Central precocious puberty in a case of SOTOS syndrome

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Background: Statural overgrowth in SOTOS syndrome is well recognised. However excessive growth away from the usual growth trajectory should prompt assessment for other causes of growth acceleration.

Case: TE was referred for a growth assessment at 6.8 years as he appeared to have grown more in the previous year. He was 142.9 cm (Ht SDS +4.32), weight 44.4kg (BMI SDS +2.85). He had no formal genetic diagnosis except that he was clearly dysmorphic with global developmental delay and had an 'overgrowth syndrome', growing very well despite his chronic respiratory symptoms in early childhood. He was delivered at 36 weeks gestation with a birth weight of 2.64 kg. He presented with sepsis at day 23 and was noted to be failing to thrive. He was treated for gastrooesophageal reflux but continue to be troubled by recurrent apnoea during feeds. Sleep apnoea was also a problem but finally resolved by age 3 years. Obstructive apnoea was problematic until his adenoidectomy at age 4 years. Due to his large size and global delay, a genetics opinion was sought at 4 years following investigations which included a normal brain MRI and array CGH. No unifying diagnosis was made apart from an overgrowth dysmorphic syndrome. Further genetic tests were organised. When he was examined at 6.8 years, it was noted that he had large hands and feet, large ears, slightly long palpebral fissures and a pointed chin. He was also hypertrichotic and in puberty Tanner A1P1G2 with bilateral 8ml testes. It was noted that he had selective eating habits.

Investigations: Bone age, pituitary MRI, tumour markers, LHRH stimulation test.

Results: Central precocious puberty was confirmed with LH peak of 9 IU/L, FSH 4.2 IU/L. Bone age was 11 years 6 months at a chronological age of 7 years 3 months. Pituitary and brain MRI was normal. Tumour markers were negative. Further genetic testing revealed a de novo loss of function mutation in the NSD1 gene consistent with a genetic diagnosis of SOTOS. These results were only available after the diagnosis of precocious puberty.

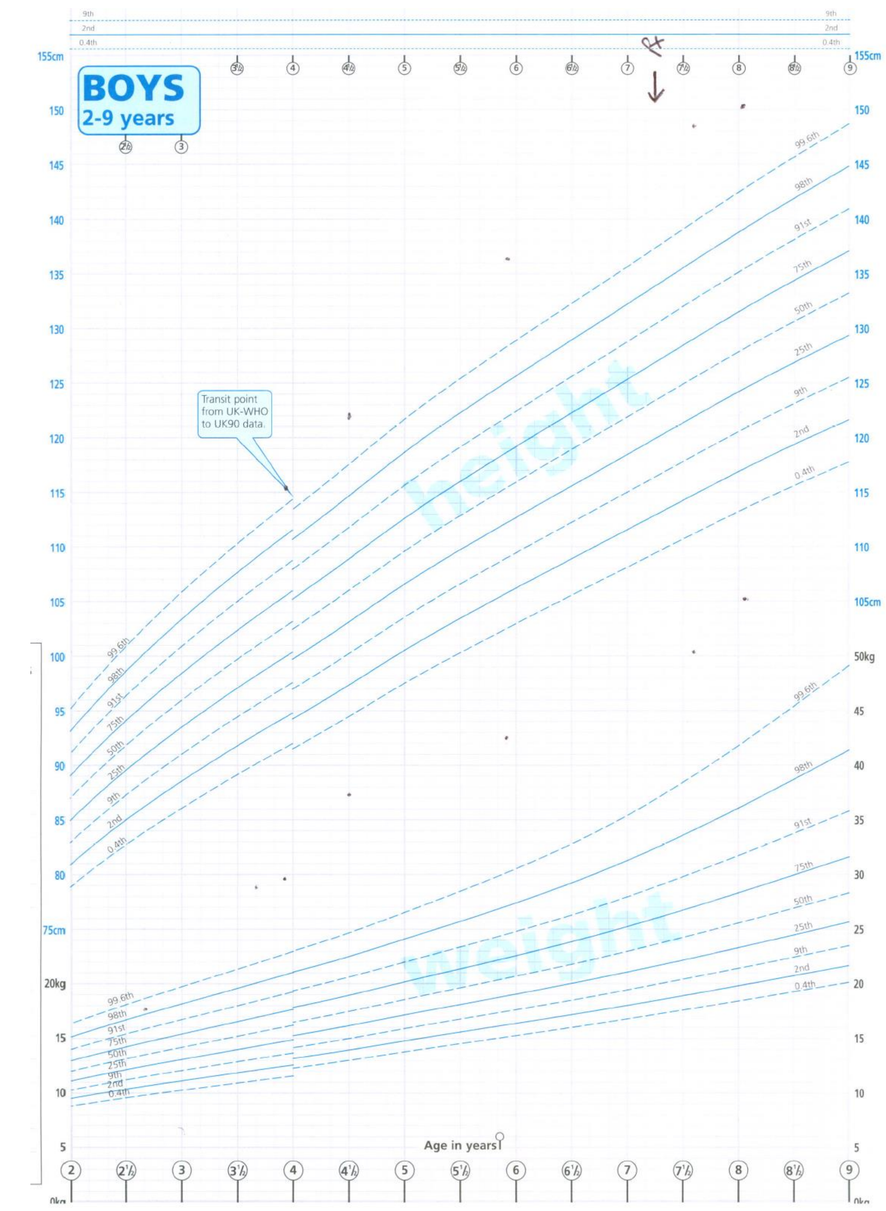
Management: TE was started on regular treatment with GNRH analogue (arrow on Growth chart) and has tolerated it so far.

LHRH stimulation test

Time	0 min	20 min	60 min
LH IU/L	0.6	8.0	9.0
FSH IU/L	2.0	2.8	4.2

Auxology

Age (years)	3.7	5.9	6.83	7.57	8.10
Ht SDS	+3.75	+4.44	+4.32	+4.42	+4.13
BMI SDS	+3.7	+3.5	+2.85	+2.87	+3.05



Growth chart

Conclusion: Growth and puberty data reported in SOTOS have not included an increased incidence of central precocious puberty although advanced bone age and early menarche can occur. Late menarche have not resulted in excessive tall final heights in women reported. Most adult SOTOS men have final heights within the normal range. In this case, excessive growth should always prompt investigation regardless of the underlying diagnosis. Advanced bone age is a common finding in SOTOS but in this case there is an endocrine cause. Although the issue of a compromised final height is not a problematic one, deciding when to cease treatment would still be tricky with this behaviour phenotype.

References

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