

Treatment of Subclinical Hypothyroidism can Improve Weight Gain in Children with Failure to Thrive: A Case Series

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Abstract

Abnormal thyroid function testing results are sometimes discovered in children with poor weight gain (failure to thrive, or FTT), although traditionally it is thought that children with hypothyroidism present primarily with poor linear growth. We report on a series of children's with FTT and subclinical hypothyroidism (SCH, or a TSH of 5-10 uIU/mL with a normal FT4), all of whom showed improvement in weight gain with thyroid hormone replacement. Recent studies documenting changes in hormone-controlled appetite signaling in children with mild elevations of TSH offer a compelling physiological explanation for these clinical findings, suggesting FTT may not be as uncommon a presenting sign of SCH as previously believed. These laboratory findings can be distinctly differentiated from the thyroid testing results seen in children with euthyroid sick syndrome. We conclude that the evaluation of a young child with FTT should include thyroid function testing. Even mild elevations of TSH (5-10 uIU/mL) can be associated with FTT, and treatment with levothyroxine may be effective in restoring normal weight gain.

Keywords: Subclinical hypothyroidism; Children; Failure-to-thrive; Euthyroid sick syndrome

Introduction

Mild elevation of TSH is sometimes discovered in children with poor weight gain (failure to thrive, or FTT). Yet traditionally it is thought that children with hypothyroidism present primarily with poor linear growth, leading many clinicians to question the significance of a mild elevation of TSH in a child with FTT [1]. When subclinical hypothyroidism (SCH, or a TSH of 5-10 uIU/mL with a normal FT4) is diagnosed in a child with FTT who does not have an underlying condition predisposing to thyroid disease, it is not clear that any treatment is needed. Many children with persistent mild elevation of TSH continue to show normal linear growth over time, and there is only very limited data suggesting that treatment of SCH improves linear growth [2,3]. There are no published studies to date assessing treatment of SCH in children with FTT.

Nevertheless, it has been our clinical experience that treatment of SCH may improve weight gain in children with FTT. We report on a series of children with FTT and SCH, all of whom showed improvement in weight gain with thyroid hormone replacement and normalization of TSH.

Case Series

Records were retrospectively reviewed from the Tripler Army Medical Center Pediatric Endocrinology Clinic for cases of FTT where the only identified diagnosis was SCH. In all of the cases presented below all other screening labs (chemistry, CBC, celiac panel, and workup for other causes of chronic disease) were normal. After treatment with a low dose of levothyroxine, each child was followed up with repeat thyroid function testing within 6 weeks, and were treated to keep the TSH in the normal range (below 5 uIU/mL). Approval for publication was obtained from the Department of Clinical Investigation at Tripler Army Medical Center.

Case #1

A 15-month-old female presented with almost no weight gain since 8 months of age and was diagnosed with FTT. Her linear growth was normal. She had a good appetite and normal intake of solid foods. Her past medical history was significant for constipation. Extensive workup showed a TSH of 7.0 uIU/mL with a normal FT4. Treatment was started with levothyroxine 25 mcg once daily. Within 6 weeks her TSH normalized to 3.9 uIU/mL, she gained over 300 grams of body weight and her constipation resolved.

Case #2

A 3-year-old male presented with dry skin, coarse hair, poor weight gain and constipation. His weight gain had slowed significantly from 2 to 3 years of age, but his linear growth was normal. TSH was found to be 5.4 uIU/mL with a normal FT4. He was not initially treated. Repeat TSH 8 months later was 6.4 uIU/mL, again with a normal FT4. He was started on levothyroxine 37.5 mcg once daily. With normalization of his TSH to 2.5 uIU/mL his weight gain improved dramatically.

Case #3

A 3-year-old male was referred for poor weight gain, poor appetite, early satiety and constipation. His weight velocity had dropped to below the 3rd percentile. Extensive workup showed normal endoscopy and normal screening for gastrointestinal disease, however his TSH was found to be 7.7 uIU/mL with a normal FT4. Treatment was started with levothyroxine 37.5 mcg once daily. He then showed an improvement in weight gain and his gastrointestinal symptoms resolved.

Case #4

A 32-month-old female presented with thinning hair and weight loss despite attempts to increase caloric intake. Her linear growth continued to

track at the 25th percentile. Laboratory evaluation revealed a TSH of 8.8 uIU/mL with a normal FT4 and positive thyroid peroxidase antibodies. Treatment was begun with levothyroxine 50 mcg once daily, with dramatic improvement in symptoms and excellent catch up growth.

Case #5

An 8-year old female presented with dry skin and poor weight gain for the last 2 years. At the time of her presentation, she had gained only 2 kg

over the last 24 months. Her linear growth rate, which had been normal until age 8, had begun to decrease as well. Laboratory evaluation showed a TSH of 6.1 uIU/mL with a normal FT4. She was treated with levothyroxine 25 mcg once daily. Her weight gain and linear growth began to improve.

Auxological and laboratory measurements for all patients are summarized in table 1. Growth charts for all patients described have been carefully reproduced in figure 1.

Case	Age/ Gender	Weight Velocity Prior to Treatment (Percentile) (4)	Weight Velocity After Treatment (Percentile) (4)	TSH (uIU/mL)	FT4 (pmol/L)	Thyroid Peroxidase Antibody (TPO)
1	15 mo M	0.68 kg/7 months (3 rd)	0.32 kg/6 weeks (50 th)	7.0	20.6	Not Checked
2	3 yr M	0.5 kg/9 months (<3 rd)	5.3 kg/12 months (>97 th)	5.4	16.7	Negative
3	3 yr M	0.9 kg/12 months (<3 rd)	1.6 kg/12 months (3 rd -5 th)	7.7	12.87	Negative
4	4 yr F	-0.7 kg/6 months (<3 rd)	3 kg/12 months (90 th)	8.8	11.6	Positive
5	8 yr F	2.6 kg/24 months (<3 rd)	2.8 kg/11 months (25 th -50 th)	6.1	11.6	Negative

Table 1: Auxological and laboratory data for cases 1 through 5. All patients had a mildly elevated TSH with a normal FT4 for their age.

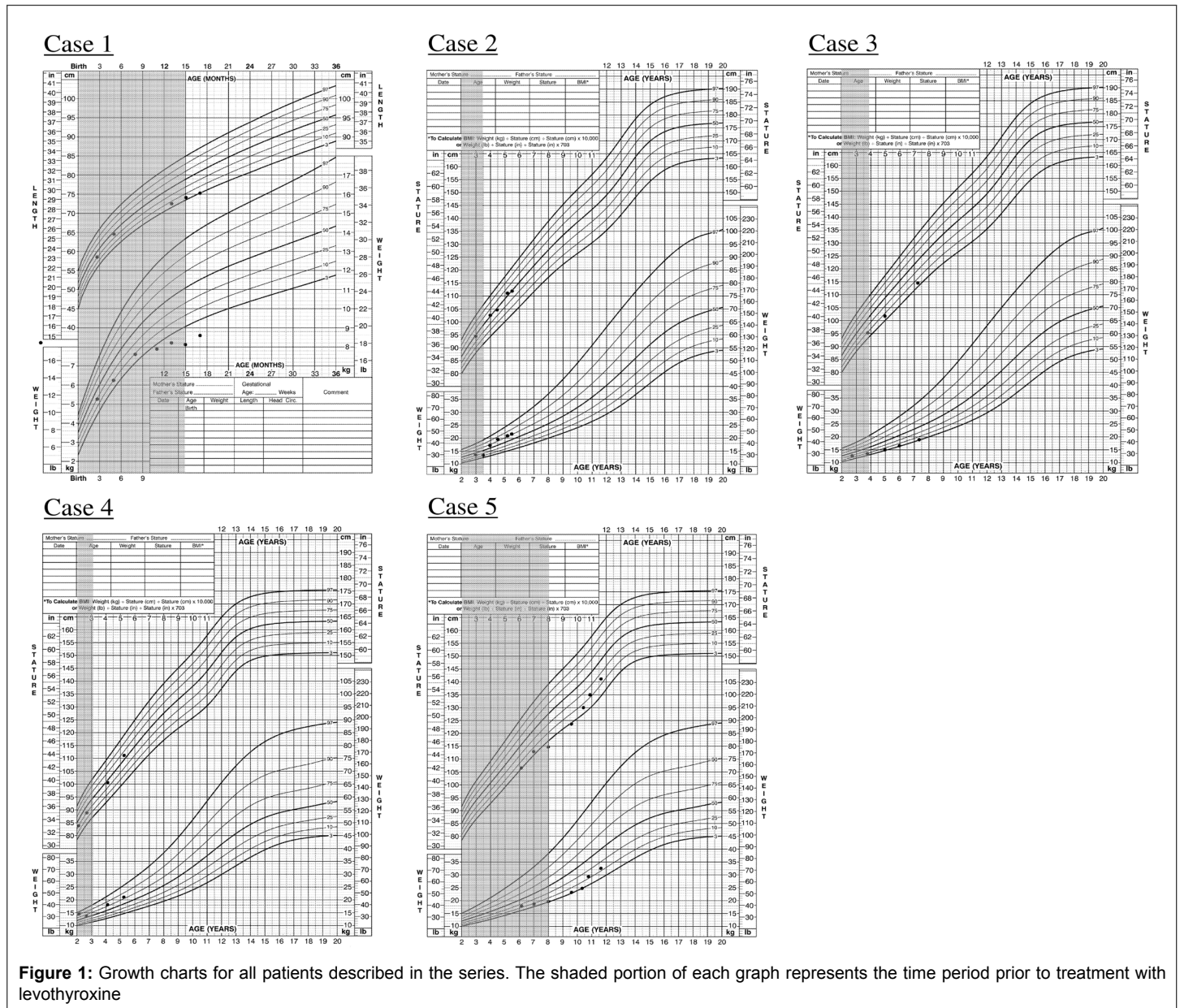


Figure 1: Growth charts for all patients described in the series. The shaded portion of each graph represents the time period prior to treatment with levothyroxine

Discussion

In each of these cases the child presented with poor weight gain as a major component of the primary complaint. Evaluation showed all of these children had very poor weight velocity for age, yet they had preservation of linear growth for a long period of time [4]. As classically described, endocrine disorders such as hypothyroidism or growth hormone deficiency are associated with poor linear growth (sometimes referred to as a Type 2 growth pattern), whereas children with primarily poor weight gain more often have poor caloric intake or gastrointestinal disease [5]. This leads us to believe that young children with FTT and SCH are a unique population because in contrast to children with overt thyroid disease, children with SCH often have mild symptoms or sometimes no symptoms at all. In many instances SCH does not cause significant disease and no treatment is needed.

There are only a limited number of studies investigating the natural history and effects of levothyroxine therapy in children with SCH [2,3,6,7]. Some authors have recommended waiting until overt hypothyroidism develops (TSH>10 uIU/mL), usually in concert with goiter or elevated thyroid antibodies before treatment is considered, as many children with SCH do not progress to developing overt thyroid disease [8]. Others have noted that in populations at high risk to develop overt hypothyroidism, such as children with type 1 diabetes or Down syndrome, treatment of SCH can be helpful [6,9].

Recent studies have documented altered levels of the appetite-suppressive gut hormone obestatin in children with SCH. Obestatin levels were shown to correlate positively with TSH in children with SCH [10]. This association of hormone-controlled appetite signaling with mild elevations of TSH offers a compelling physiological explanation for our clinical findings, suggesting FTT may not be as uncommon a presenting sign of SCH as previously believed. Although we did not specifically measure markers of appetite or track changes in caloric intake, it may be that this distinctive presentation of SCH in very young children compared to older children or adults is potentially explained by an increased sensitivity to these altered hormonal levels. Additional study is needed to determine how these changes in TSH correlate with changes in nutritional status in children with FTT.

Previous studies have documented changes in TSH levels with anorexia or chronic malnutrition, and have attributed abnormal thyroid function testing results to sick euthyroid syndrome [11]. However, in sick euthyroid syndrome, TSH is typically normal or reduced, and is sometimes markedly low [12]. Elevation of TSH above normal commonly occurs transiently as patients recover from sick euthyroid syndrome, not during the acute illness [12]. Given that all of the children described above were still growing poorly during their evaluation, it is unlikely that they were in the recovery phase of sick euthyroid syndrome.

Our clinical experience suggests that in children with FTT and SCH, small doses of thyroid hormone replacement may help to restore normal weight gain. We recognize the many limitations of this analysis, in that many children with FTT will eventually show improvements in weight gain over time regardless of the underlying diagnosis [13], and that some of the patients described here only showed a marginal response (such as case #3). The varied response could be due to other factors that involved attempts to improve feeding and caloric intake in these children. In addition, we do not have long term follow-up for these cases. Future longitudinal studies with large numbers of cases are necessary to prove our hypothesis. Nevertheless, the improvement in weight gain shown in these patients suggests that children with FTT should have screening thyroid function testing performed, and treatment with levothyroxine can be initiated if TSH is found to be above the normal range.

Conclusion

The evaluation of a young child with FTT should include thyroid function testing. Even mild elevations of TSH (5-10 uIU/mL) can be associated with FTT, and treatment with levothyroxine may be effective in restoring normal weight gain.

Conflict of Interest

The authors have no relevant disclosures and no conflict of interest to report.

Disclaimer

The views expressed in this manuscript are those of the author and do not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government.

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