a rate of 102x/min, an increase in the respiratory rate of 28x/min and changes in mental status. The diagnosis of thyroid storm is based on clinical findings and not only on the severity of thyrotoxicosis. The Burch-Wartofsky Point Scale (BPWS) helps assess the likelihood of thyroid storm independently of thyroid hormone levels by assigning numerical values to specific clinical signs and symptoms. These criteria include hyperpyrexia, tachycardia, arrhythmia, congestive heart failure, agitation, delirium, psychosis, stupor, and coma, as well as nausea, vomiting, diarrhea, liver failure, and the presence of an identified precipitant. Points in the BWPS system are based on the severity of an individual's manifestations, with a point total of ≥45 consistent with a thyroid storm, 25-44 points classified as an impending thyroid storm, and <25 points making a thyroid storm likely. Based on the buch wartofsky scale this patient showed a score of 55 points which was interpreted as having a thyroid storm.[8,9]

Common clinical symptoms of DKA are weakness, dehydration, tachycardia, hypotension and in severe cases, shock. Dull, acetone-smelling breath, nausea and vomiting and abdominal pain are also common in DKA patients due to ketosis and acidosis. Fever may occur in patients due to infection. The neurological status of DKA patients varies greatly from fully conscious to lethargy and coma. The cause of altered mental status in patients with DKA is still unknown but pH changes in acidosis are suspected to be the main cause. It is believed that changes in mental status are caused more by changes in pH rather than changes in blood glucose levels.[10,11]

In the potassium examination, the patient obtained an increase of 5.4mmol/L, hyperkalemia in this patient was due to metabolic acidosis with a pH of 7.17. In KAD, potassium levels can vary from normal to elevated. In patients who experience metabolic acidosis will cause an increase in

H +, and to compensate the body will pump K + out and enter H +. thus causing hyperkalemia in the extracellular.

In patients with DKA, fluid deficit can reach 10-15% of body weight. Immediate fluid resuscitation is essential to correct hypovolemia, restore tissue perfusion, and clear ketones. Hydration also helps improve glycemic control independent of insulin.[1] The first choice of therapy is isotonic fluids where in this patient 0.9% NaCl was chosen with 15-20ml/KgBB administration for 1 hour. This patient received loading NaCl 0.9% 2L in 2 hours followed by 30 drops per minute because in the first 1 hour the patient's blood sugar was still high so the NaCl administration was repeated for up to 2 hours and the total loading became 2L. Furthermore, the patient's fluid was given maintenance 30 drop per mnutes to replace the fluid and sodium deficit that the patient could experience for 12-24 hours.

The patient also received antibiotic therapy, levofloxacin and ceftriaxon for pneumonia infection which is one of the triggers of DKA. Where floroquinolone antibiotics are the first line of therapy in hospitalized patients with pneumonia. And also given a combination of ceftriaxon 2x1gr which is a 3rd generation cepalosporin. In addition, appropriate and adequate antibiotic administration is also believed to reduce mortality rates in DKA patients.

Blood glucose regulation is critical in the co-occurrence of DKA and Thyroid Crisis. In this patient, insulin drip was administered with a target blood glocose reduction of 50-75mg/dL/hour and a maintenance blood glucose target of 140-180mg/dL. Previous treatment protocols recommended an initial bolus of 0.1 U/kg, followed by an infusion of 0.1 U/kg/hour. A more recent randomized prospective trial showed that boluses were not necessary if patients were given hourly insulin infusions at a dose of 0.14 U/kg/hour. In this patient, insulin drip of 6IU was immediately given and insulin levels were checked every hour until after 8 hours of insulin drip, the patient's blood glocose was 197mg/dL and insulin drip was replaced with basal and prandial insulin.[1] After insulin drip was stopped, the patient was given basal and prandial insulin, at basal 10 IU and prandial 4 IU and monitoring was carried out the next day for fasting and post prandial blood sugar checks. This is in accordance with insulin therapy guidelines where basal is given 5-10 IU / day and can be adjusted by 10-15% or 2-4 IU. As for prandial insulin, the initial dose can start with 4 IU or 0.1IU / kgBB or 10% of the basal dose for adjustment can be given 10-15% or 1-2 IU. Furthermore, close monitoring of patients is carried out to see signs of resolution in DAK, which is evidenced by blood sugar <200mg/dL, serum bicarbonate ≥15 mEq/L pH>7.3, and anion gap ≤12 mEq/L.1,15,16

For the management of thyroid crisis in this patient, PTU 100mg every 4 hours, propanolol 10 mg every 12 hours and hydrocortisone 2x100mg were given. PTU was chosen because PTU prevents the conversion of T4 to T3 in the periphery. Beta blocker therapy, namely propranolol in this patient, was given to overcome the patient's tachycardia condition, besides that propranolol can also inhibit type 1 deiodinase thus reducing the conversion of T4 to T3, lower dose was given as the initial dose to avoid vascular colapse in this patient.

Corticosteroids will inhibit the conversion of T4 to T3 in the periphery so that it will provide a better outcome. Hydrocortisone is an option in this patient given 100mg every 6 hours and can be continued until the symptoms of thyroid crisis disappear. This patient was given 100mg of hydrocortisone every 6 hours, on day two tapering was done to 100mg every 12 hours and the administration of hydrocortisone was stopped on day four because the symptoms of thyroid crisis were no longer found in the patient.

The administration of corticosteroids in the management of thyroid crisis will increase the patient's glucose levels so it is necessary to monitor blood glucose levels closely along with dose

adjustments in the administration of insulin therapy. In patients receiving steroid therapy, hyperglycemia management is recommended using basal and prandial insulin and adjusted to the results of blood glucose result where the initial dose is recommended to be 10IU and can be increased up to 10-20% according to the results of the patient's blood glucose test.

CONCLUSION

A 57-year-old female patient was reported to have coincident DKA with thyroid crisis triggered by pneumonia. The patient was treated for DKA and thyroid crisis as both conditions are life-threatening emergencies. Tight blood glucose regulation was performed on the patient as corticosteroid administration in thyroid crisis can increase the patient's blood glucose. By correcting fluid and electrolyte balance disorders, tight blood glucose regulation, administration of atintyroid and corticosteroids at optimal doses and handling pneumonia with adequate antibiotics, the patient had a good outcome.

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