Thyroid ultrasonography in congenital isolated thyroid stimulating hormone deficiency

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Abstract
The effects of thyroid stimulating hormone (TSH) deficiency on thyroid development was examined using ultrasonography in a child with congenital isolated TSH deficiency. Ultrasound revealed the thyroid gland was one sixth normal volume, suggesting that TSH plays an important part in thyroid growth, but not a critical role in differentiation. (Arch Dis Child 1995; 72: 439-440)

Keywords: thyroid stimulating hormone deficiency, thyroid ultrasonography, thyroid growth.

Congenital isolated thyroid stimulating hormone (TSH) deficiency is a rare autosomal recessive disease characterised by typical signs and symptoms of cretinism. It has been shown that congenital isolated TSH deficiency in Japan is caused by a point mutation in the codon for the 29th amino acid of the TSH beta subunit. This results in conformational changes of the beta subunit that preclude its association with the alpha subunit. The disease provides a model for considering the effects of TSH on how the thyroid gland develops. We describe a child with congenital isolated TSH deficiency whose thyroid gland was found to be hypoplastic on ultrasound examination.

Case report
The patient was a 10 year old girl whose congenital hypothyroidism had been diagnosed as a neonate. She had been born after an uncomplicated full term pregnancy and delivery and weighed 2983 g. The patient was admitted to our hospital at 10 days of age because of jaundice and poor appetite. Thyroid hormone studies showed a depressed triiodothyronine uptake of 19% (normal range 25–35), a thyroxine concentration of 34.7 nmol/l (72-1–139.0), and TSH of 2 mU/l (<12). Scintigraphy and thryrotrophin releasing hormone (TRH) stimulation test were not performed. Thereafter, she was treated with standard therapeutic doses of L-thyroxine, monitored periodically by determining the serum concentration of thyroxine. At 10 years of age, the dosage of L-thyroxine was gradually tapered for six months to exclude the possibility of transient hypothyroidism, but serum concentrations of thyroxine and TSH remained low and the patient complained of fatigue. Before the dose of L-thyroxine was increased, TRH stimulation test, luteinising hormone releasing hormone stimulation test, and insulin provocative growth hormone secretion test were performed. The results of these disclosed adequate secretion of hormones other than TSH, indicating that the most likely diagnosis was congenital isolated TSH deficiency.

Methods and results
DNA analysis
Genomic DNAs were extracted from peripheral blood by standard techniques. Polymerase chain reaction (PCR) and MaeI digestion were carried out as previously reported with modification. In summary, a 0.85 kb fragment of the TSH β gene was amplified by 30 cycles of PCR using pTSH621p and pTSH1471r. After digestion with MaeI, the PCR products were analysed by electrophoresis on 2% agarose gel containing ethidium bromide, then photographed. A 0.85 kb fragment produced by PCR was cleaved into two fragments of 0.71 kb and 0.14 kb only when it harboured a missense mutation from a codon GGA (glycine) to AGA (arginine), generating a de novo MaeI cleavage site. As shown in the figure, the MaeI cleavage profile of PCR products showed that the patient was homozygous, whereas other family members were heterozygous, with respect to the mutated allele.

Ultrasonography
The ultrasonic scanner used was an Aloka SSD-650 unit (Aloka Co) equipped with real time 5.0 MHz and 7.5 MHz transducers. The child was placed supine with her neck hyper-extended to measure the long axis diameter (D1), the short axis diameter (D2), and the

MaeI cleavage profiles of PCR products. Genomic DNAs extracted from peripheral blood were analysed by PCR using pTSH621p and pTSH1471r followed by MaeI digestion.
thickness (D3) of both lobes and the isthmus. The measured values were (cm): isthmus, 
$D1=1.0$, $D2=0.7$, $D3=0.2$; right lobe, 
$D1=1.8$, $D2=0.7$, $D3=0.2$; and left lobe, 
$D1=2.3$, $D2=1.0$, $D3=0.7$. As in Ueda’s 
study, the volume of the thyroid gland was 
determined using a standard geometric 
formula, in which each lobe of the thyroid 
gland was assumed to be a prolated spheroid 
(volume of a prolated spheroid=$D1\times D2 \times 
D3/n/6$). The total volume of the patient’s 
thyroid gland was calculated as the sum of each 
lobe. The result was 1.04 cm$^3$, obviously a 
small thyroid gland compared with the thyroid 
gland size derived from healthy children with 
the same body height (mean (SD) $6.3 (2.0)$ 
cm$^3$).

Discussion
There are fundamental questions about the 
control of thyroid cell growth and multiplica-
tion and differentiation. In our patient we 
confirmed that TSH has a developmental role 
in thyroid growth. It is true that goitre is 
induced by an increased TSH concentration in 
response to any interference with thyroid hor-
monic secretion or synthesis, such as iodine 
deficiency, but there have been methodological 
difficulties in evaluating how TSH acts on fetal 
thyroid development. With ultrasonography, 
however, we could examine the effects of TSH 
on the developing thyroid gland in this child in 
whom TSH had been deficient since the fetal 
stage. In studies of aborted human fetuses, thy-
roid hormone synthesis has been demonstrated 
in the 11th week, whereas pituitary TSH was 
detected at 8–10 weeks and serum TSH at 
10–12 weeks, showing that TSH plays a 
minimal part in the differentiation of the 
thyroid gland.

Our ultrasound study of this patient revealed 
a hypoplastic thyroid gland of one sixth normal 
volume. Although findings in a single case 
must be interpreted with caution, we conclude 
that TSH plays an important part in thyroid 
growth and function, but that it is not indis-
 pensible for differentiation.

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