Case Report
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Sotos Syndrome: A Case Report

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Sotos syndrome is an overgrowth condition accompanied by macrocephaly, distinctive facial appearance and mental retardation. It usually occurs sporadically.

The aim of the current case report was to emphasize the necessity of detailed evaluation, including genetic testing, in patients who have overgrowth combined with other dysmorphic features.

Keywords: overgrowth, mental retardation, Sotos syndrome

Introduction

The syndrome which includes overgrowth, acromegaly and mild mental disabilities was described in 5 patients by Sotos, in 1964 [1]. Although, there had been reported six generation family members with Sotos syndrome inherited by autosomal dominant type, most cases of disorder are sporadic. Its estimated incidence is 1:10000-1:50000.

Diagnostic criteria of Sotos syndrome are receding forehead hairline, macrocephaly, frontal bossing, long narrow face, sparse hair, characteristic chin, distinctive facial appearance, advanced bone age, and mental retardation [2,3]. Patients usually have excessive occipitofrontal circumference. Eye symptoms are often presented by nystagmus and strabismus. Anomalies of skeletal, cardiovascular, central nervous and urogenital systems can be also detected. The skeletal features include scoliosis, large hands and feet. There are numerous cardiovascular findings which may be presented in form of hypotonia, trioventricular septal defect, ventricular septal defect, patent ductus anteriorus, and microvalval prolapses in tricuspid valve in 8 % of patients [4].

The morphological changes of the brain are detectable on MRI and include ventriculomegaly in 60-80% of patients and dysgenesis of corpus callosus. Impairment of cognitive functions such as learning disabilities and speech problems may also be observed.

Case Report

A 13 year and 8 month old male patients were admitted to the Department of Pediatric Endocrinology of 19 Mayis University for overgrowth. The state of excessive growth had been observed for the last two years. Increase in body weight was not observed. No other complaints like headache, nausea, vomiting, fatigue, joint pains, excessive perspiration, thirst, urination, vision impairment or smell disturbances were found.

There was no history of drug intake, specific infections or prenatal trauma. Patient's weight at birth was 4800 g; however the height was not recorded. He began to speak when he was 1 year old and walk when he was 4 years old. He underwent appendectomy, tonsillectomy and adenoidectomy. He has been under neurologist's control since school years because of difficulties in learning which was diagnosed as a slight mental retardation.

The family history revealed that the patient's uncles were quite tall. The heights of the parents were normal and recorded as 152.1 cm for mother and 182.3 cm for father.

Physical examination revealed dysmor-

phic features, including sparse hair, long narrow face, large nose and chin, prominent forehead, and large sized head. In addition to these, prognathism and high arched palate were found (Fig. 1). According to the patients' parents all these features has been observed since his birth.

His anthropometric values were as following: height 178 cm (<97th percentile) with z-score 2, and body weight 75.7 kg (<90th percentile), occipitofrontal circumference 57 cm (<97th percentile), calculated target height 173.7 cm with z-score -0.37, height age 18 years and skeletal age 14 years.

The results of biochemical blood tests, including levels of Na, K, Cl, glucose, creatinine, Ca, P, ALT and AST (aspartate and alanine transaminases), triglyceride, cholesterol, HDL and LDL (high and low density lipoproteins), thyroid hormones, prolactine, total testosterone, FSH (follicle-stimulating hormone), cortisol and ACTH (adrenocorticotropic hormone) were normal. However, growth hormones levels showed slight elevation: GH (growth hormone) 4.27* (range 0-3) ng/mL, GH (after 30 minutes) 5.64* (range 0-3) ng/mL, IGFBP-3 (insulin-like growth factor-binding protein) 7.25* (range 2.4-7.0) mg/mL, IGF (insulin-like growth factor) 1537 (range 183-850) ng/mL.

Genetic analysis using FISH (fluorescence in situ hybridization) method has revealed mutation of NSD-1 gene, located on chromosome 5, q35. Due to results of genetic analysis and characteristic clinic findings, i.e. dysmorphic features, mental retardation, high anthropometric values and exclusion of other causes of overgrowth, the patient was diagnosed to have Sotos syndrome.

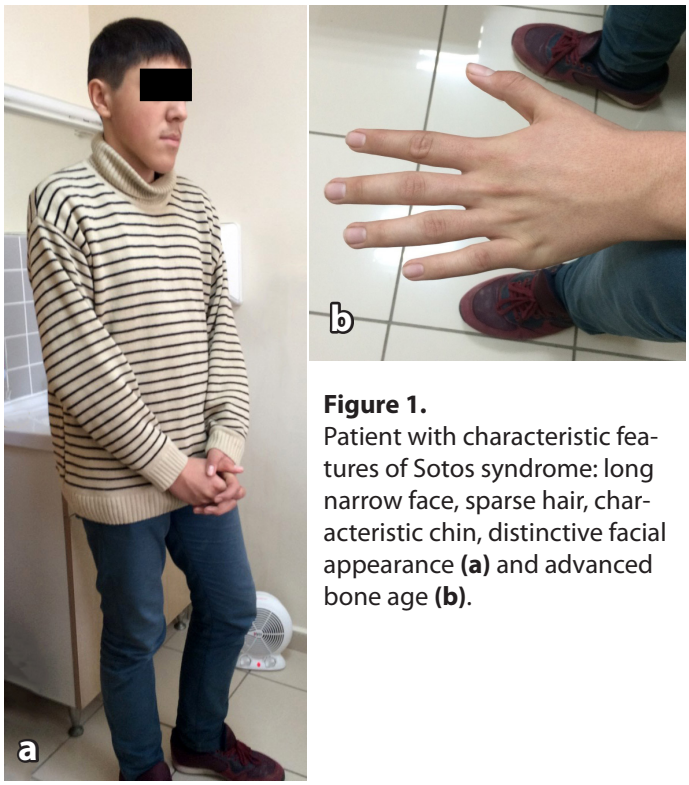

Figure 1.
Patient with characteristic features of Sotos syndrome: long narrow face, sparse hair, characteristic chin, distinctive facial appearance **(a)** and advanced bone age **(b)**.

Discussion

Abnormal growth and dysmorphic signs such as macrocephaly, prominent forehead and chin can be signs of a genetic syndrome. Examples of common overgrowth syndromes, among some with rare conditions, include Beckwith-Wiedemann syndrome, Marfan syndrome, fragile X syndrome, homocystinuria and Sotos syndrome.

Beckwit-Wiedemann syndrome is characterized by macrosomia, macroglossia, abdominal wall defects and hepatosplenomegaly.

Fragile X syndrome is associated with macrocephaly, moderate to severe mental retardation and delayed developmet.

Marfan syndrome is associated with connective tissue dysplasia and characterized by blue sclera, ocular lens dislocation, hearth defects, pulmonary, skin signs, dural ectasia at lumbosacral level of spinal column.

Homocystinuria is a disorder of methionin metabolism characterized by mental retardation and recurrent venous thrombosis.

In case of absence of dysmorphic features, one has to differentiate between familial tall stature, precocious puberty, excess of gonadotropin hormone, hyperthyroidism and some other rare conditions.

In our case parents' height was normal. Values of the sex hormones and results of thyroid function tests were in acceptable ranges. The presence of dysmorphic features allowed us to suspect genetic disorder, which was further confirmed by the results of genetic test. The mutation of NSD-1 gene located at 5q35 locus was discovered. NSD-1 gene encodes histone methyltransferase. Deletions of this gene, which is located at 5q35 locus, are responsible for 75% of cases of Sotos syndrome [5]. However in 55% of Asians (especially in Japanese) and 10 % of Europeans, the negative results of genetic analysis don't deny the diagnosis.

Conclusion

Patients with increased height especially if this is combined with dysmorhic features and abnormal growth rates should be carefully investigated. It must be particularly emphasized, that in case of overgrowth combined with macrocephaly, dysmorphic features and mental retardations an investigation for Sotos syndrome is necessary for establishing proper diagnosis.

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