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Case Report

An Indonesian adolescent with Turner syndrome and β-thalassemia in low-resource setting: A case report and literature review article

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ABSTRACT

Background: Turner syndrome and β-thalassemia very rarely occur together in an individual.
Case presentation: An Indonesian adolescent, 18 years old, complained is fatigue a week ago. She has a medical history of β-thalassemia for age 6 months and Turner syndrome identification for age 16 years. Meanwhile, she regular consumes deferasirox 500 mg every day. Physical examination showed pale conjunctiva and pale face. Body view similar children aged 13 years old. Laboratories investigation values included Hb of 7.7 gr/dL, MCV of 79.5 fL, MCH of 25.9 pg, MCHC of 28.6%, WBC of 6780/mm^3, PLT of 242,000/mm^3, AST of 15 U/L, ALT of 20 U/L, Ferritin of 1692.32 ng/mL, growth hormone of 0.468 ng/mL, Estradiol of <11.80 pg/mL, luteinizing hormone of 53.50 mIU/mL, and follicle-stimulating hormone of 115.19 mIU/mL. Chromosomal analysis showed Turner syndrome. The patient received a packed red cell transfusion of up Hb of 10 gr/dL, deferasirox 500 mg daily, and a contraceptive tablet. Due to financial issue in Indonesia, patient with Turner syndrome does not get proper hormonal therapy such as growth hormone, vitamin D supplementation, and other hormone replacement therapy.
Discussion: Turner syndrome and thalassemia in low-resource settings are challenges in themselves, so in their implementation, only thalassemia can be controlled, but for therapy, it does not show an improvement in prognosis.
Conclusion: Turner syndrome and thalassemia both worsen the patient's condition.

1. Introduction

Turner syndrome is a sex chromosome disorder that affects females. This abnormality affected 1:2500 female birth. More than half of Turner syndrome patients are diagnosed after 12–14 years old, with the main complaints being amenorrhea and lack of spontaneous pubertal signs [1]. However, thalassemia is an X-linked hereditary disorder that affects globin chain synthesis. This disease predominantly suffers people around the Mediterranean, Middle East, or Asia. In Indonesia, there are almost 2000 new thalassemia patients every year [2,3]. Cases of Turner syndrome and thalassemia are rare, and there are very few reports of such cases [4]. Based on the description above, we are interested in reporting an Indonesian adolescent with Turner syndrome and β-thalassemia. The report is based on the CARE guidelines [5].

2. Case presentation

An Indonesian adolescent, 18 years old, complained is fatigue a week ago. She does regular transfusions every two months due to β-thalassemia since she was six months old. Meanwhile, she regular consumes deferasirox 500 mg every day. When she was 16 years old, she had amenorrhea and breast, not growth, so some examination and chromosomal analysis showed Turner syndrome. None of the families had similar health problems to the patients.

Physical examination showed pale conjunctiva and a pale face. Anthropometric examination revealed a discrepancy between the patient's age and growth which a body weight of 26 kg, body height of 126.5 cm, BMI of 16.2 kg/m^2 (underweight), body surface area of 0.69 m^2, a chest circumference of 66 cm, chest width of 28 cm, nipple space of 18 cm, abdomen circumference of 64 cm, the pelvic circumference of 66 cm, arm length of 37 cm, and manus length of 8 cm. Physical condition similar child aged 13 years old. Laboratories investigation values

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included Hb of 7.7 gr/dL, MCV of 79.5 fL, MCH of 25.9 pg, MCHC of 28.6%, WBC of 6780/mm^3, PLT of 242,000/mm^3, AST of 15 U/L, ALT of 20 U/L, Ferritin of 1692.32 ng/mL, growth hormone of 0.468 ng/mL, Estradiol of <11.80 pg/mL, luteinizing hormone of 53.50 mIU/mL, and follicle-stimulating hormone of 115.19 mIU/mL.

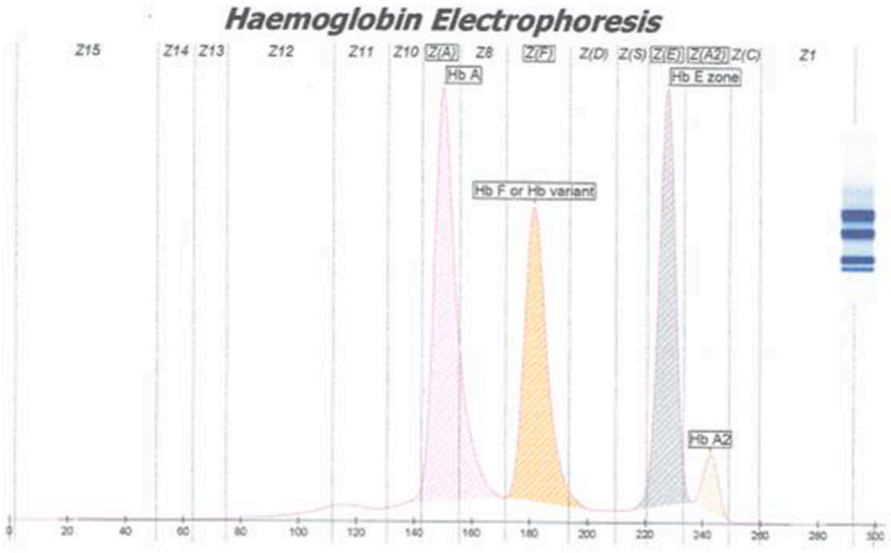
Abdominal ultrasonography showed her uterine size was 7 mm and cervix size was 2.9 mm. There were no cystic or solid lesions. The patient's bone age was similar to 13 years old girls when she was 16 years old. Every epiphyseal cartilago was thinner except in radius and ulna bones. Her intelligence quotient was 93, which is a low average level, her understanding ability was good, her verbal ability was enough, her motoric ability was good, her logical ability was enough, abstraction ability was poor, and her reasoning ability was enough. Her haemoglobin electrophoresis revealed increasing in HbF and HbE (Fig. 1). Chromosome analysis configuration was mos 46 X, idic(Y)(q11.22)[27]/45X [7]/47X, idic(Y)(q11.22)x2 [6]. Thus she was diagnosed with Turner syndrome (Fig. 2). She also went to echocardiography and revealed a secundum atrial septal defect left to right shunt, mild tricuspid regurgitation, and an ejection fraction of 69.30%.

She underwent two bags of packed red cells transfusion until her hemoglobin level reached 10 gr/dL, continuing deferasirox 500 mg daily for iron chelation agent and the contraceptive pill. The patient to regular blood transfusion every 2 months with average haemoglobin of around 7 gr/dL. The patient did not continue the contraceptive pill because she felt dizziness and nausea because of the side effect. Due to financial issue in Indonesia, patient with Turner syndrome does not get proper hormonal therapy such as growth hormone, vitamin D supplementation, and other hormone replacement therapy.

3. Discussion

Turner syndrome was diagnosed when there was a partial or complete absence of one X chromosome (45, X karyotype). It is a sex chromosomal disorder that affects 1/2500–3000 females. The variability of clinical manifestation usually includes short stature, a broad chest, widely spaced nipples, cubital joint cubital, called cubitus valgus, lymphedema, congenital, and lack of spontaneous pubertal development and ovarian sex hormone insufficiency. There are no maternal risk factors to estimate a baby with Turner syndrome. Characteristics of Turner syndrome in children are mentioned above, while amenorrhea is the main complaint that makes physicians seek Turner syndrome in teenagers. Short stature in tuner syndrome has been developed when the patient is still in intrauterine. The average height of Turner syndrome subjects without growth hormone therapy is about 143 cm or 20 cm shorter than the average population [6,7]. However, β-Thalassemia major is a hemoglobin hereditary disorder which results in impaired beta-globin chain synthesis. That such a disorder leads to hemolytic anemia. Typically, human haemoglobin contains heme and globin, built by two pairs of α chain and β chain. There are two genes involved in the production of hemoglobin. There are located at the short arm of chromosomes 16 for α chain and 11 for β chain. Thalassemia leads to the disorder of α and β chain biosynthesis, which decreases haemoglobin tetramer production. Usually, patients come with the main complaint of pallor or anemic, enlargement of the abdomen, and delayed growth. This complaint occurs in a six-months-old patient [2,3,8].

Girls with Turner syndrome have normal external genitalia while their ovarium is not function. Ovarian failure leads to decreased hypothalamus-hypophysis axis, marked by increased FSH and LH levels. Estrogen production is low due to gonadal dysgenesis, leading to a lack of spontaneous pubertal signs. Ultrasonographic imaging of the pelvic organs is essential to know about the maturation of the gonads. During childhood, the appearance of ovarian is in size from lining organs with fibrotic tissue. Evaluation of uterine development is also essential. Uterus was evaluated in length, volume and shape by the ratio of the upper to lower uterine [9]. Pharmacological growth hormone treatment is essential to optimizing stature. Consideration to give estrogen hormone therapy as soon as possible when the patient is of pubertal age usually allows the growth of long bone. The recommendation for estrogen hormone therapy is between the age of 12–15 years with low dose estrogen and increased gradually when feminization is reached.



Name	%	Normal Values %
Hb A	39.4	
Hb F or Hb variant	27.6	
Hb E zone	29.5	
Hb A2	3.5	

Fig. 1. Haemoglobin electrophoresis revealed that the patient suffers from Thalassemia HbE disease.

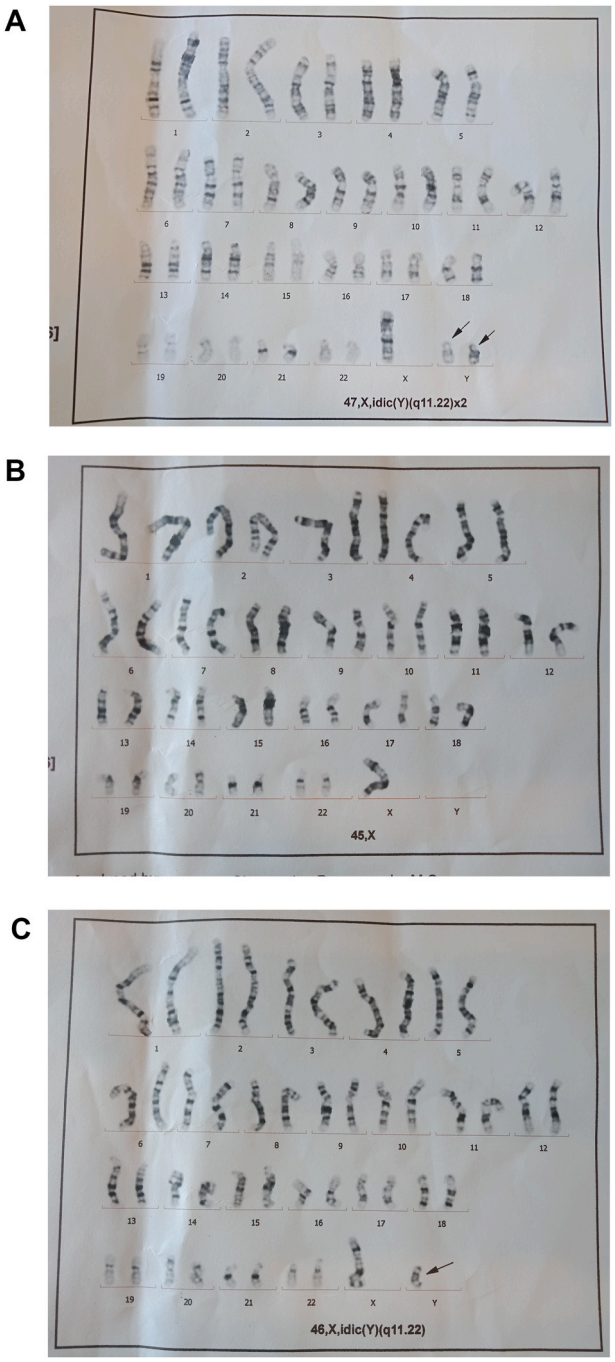


Fig. 2. Chromosome analysis showed isodycentric Y chromosomal abnormalities such as Turner syndrome.

Cyclic progestin is added after 12–24 months. The average age of initiation in community-treated patients was relatively late at almost 16 years of age to optimize stature by the effect of growth hormone [10,11]. Girls with Turner syndrome have average intelligence (mean full-scale IQ of 90); however, they usually have difficulty in nonverbal language, social, and psychomotor skills [6].

β-thalassemia major patient needs a regular transfusion to life survive. Iron chelator drugs that are available for clinical use such as desferrioxamine (DFO), deferiprone (DFP) and deferasirox (DFX). DFX is a once-daily oral iron chelator. It was introduced as first-line therapy for patients over 2 years of age with chronic iron overload due to blood transfusions in 2005. Some studies showed that DFX strongly affects liver iron and results in high patient compliance [12–14]. Multi disciplines management should be undergone for the patient with Turner syndrome. Psychosocial counselling is essential due to the short stature concerning school admission, failure to puberty problems and sterility. Severe thalassemia beta mayor is also characterized by growth retardation. Estrogen replacement therapy is essential to induce pubertal development, prevent osteoporosis, and reduce cardiovascular disease risk. Growth hormone therapy is given as soon as possible (12–24 months of age). The average adult height in Turner syndrome patients is 140 cm without hormonal therapy, while the mean adult height reaches 150 cm with growth hormone and estrogen therapy. Growth hormone therapy should be discontinued after the bone age patient is likely 14 years, while sex hormone therapy should be continued for a long time. Calcium and vitamin D supplements should be given to prevent osteoporosis starting at ten years old [15,16].

4. Conclusion

Multiple genetic disorders such as sex chromosome abnormalities and other gene disorders may appear with some overlapping clinical manifestations. Recognition of signs and symptoms may be confusing. Thus, we need molecular or chromosome analysis to diagnose the genetic disorder. Both Turner syndrome and β-thalassemia major patient needs a regular transfusion to live to survive thalassemia in this patient can worsen the clinical manifestation by each other.

Ethical approval

This case report does not require any ethical approval.

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Author contribution

All authors contributed to data analysis, drafting and revising the paper, giving final approval of the version to be published, and agreeing to be accountable for all aspects of the work.

Guarantor

Hermina Novida is the person in charge of the publication of our manuscript.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Consent

Written informed consent was obtained from the patient to publish this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Research registration

Not applicable.

Declaration of competing interest

Nila Maharani and Hermina Novida declare that they have no conflict of interest.

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