Paediatrica Indonesiana

p-ISSN 0030-9311; e-ISSN 2338-476X; Vol.63, No.2(2023). p.155-9; DOI: 10.14238/pi63.2.2023.155-9

Case Report

Hyperthyroid crisis with cholestasis in a 12-year-old girl: a case report

Celine Celine, Ni Made Dwiyathi Utami

Hyperthyroidism is considered to be an emergency in children. Death can occur in 10-20% of cases. This condition is found more often in adolescents and girls. Cholestasis may be caused by the hyperthyroidism or side effects of anti-thyroid drugs. Increased hepatic blood flow without adequate oxygen supply as a result of a hypermetabolic state affects the transport of bilirubin, leading to cholestasis. **[Paediatr Indones. 2023;63:155-9; DOI: 10.14238/pi63.2.2023.155-9**].

Keywords: hyperthyroid crisis; cholestasis; children; case report

A thyroid crisis is an emergency situation in children. Graves' disease is the most common cause of hyperthyroidism in children, and occurs because of the presence of antibodies to the TSH receptor, which stimulate excessive thyroid hormone production. The prevalence of Graves' disease was found to be 1 per 10,000 children in the United States. Death can occur in 10-20% of cases. This condition is mostly found in adolescent girls.[1,2]

Hyperthyroidism has been associated with liver function abnormalities, however, cholestasis as the presenting feature of pediatric Graves' disease has not been previously reported. Impaired liver function and cholestasis, though not yet fully understood, can be caused by either hyperthyroidism or the use of anti-hyperthyroid drugs. Increased hepatic blood flow without an adequate oxygen supply as the result of hypermetabolic conditions affects bilirubin transport, leading to cholestasis.[3] Once hyperthyroidism is controlled, cholestasis will improve.

Management of Graves' disease includes anti-hyperthyroid drugs, use of radioactive iodine, and/or surgery. Propylthiouracil (PTU) and methimazole are commonly used as first-line anti-hyperthyroid therapy. Past studies do not recommend the use of PTU in children because of its hepatotoxic effect.[4,5]

The case

A twelve-year-old girl was brought to Karitas Waitabula Hospital, Southwest Sumba, East Nusa Tenggara, by her parents with a lump in her neck as her chief complaint. The lump had enlarged over the past one year and was accompanied by palpitations, protruding and yellowish sclera, nausea and anorexia for the previous three months, as well as weight loss. She had no history of fever and similar symptoms in her family history were denied.

On physical examination, the child's general condition appeared to be moderately ill and fully

From Karitas Hospital Southwest Sumba, Southwest Sumba, East Nusa Tenggara, Indonesia.

Corresponding author: Celine, Karitas Hospital, Jalan Bulgur No.01, Tambolaka, Southwest Sumba, Telp. +62 8118450951; Email: celinesiauw20@gmail.com

Submitted March 23, 2021. Accepted April 10, 2023.

alert. She had tachycardia (heart rate 130 beats/min), tachypnea (respiratory rate 26 times/min), and subfebrile axillary temperature of 37.8°C. The girl was malnourished, with 23 kg body weight and 137 cm body height. Physical examination was remarkable for bilateral exophthalmos, icteric sclerae, a diffuse mass in the thyroid region (5 x 4 cm) that moved with swallowing, and hepatomegaly.

Laboratory examinations included complete blood count, liver enzymes, total serum bilirubin, direct serum bilirubin, and thyroid hormone tests. The results showed microcytic hypochromic anemia (hemoglobin 8.3 g/dL), negative malaria, non-reactive HbsAg, and elevated total serum bilirubin with direct hyper bilirubinemia (direct serum bilirubin 13.3 mg/dL). Thyroid hormone test results showed an increase in free T4 (FT4) > 7.77 ng/dL and TSH <0.005 IU/mL (**Table 1**).

Patient's electrocardiography result (**Figure 1**) showed normal position of the heart (axis 60-90°), sinus rhythm, tachycardia, PR interval within normal limits (0.14s), no abnormal morphology of P waves, QRS complex or T waves. No signs of ventricular hypertrophy. Significant ST images of elevation or depression were also not seen on the ECG results.

Table 1. Laboratory test results

Parameters	Value	Reference range
Hemoglobin, g/dL	8.3*	12-16
Hematocrit, %	24.1	35-45
Leukocytes, /mm^3	5,000	5-10,000
Erythrocytes, million/mm^3	2.66	4-5
Platelet count, /mm^3	153,000*	150,000-350,000
SGOT, μ/L	467*	6.7-8.6
SGPT, μ/L	268*	5-35
Total bilirubin, mg/dL	19.2*	0.1-1.2
Direct bilirubin, mg/dL	13.3*	0.1-0.4
Thyroid hormone		
FT4, ng/dL	>7.77*	1-2
TSH, IU/L	<0.005*	0.5-4.7

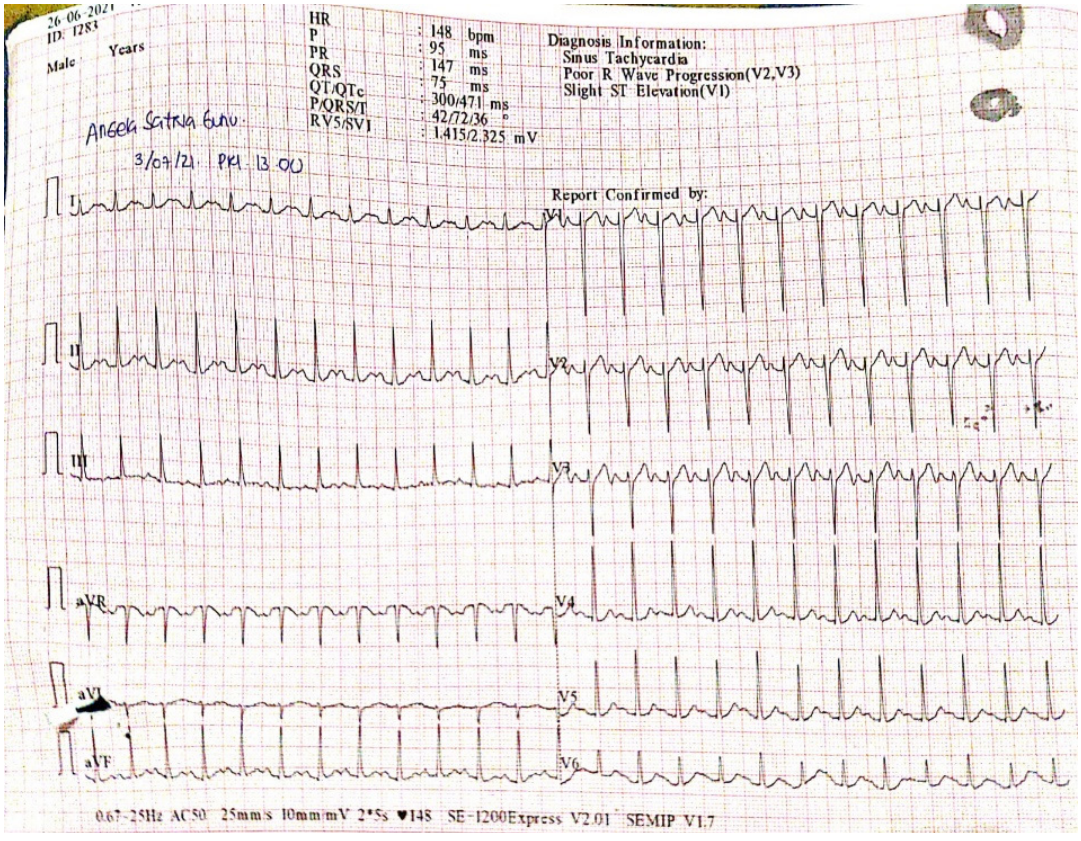

Figure 1. Patient's ECG

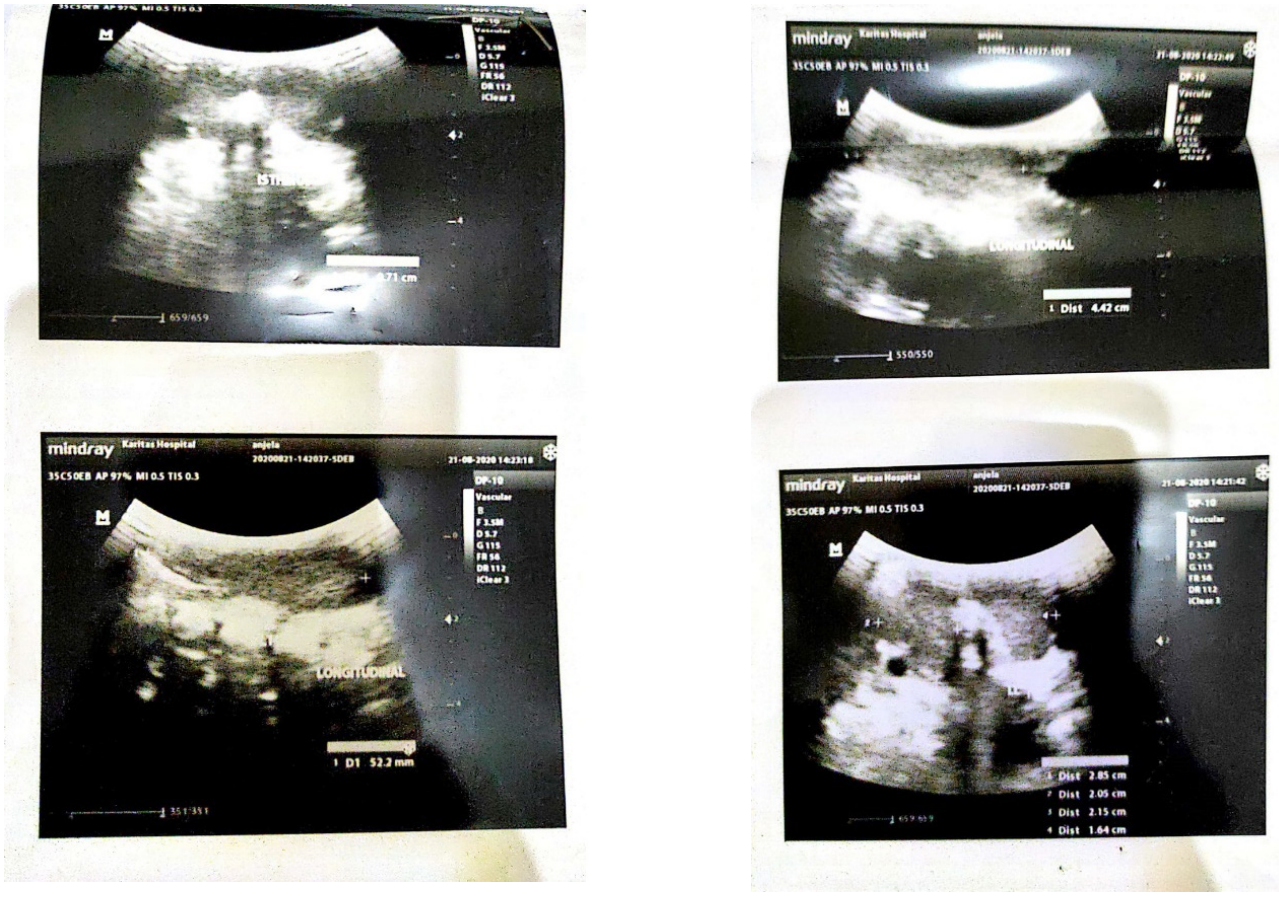

Figure 2. Thyroid ultrasound results using a curved probe

Thyroid ultrasound revealed diffuse enlargement of the thyroid with a right lobe size of 2.85 x 2.05 x 4.42 cm and a left lobe size of 2.15 x 1.64 x 5.22 cm (**Figure 2**). A liver ultrasound ruled out other etiologies for the hepatomegaly appreciated on the physical exam. Based on these findings, the patient was diagnosed with a hyperthyroid crisis with cholestatic jaundice. The patient was given PTU as an anti-thyroid agent 50 mg every 8 hours (7 mg/kg/day), propranolol 10 mg every 12 hours (1 mg/kg/day), ursodeoxycholic acid 250 mg every 8 hours (10 mg/kg/dose), and dexamethasone as glucocorticoid 5 mg every 8 hours (1 mg/kg/day; max dose 15 mg/day). The patient underwent treatment for 4 days in the hospital.

After discharged, patient routinely scheduled as pediatric outpatient clinic every week for clinical evaluation. Patient continued PTU and urseodeoxycholic acid for the treatment. The scleral jaundice and exopthalmos improved after 2 weeks for treatment (**Figure 3**). Patient was encouraged to do monthly visits for clinical and therapeutics follow-up.

Discussion

A thyroid crisis is a life-threatening condition as a result of a hypermetabolic state triggered by excessive thyroid hormone release. Hyperthyroidism is associated with impaired liver function, including increased transaminase enzymes, alkaline phosphatase, prothrombin activity, bilirubin as well as hypoalbuminemia. Increased hepatic blood flow and increased oxygen demand in hepatic tissue that is not fulfilled as a result of the metabolic conditions of hyperthyroidism can lead to liver cell damage. This condition then affects bilirubin transport, causing cholestasis.[3] Cholestasis can be progressive, as in our patient who had complaints for the previous 3 months. Due to economic, educational, and cultural factors, her family provided traditional medicines as first-line therapy and only sought treatment from the community health facility when her symptoms worsened.

Figure 3. The improvement in exopthalmos and scleral jaundice after two weeks of antithyroid treatment [3A=frontal view; 3B=side view]

Cholestasis in children can be caused by several etiologies such as infection, drug effects, genetics, immunology, metabolic problems, and malignancy. Our patient had no signs of infection such as fever and her laboratory test results showed no increase in white blood cells count. Liver infection and inflammation can be caused by parasites, including malaria and hepatotropic viruses such as Epstein-Barr virus, as well as hepatitis A, B, and C. HBsAg tests were performed to rule out hepatitis B infection, but hepatitis A and C examinations were not performed. Generally, cholestasis caused by viral infection of the liver appears in chronic cases and lasts 4-30 days, whereas in acute cases cholestasis symptoms improve within 2 weeks of treatment. A malaria examination was also performed with a negative result, since Southwest Sumba district is an endemic area.[6]

Our patient was diagnosed with a thyroid crisis using the Burch-Wartofsky scoring tool[7] based on clinical symptoms and laboratory findings including temperature 37.8°C (score 10), tachycardia 130 bpm (score 20), and jaundice (score 20), with a total score of 50 (> 45) (**Table 2**). The child had no central nervous system disorders or other precipitating factors.[2]

Cholestasis can also occur because of anti-thyroid agent use. Past studies showed high hepatotoxic effects in patients treated with PTU, so it is no longer recommended for children.[2,5] Methimazole (MMI) is currently the recommended anti-thyroid agent for children. However, in the absence of MMI, the Indonesian Pediatrics Society still recommends PTU to treat a thyroid crisis in order to block the conversion of T4 to T3. The recommended initial PTU dose is 5-7 mg/kg BW/ day divided into 3 doses,

Table 2. Thyroid crisis scoring[2]

Criteria	Patient condition	Score
Thermoregulatory dysfunction (body temperature	37.8°C	10
Central nervous system dysfunction	Absent	0
Cardiovascular dysfunction		
Heart rate	130 bpm	20
Atrial fibrillation	Absent	0
Congestive heart failure	Absent	0
Gastrointestinal and hepatic dysfunction	Unexplained jaundice	20
Precipitant history	Absent	0
Total score		50

followed up with close monitoring, especially of liver function. Other treatment choices, such as iodides, were not given because of unavailability, and the fact that radiotherapy is not recommended as first-line therapy in Indonesia.

Our patient had never taken PTU before this crisis, so the main cause of cholestasis was probably due to the hypermetabolic effects of the thyroid crisis. Follow-up results one week after hospital discharge showed clinical improvement in cholestasis, no jaundice, and no signs of acute liver injury, so PTU could be continued as anti-thyroid therapy. Our follow-up plan was to control the child's thyroid hormone levels and to establish the cause of the hyperthyroidism. The patient also routinely took her medication every month and showed good improvement.

The prognosis of a thyroid crisis can be good if the main cause can be clearly found and the patient undergoes regular treatment. Physicians should also consider other factors such as family financial status and family support, which might prevent the patient from receiving complete therapy.

In conclusion, a thyroid crisis is an emergency that should be treated immediately. Cholestasis can be found in thyroid crisis patients as a result of hypermetabolic conditions or hepatotoxic effects of anti-thyroid drugs. Rapid diagnosis and aggressive therapy are important to improve clinical outcomes from this potentially devastating illness.

Conflict of interest

None declared.

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