Case Report

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Turner Syndrome and Beta Thalassemia Major: A Rare Association

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Received: 31 July 2022 **Revised:** 24 September 2022 **Accepted:** 07 November 2022

ARTICLE INFO

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Keywords:
Turner syndrome;
β-thalassemia;
Transfusion;
Therapy

ABSTRACT

Background: Turner syndrome (TS) is the most common genetic disorder affecting only females. The criteria for diagnosis include the complete or partial absence of the second sex (x) chromosome (with or without cell line mosaicism) plus short stature and primary ovarian failure with or without the presence of other phenotypic TS features. The genotype in TS, as tested in peripheral blood, is most commonly 45xo. β-thalassemia major or transfusion-dependent thalassemia refers to severe β-thalassemia that requires early transfusion therapy. The association between Turner syndrome and thalassemia major is rare, which may result from transcription factor gene mutation.

Case Report: We report a girl with thalassemia major who was treated by recurring monthly transfusions since the age of six months. Short stature, triangular face, low set ear, hypertelorism, webbed neck, lordosis and genu valgum were observed in the examination. The patient was diagnosed with Turner syndrome, and her karyotype also was defined as 45xo.

Conclusion: In the case of Turner syndrome and β-thalassemia major association, a mutation in the transcription factor gene is proposed, which can be confirmed by genetic testing.

Introduction

Turner syndrome (TS) is caused by complete or partial monosomy of the x chromosome.[1] About half the patients with TS have a 45xo chromosome complement.[2,3] Turner syndrome occurs in 1 of 2000 to 4000 live female births.[4,5] It is also defined by a combination of phenotypic features. Small size for gestational age, webbed neck, protruding ears, and lymphedema of the hands and feet are the clinical signs of Turner syndrome. However,

many infants are phenotypically normal. Older children and adults have short stature and show variable dysmorphic features. Structural renal anomalies (60%) and congenital heart defects (40%) are common features of TS. Bicuspid aortic valves and coarctation of the aorta are the most common heart defects. Following gonads' replacement by fibrous streaks, primary amenorrhea and lack of secondary sex characteristics happen.[6] Chromosome analysis must be considered routinely in short females. Ultrasonography of the heart, kidneys, and ovaries is recommended after the diagnosis is established. Plasma levels of gonadotropins, particularly follicle-stimulating hormone (FSH), are markedly increased by 10-11 years of age.[7]

To detect autoimmune thyroiditis, thyroid function tests should be checked regularly. Measuring tissue transglutaminase immunoglobulin A antibodies, Turner syndrome females should be screened for celiac disease. Initial testing should be done around age four and repeated every 2-5 years.[7]

Treatment with recombinant human growth hormone increases height velocity in children with Turner syndrome. Replacement therapy with estrogens is indicated at 12-13 years.[7]

On the other hand, thalassemia represents a group of genetic disorders of globin-chain production resulting from an imbalance between α-globin and β-globin chain production.[8,9] β-thalassemia syndromes originate from a genetic deficiency in the synthesis of beta-globin chains. There are more than 200 different mutations leading to absent or decreased globin production. Inadequate β-globin gene production leading to decreased levels of normal hemoglobin (HbA) and unbalanced α and β-globin chain production leading to ineffective erythropoiesis are two related features that contribute to the sequelae of β-thalassemia syndromes.[3]

If not treated, children with homozygous β-thalassemia usually become symptomatic from progressive anemia during the 2nd 6 mo of life. Chronic transfusion therapy dramatically improves the quality of life and reduces the complications of severe thalassemia.

Transfusion induces hemosiderosis, which becomes the major clinical intricacy of transfusion-dependent thalassemia.[3]

Case Report

A four-year and seven-month-old girl with thalassemia major who was treated by recurring monthly transfusion since the age of six months had been referred to the endocrine clinic. Her parents were consanguineous. In the examination, triangular face, low set ear, hypertelorism, webbed neck, lordosis, and genu valgum were observed. Her weight and height were measured as 11kg (< 5%) and 91cm (< 5%, SDS = -3.5), respectively. The patient was diagnosed with Turner syndrome, and her karyotype was also defined as 45xo. Her kidney sonography, echocardiography, and thyroid were normal. The patient's laboratory tests for celiac disease were also negative. In the patient's follow-up examinations at ten years of age, her growth velocity was low, and the results of her paraclinical tests were as follows:

Table1. The Results of Paraclinical Test

Paraclinical tests of the patient		
LH		3.7 U/L
FSH		29.5 U/L
Estradiol		< 5 pg/ml
BMD	Lumbar spine	-3.1
	Femur	-3.5

Discussion

Turner syndrome (TS) is a rare chromosomal disorder affecting females and is characterized by short stature and lack of sexual development at puberty. Patients with TS have an abnormal karyotype involving the X chromosome.[10] Many patients with Turner syndrome are identifiable at birth because of a characteristic edema of the dorsum of the hands and feet. Low birth weight and reduced birth length are common. Characteristic appearance in childhood includes webbing of the neck, a low posterior hairline, a small mandible, prominent ears, epicanthal folds,

high arched palate, a barrel chest, widely spaced nipples, cubitus valgus and hyperconvex fingernails. The diagnosis is often first suspected at puberty when breast development fails. Short stature, the cardinal finding in all females with Turner syndrome, may be present with little in the way of other clinical manifestations.[11]

Our patient's karyotype was 45xo, and ultrasonography of the heart and kidneys was normal. The results of her thyroid and celiac disease were also normal. In follow-up at ten years, growth velocity was low and primary hypogonadism was diagnosed according to laboratory test results.

Thalassemia is a group of disorders resulting from an inherited abnormality of production of the globin moiety of hemoglobin. Thalassemia syndromes are characterized by varying degrees of ineffective hematopoiesis and increased hemolysis.[12]

Turner syndrome and thalassemia major association are rare, which may result from transcription factor gene mutation. Our patient was not investigated for genetic tests due to the high cost.

Conclusion

In the case of Turner syndrome and beta-thalassemia significant association, a mutation in the transcription factor gene is proposed, which can be confirmed by genetic testing.

Conflict of Interest

The authors have no conflict of interest.

Acknowledgments

The authors thank the patient’s family for their cooperation in this study.

The present study was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences (IR.SSU.REC.1401.070).

How to Cite: Mirhosseini NA, Mirhosseini S, Saeida-Ardekani M. Turner Syndrome and Beta Thalassemia Major: A Rare Association. World J Peri & Neonatol 2022; 5(2): 99-101.
DOI: 10.18502/wjpn.v5i2.11997

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