REFERENCE

1. Indian Council of Medical Research. National Ethical Guidelines for Biomedical and Health Research Involving Human Participants. New Delhi: Indian Council of Medical Research; 2017. Available from: *https://www.icmr.nic.in/sites/ default/files/guidelines/ICMR_Ethical_Guidelines_2017.pdf*. Accessed May 21, 2019.

Precocious Puberty in an Infant with Sotos Syndrome

Sotos syndrome is a rare genetic disorder characterized by statural overgrowth, distinctive appearance (downslanting palpebral fissures, long narrow face and chin, broad forehead, dolichocephalic large head), developmental delay, and intellectual disability [1]. The endocrine manifestations are rare.

A 3-month-old boy presented with enlargement of genitalia and rapid growth noticed since birth. There was no history of visual disturbances, seizures, head injury, or drug intake. He weighed 3.7 kg (Z-score +0.71) at birth and had delayed development. The weight, height and head circumference were 6.65 kg, 66.0 cm and 42.0 cm corresponding to +0.28, +2.12 and +0.41 Z-scores, respectively. The upper-to-lower body segment ratio was 2.5:1 (normal 1.7:1). He had broad prominent forehead, dolicocephaly, large ears and long chin. The stretched penile length was 4.9 cm (+2 Z-score), testicular volume was 10 cc, and there were no pubic hairs. A diagnosis of Sotos syndrome was considered in view of distinct facial features, overgrowth and developmental delay.

The routine hematological and biochemistry investigations were normal. Bone age was advanced (3 years). Serum prolactin, growth hormone, thyroid profile and tumour markers were normal. Baseline luteinizing hormone (LH) and follicle stimulating hormone (FSH) were 1.95 IU/L (normal 0.02-3.2 IU/L) and 1.59 mIU/mL (normal 0.10-1.5 IU/L), respectively. GnRH stimulated peak concentrations of these hormones were 17.02 IU/L and 5.01 IU/L, respectively confirming central precocious puberty. The pituitary MRI and cardiac echocardiography was normal. Clinical exome sequencing identified a pathogenic heterozygous stop gain mutation in the *NSD1* gene (c.2362C>T; p.Arg788Ter), confirmed by Sanger sequencing.

Child was started on 3-monthly injections of Leuprolide. Testicular volume regressed to 5 cc over next 8 months. At age of 4 years and 9 months, his weight, height, and head circumference were 19 kg (+0.97 Z-score), 112.6 cm (+1.77 Z-score) and 56 cm (+3.84 Z-score), respectively, and testicular volume was 4 cc.

Sotos syndrome shows clinical overlap with Weaver syndrome and other overgrowth syndromes during infancy, and the confirmation of diagnosis depends on the presence of *NSD1* mutations [1]. An increased upper-to-lower segment ratio is helpful in differentiating it from usual causes of infantile overgrowth [2]. The endocrine problems in Sotos syndrome include hypothyroidism, cryptorchidism, hypospadias, and hyperinsulinism [1,3]. Central precocious puberty has been reported very rarely [4,5]. Although bone age advancement due to accelerated growth velocity is common in Sotos syndrome, an unusual advancement as seen in our patient may indicate central precocious puberty [4].

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REFERENCES

1. Tatton-Brown K, Cole TRP, Rahman N. Sotos Syndrome. *In*: Pagon RA, Adam MP, Ardinger HH, *et al., editors*. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2019. 2004 Dec 17 [updated 2015 Nov 19].
2. Dayal D, Soni V, Das G, Bhunwal S, Kaur H, Bhalla AK. Longitudinal observations on growth patterns of obese infants: Developing country perspectives. Preliminary study. Pediatria Polska. 2017;92:397-400.
3. Cerbone M, Clement E, McClatchey M, Dobbin J, Gilbert C, Keane M, *et al*. Sotos syndrome presenting with neonatal hyperinsulinaemic hypoglycaemia, extensive thrombosis, and multisystem involvement. Horm Res Paediatr. 2019 Mar 15:1-7. [Epub ahead of print].
4. Bertelloni S, Baroncelli GI, Tomasi O, Sorrentino MC, Costa S, Saggese G. [Sotos syndrome: follow-up of a case with precocious puberty]. Pediatr Med Chir. 1995;17:353-7.
5. Lim S. Central precocious puberty in a case of SOTOS syndrome (abstract). *In*: 53rd Annual Meeting of the European Society for Paediatric Endocrinology (ESPE). Dublin, Ireland, September 18-20, 2014: Horm Res Pediatr. 2014;82:1-507.