CASE ILLUSTRATION

Graves disease in a 16 year-old female: A case report

Ni Wayan Yuliandari,* I Made Arimbawa

ABSTRACT

Graves’ disease is an autoimmune disease originating from production of thyroid stimulating immunoglobulin leading to overproduction of thyroid hormone. Most Graves’ disease case reported to date are associated with adults, which makes extrapolation of the result to children and adolescents particularly challenging. A 16-year-old female presented with a slowly-enlarging painless mass in her front neck over a three-year period, sensation of food get stuck in the upper throat, lack of concentration and attentiveness, and fatigue. Thyroid ultrasound, thyroid function tests, thyroid peroxidase antibody, and thyroglobulin antibody tests revealed Graves’ disease. She takes 5 mg of Thiamazole once daily and shows improvement after four weeks.

Keywords: Graves’ disease, autoimmune, family history


INTRODUCTION

Graves’ disease is an autoimmune disease which is originated from production of Thyroid-Stimulating Immunoglobulins (TSI), which binds to Thyroid-Stimulating Hormone (TSH) receptor, leading to overproduction of thyroid hormone. This condition manifest as increasing level of blood T3 and free T4 hormone levels, with low or normal plasma TSH level.1-3 Most Graves’ disease cases reported to date are associated with adults, which makes extrapolation of the result to children and adolescents particularly challenging. Females are reported to suffer from this disease more commonly than men.1,4 Most Graves’ disease leads to several complications. These including enlargement of thyroid glands, severe ophthalmologic graves that possibly leads to blindness, and other complications reported were endocrinology and cardiology complications.4-7

Management of Graves’ disease including treatment using anti-thyroid therapy, radioactive iodine therapy and surgical thyroidectomy.2,8,9 Monitoring is mandatory as this is an autoimmune condition, and no exact finish line as the remission will achieved.

Herein, we reported a rare case of Graves’ disease which inflicts a female Indonesian adolescent. Despite this lack of reliable information to suit the case of our finding, the importance of proper early diagnosis for the disease remains crucial to give proper treatments.

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A 16-year-old female came to Sanglah Public Hospital on October 2016, presented with a slowly-enlarging painless mass in her front neck. This mass had grown over a three-year period. This mass initially was egg-sized, symmetrical in both side of
A 16 year-old female

Figure 1

Thyroid Ultrasonography (Result: Graves' Disease)

Figure 2

upper throat, but no swallowing difficulties, and no voice changes was complained.

She was also complaining lack of concentration and attentiveness. She also easily gets fatigue, but no complains of palpitation. She was still able to do her normal activity such as go to school and other social activity in her neighbourhood. But she tends to easily get tired when do excessive exercise. No complains of fever, cough, shortness of breathing, nausea, and vomiting. There were no complains of sudden body weight loss, no rash in face, nor hair easily removed.

She has menarche at 14 years old. Her menstrual period was regular every month, with duration 5-7 days each period. No history of hospital admission before this complain. Her perinatal history was unremarkable. Her immunization schedule was according to national immunization programme. She also has normal nutritional history, as well as her growth and developmental. She is the first born of three siblings. Her aunt had a history of struma treated by surgical management. She is now at the first year of senior high school in Badung regency.

On physical examination, she had normal blood pressure (120/80 mmHg), no tachycardia (98 beat/minute), no tachypnoea (20 times/minute) and normal body temperature (36.9°C). No exophthalmos was found. Her thyroid gland was palpable, enlarged with size of 8x5x2cm, mobile, not tender, warm and moist. No lymph node enlargement was found. Cardiovascular examination revealed a regular heart rate without murmur and gallop. Her pulmonary and abdominal examination was within normal limit. Her pubertal examination found she is on tanner 4. Her weight is 44 kg, height 158 cm, the Body Mass Index (BMI) is 17.8 and it is normal according to her age, and Waterlow Scale is 104% (well-nourished). Her Genetic Height Potential is within the mid-parental height (159.5 cm ± 8.5 = 151 cm – 168 cm).

We performed several examinations to establish the diagnosis and to find out her future management strategies. The admission of thyroid function tests were TSH 0.021 µIU/mL (normal 0.35-4.94 µIU/mL), T3 2.97 pg/ml (2.27-4.47 pg/ml), Free T4 1.94 ng/dL (normal 0.79-1.34 ng/dL), Thyroid Peroxidase Antibody (TPOAb) was positive 554.7 IU/ml (normal Negative IU/ml). Thyroglobulin Antibody (TgAb) 507 IU/ml (normal 0-40 IU/ml). Electrocardiography was normal. Thyroid ultrasound revealed Graves' disease.

Both physical and laboratory examination results indicate that the patient is inflicted with Graves' disease, a particularly rare case considering that most Graves' disease cases reported to date are associated with adults.
CASE ILLUSTRATION

These results prompted the author to treat the patient with 5 mg of Thiamazole once daily. The patient currently shows improvement in her condition after four weeks. Close monitoring of the disease and laboratory finding was done, as her condition is getting better and laboratory changes are presented on Table 1.

DISCUSSION

Graves’ disease is the most common cause of hyperthyroidism in children and is due to the effect of thyroid stimulating hormone (TSH) receptor stimulating antibodies which stimulate the thyroid to produce excess hormones. The incidence of Graves’ disease is believed to be between 0.1 and 3/100,000 children with a prevalence of 1 in 10,000 children in the United States. In Indonesia, the case is found approximately in 1/100,000 children. Female is predominantly affected by this disease. Familial inheritance also reported in several cases. The clinical manifestations of Graves’ disease are variably in many different age range. Although presenting symptoms are like the adult population in many ways, children and adolescents may present with non-specific symptoms that can be overlooked or attributed to normal changes children go through, such as nervousness, fatigue, sleep disturbances, or behavioral and learning disorders.

Graves’ disease is a common risk factor of hyperthyroidism. The laboratory result of this disease is low level of Thyroid Stimulating Hormone (TSH), high level of free T4 and low to normal level of blood T3.

Hwang et al. reported the time of normalization of T3/fT4/TSH had no significant correlations with other variables such as age, sex, a family history of thyroid diseases, thyroglobulin, thyroid-stimulating immunoglobulin, or antithyroglobulin antibody. Higher serological titers of Anti-microsomal Antibody (AMA) at diagnosis may have prognostic value in the response to initial methimazole treatment in pediatric Graves’ disease patients.

The various options for treatment of Graves’ disease in children include antithyroid drugs, radioactive iodine ablation, and thyroidectomy. In most centers, the majority of children with Graves’ disease are initiated on antithyroid drugs with Radio Active Iodine (RAI) ablation and surgery being reserved for children who do not achieve sustained remission with anti-thyroid drugs.

Anti-thyroid medications alone are not curative therapy, they simply mitigate the symptoms of hyperthyroidism until the Graves’ Disease goes into spontaneous remission or a definitive treatment is chosen. Considering the adverse effects of ATD especially fatal liver injury with propylthiouracil (PTU) and the fact that <30% of children achieve sustained remission with ATD, there is increase in the number of children subjected to RAI. Still, ATD forms the initial therapy for pediatric Graves’ disease in a significant proportion of subjects.
The recommended starting dose is 0.5–1.0 mg/kg/day for MMI and 5–10 mg/kg/day for PTU. In a study comparing low and high dose MMI (<0.5 mg/kg vs. >0.5 mg/kg), more subjects (82%) responded to the higher dose than the lower dose (42%). The medications are initiated at this dose and reduced every 4–8 weeks after documenting resolution of symptoms and thyroid function tests. In most patients with Graves’ Disease, there is early reduction of T3 and T4 to normal levels correlating with resolution of symptoms. Recovery of suppressed TSH to normal levels occurs gradually. Continued suppression of serum TSH in patients with Grave’s Disease during ATD treatment is related to thyroid binding inhibiting immunoglobulin, pre-treatment severity of hyperthyroidism, and time to normalization of serum T3 and T4.

The doses of ATD are progressively reduced and maintained at minimum doses required to maintain a clinical and biochemical euthyroid (Normal T3 and T4) for a period of 12–24 months. Following that the ATD is discontinued, and patient kept under follow-up for recurrence of symptoms. In the block and replace method, both ATD and thyroxine are supplemented to maintain euthyroid. However, this approach needs a higher dose of ATD and hence vulnerable to the adverse effects. The rate of remission in this approach is not superior to the traditional approach described above.

In the study by Rabon et al. reported 268 patients were started on an antithyroid drug and 23 underwent thyroid ablation or thyroidectomy. Fifty-seven (21%) children achieved remission and 16 (28%) of these patients relapsed, almost all within 16 months. Gender and ethnicity did not affect rates of remission or relapse. Of 251 patients treated with methimazole, 53 (21%) had an adverse reaction, including rash, arthralgias, elevated transaminases, or neutropenia. Most children with Graves’ disease treated with ATD do not experience remission, but most remissions do not end in relapse. Adverse reactions to methimazole are common but generally mild.

In our case, the patient treated with antithyroid drug, which is daily Thiamazole 5 mg. Along monitoring of the disease, the patient shows significant positive changes along the treatment. Her palpitation, and tachycardia relieves. The size of her thyroid gland initially reduced, and she start to have her body more relax, without disturbance of concentration in her daily activity. No adverse event was found on her.

Other therapeutic option in managing patient were surgical and radiotherapy. These two optional therapies usually considered when treatment with antithyroid therapy failed to achieve remission. In our case, the patient shows improvement after four weeks treatment with antithyroid drugs, thiamazole, that the surgical and radiotherapy option is not considered. In the future if the treatment of antithyroid drugs failed to relieve the disease, surgical or radiotherapy may decide.

Elfenbein et al. showed failure of antithyroid medications was the indication for surgery in 55% of the children vs 36% of adults (p=0.05). Mean duration of medications prior to surgery was similar. No children had failed Radioactive Iodine (RAI) therapy prior to surgery, but 12.5% of the adult population had (p=0.04). Surgical outcomes were similar. Clinicians may be more likely to refer children who fail medical treatment to surgery over RAI. Thyroidectomy at a high-volume hospital should be discussed as a treatment option for children with Graves’.

The study from Wu et al. showed a higher proportion of pediatric Graves’ Disease patients underwent thyroidectomy than 131I therapy. Rapid turnover suggested more effective initial management with operation than 131I therapy. Although transient operative complications were high, 131I therapy complications included worsening of Graves orbitopathy among those with pre-existing orbitopathy.

The natural history of untreated Graves’ disease in children is not well described. A patient is considered to be in remission if T3, T4, and TSH remain normal 1 year after discontinuation of antithyroid therapy. The remission rates in various studies. The remission rates in adults with Grave’s Disease seem to be variable with studies from US reporting it at 20–30% remission after 12–18 months of dedication. European study indicated a 50–60% remission rate after 5–6 years of treatment. The remission rates in children seem to be lower than in adults. Remission rates in children with Graves disease are around 20–30% and seem to be worse for patients with large glands, high antibody levels or very high free T4 levels at diagnosis. Younger children have lower remission rates and higher relapse rates than older adolescents and adult patients.

In our case, the patient showed clinical and laboratory improvement. Her clinical manifestations at her first admission relieve, as the laboratory result leading to normal level of thyroid function.

**SUMMARY**

Regardless the rarity of the cases, proper early diagnosis of the disease is of utmost importance to give the patient with the correct treatment, as illustrated promptly in a 16-year-old female patient. Both physical and laboratory examination results indicate that the patient is inflicted with Graves’ disease.
With 5 mg of Thiamazole once daily, she showed improvement in her condition after four weeks. Thyroid function monitoring is important since the diseases in an ongoing condition which needs lifelong treatment.

REFERENCES
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