We have no good explanation for the early menstruation in our patients, but believe that it may be due to increased sensitivity of the endometrium to circulating levels of oestrogens which are too low to produce breast development. Certainly, the oestrogen values obtained in 2 of the patients were far below the levels found in normal ovulatory cycles. Case 4 apparently had a peak of urinary LH excretion on the 11th day of one of her menstrual cycles which was preceded by a peak of urinary oestrogen excretion on the previous day. The brisk rise in FSH after LRH stimulation in our Case 3 is surprising and is not in keeping with the very modest basal FSH levels found in 2 of the other cases. Further studies are obviously needed to establish whether this pronounced rise in FSH after LRH is

a consistent feature in girls with early isolated menstruation.

We thank our colleagues for referring their patients for investigation.

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Correspondence to Dr D. B. Grant, The Hospital for Sick Children, Great Ormond Street, London WC1N 3JH.

A boy with low-TSH hypothyroidism

P. J. SMAIL, T. E. ISLES, AND R. S. ACKROYD

Departments of Child Health and Biochemical Medicine, Ninewells Hospital and Medical School, Dundee

SUMMARY A case of long-standing mild hypothyroidism is described. This was caused by partial TSH deficiency probably of hypothalamic origin, with no other pituitary hormone deficiencies, although with a decreased response of FSH and LH to LHRH.

Low thyroid-stimulating hormone (TSH) hypothyroidism of hypothalamic or pituitary origin is usually accompanied by other pituitary hormone deficiencies (Kaplan, 1975), isolated TSH deficiency in childhood having been described in only one report since the advent of modern TSH assays (Miyai *et al.*, 1971). We report a case of low-TSH hypothyroidism in a child without evidence of other pituitary deficiencies although with decreased response of luteinising hormone (LH) and follicle-stimulating hormone (FSH) to luteinising hormone-releasing hormone (LHRH).

Case report

A 6-year-old boy was admitted with a febrile illness. He was noted to have a deep voice, a protuberant abdomen, and an exaggerated lumbar lordosis. His height was on the 25th centile. He had not developed his first tooth until age 13 months and was said always to have been intolerant of cold. Serum thyroxine (T4) was 42 nmol/l (3.2 µg/100 ml). Our laboratory mean is 110 nmol/l (8.5 µg/100 ml) and range ± 2 SD 75–145 nmol/l (5.8–11.2 mg/100 ml).

Other thyroid function studies included serum triiodothyronine (T3) 2.1 nmol/l (1.37 µg/100 ml), T3 index 109%, free T4 index 39, and TSH <0.6 mU/l. Antithyroid-cytoplasmic antibody (by fluorescent antibody technique) and antithyroglobulin antibody (by tanned red cell test) were negative. A ⁹⁹technetium scan showed a normally placed thyroid gland. The responses of serum TSH, T4, T3, T3 index, and free T4 index to an IV dose of 200 µg thyrotrophin-releasing hormone (TRH) are shown in the Table. Serum TSH increased to a maximum of 5.2 mU/l at 20 minutes. Bone age was 3.3 years at a chronological age of 6.3 years (Tanner Whitehouse) and skull x-ray was normal. X-ray of the hips showed advanced changes of Perthes's disease bilaterally. His intelligence was within the normal range although he was having coaching at school for reading and arithmetic.

After 0.25 mg tetracosactrin IM, serum cortisol rose from 343 nmol/l (12.3 µg/100 ml) to 723

Table Response to an intravenous dose of 200 µg thyrotrophin-releasing hormone

	Time (min)				Laboratory	
	0	20	60	180	Mean	Range ± 2 SD
TSH (mU/l)	3.5	5.0	2.4	1.7	—	0–5
T4 (nmol/l)	58	69	47	56	110	75–145
T3 (nmol/l)	2.0	2.1	2.1	2.2	1.7	1.0–2.4
T3 uptake %	106	109	104	105	105	97–113
Free T4 index	55	63	45	53	103	70–135

Conversion: SI to traditional units—thyroxine: 1 nmol $\approx$ 0.077 µg/100 ml, triiodothyronine: 1 nmol/l $\approx$ 0.65 µg/100 ml.

Figure The patient before and 6 months after treatment with thyroxine.

nmol/l ($26.0 \mu\text{g}/100 \text{ ml}$) at 30 minutes. Basal serum LH was 1.5 U/l and basal FSH 0.9 U/l with no significant rise of either after an IV dose of $100 \mu\text{g}$ LHRH. Basal serum testosterone was 3120 nmol/l (0.9 ng/ml), basal serum prolactin 260 mU/l , and the maximum serum growth hormone (GH) response in an insulin tolerance test producing adequate hypoglycaemia was 9.6 mU/l , and the maximum serum cortisol $46.7 \mu\text{g}/100 \text{ ml}$ (1298 nmol/l). A stimulated GH level of 16 mU/l is regarded by our laboratory as excluding significant deficiency. An exercise test GH level after treatment with thyroxine was 18.7 mU/l , showing that the previous poor stimulation by hypoglycaemia was due to thyroxine deficiency and not to lack of GH. Treatment was begun with oral L-thyroxine increasing to 0.2 mg daily with a resultant rapid change in body habitus and general increase in level of activity (Figure). The height velocity during the first year of treatment was 7.6 cm (equivalent to the 97th centile) and his achievement at school improved considerably with capabilities now described as well above average; special teaching was no longer required. The TRH

stimulation test was repeated after one year of treatment (thyroxine being withheld for 8 weeks before the test) as it has been suggested (Boehm *et al.*, 1976) that an improvement in TSH response may occur in isolated TSH deficiency after treatment with thyroxine. Serum TSH rose from a basal level of 2.2 mU/l to a maximum of 4.3 mU/l at 20 minutes, serum prolactin rising from 165 to 750 mU/l . Bone age was 4.4 years at a chronological age of 7.7 years, an advance of 1.1 after 12 months' treatment.

Discussion

We interpret the results in this patient as indicating partial TSH deficiency, possibly of hypothalamic origin, without other clinical evidence of pituitary hormone deficiencies. The response of TSH during the TRH test suggests the presence of some active TSH, while the levels of serum T3 and free T4 index do not suggest either an abnormality of thyroxine protein binding or a defect of peripheral thyroxine metabolism. It is difficult to interpret the significance

of the decreased response of LH and FSH to LHRH in a child of this age. The two sisters reported by Miyai *et al.* (1971) were said at the age of 12 and 14 years respectively to have early breast development and detectable urinary LH and FSH. Our patient seems similar to Case 23 of Chaussain *et al.* (1974) who had TSH deficiency with a normal response to TRH but no significant rise of LH and FSH with LHRH.

That this sort of case and other cases of congenital secondary hypothyroidism may be missed, is an objection to the use of TSH rather than T4 as the primary test in screening for neonatal hypothyroidism. However, although this patient has a history of hypothyroidism dating back to neonatal life or at least to early infancy, the hypothyroidism was of mild degree with no deficit in intelligence.

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Correspondence to Dr P. J. Smail, Department of Child Health, Ninewells Hospital and Medical School, Dundee DD1 9SY.

Ring 20 chromosome in a child with seizures, minor anomalies, and retardation

JANET M. STEWART, NICHOLAS CAVANAGH, AND DAVID T. HUGHES

Institute of Child Health, and The Hospital for Sick Children, London

SUMMARY A patient is reported with seizures, developmental delay, and minor physical anomalies. Karyotype showed a ring formation of chromosome number 20. Previously reported patients with this chromosomal aberration have typically had seizures and behavioural disorders with considerable variation in the degree of physical abnormality and mental retardation. A correct diagnosis in such a case is important for accurate genetic counselling.

Many new chromosomal syndromes have been reported since the introduction of banding. Most of these are associated with dysmorphic features, multiple anomalies, and mental retardation. A ring formation of chromosome 20, on the other hand, has been reported in patients with negligible physical anomalies, severe seizures, and variable retardation (Table). We report an additional case to emphasise that seizures with slight dysmorphism may be a manifestation of a chromosomal abnormality.

Case report

Case 1 was the product of an uncomplicated, term pregnancy and weighed 2800 g at birth. He was a

slow feeder initially. He smiled at 7 weeks, sat unsupported at 10 months, crawled at 14 months, and pulled to stand at 20 months. He had no speech at 25 months. At 12 months he was noted to have episodes lasting 30 minutes in which his head turned to the left and his eyes were glazed. By 14 months he was having spells lasting 20 seconds with mouthing movements and twitching of the right arm and leg, followed by excitement. These occurred up to 5 times daily and continued when he was placed on phenobarbitone.

His mother was 36 and his father 39 at the time of his birth. His mother had a nodular goitre. She had had one miscarriage before the patient's birth and has had one subsequently. She has a brother with a cleft lip and palate and an uncle with well-controlled epilepsy. There was no consanguinity.

When examined at 16 months, his weight was at the 10th centile, height at the 25th, and head circumference between the 10th and 25th (46.5 cm) (Fig. 1). Although his face was not strikingly unusual, he did not resemble either parent. He had a sloping forehead, synophrys, long eye lashes, and no epicanthic folds. The nose was small and flattened and he had a long philtrum. The palate was