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Clinical Utility of Thyroid Ultrasonography in the Diagnosis of Congenital Hypothyroidism

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Abstract. To determine the clinical utility of thyroid ultrasonography in the diagnosis of congenital hypothyroidism (CH) before initiation of therapy, ultrasonographic images of the thyroid gland with a high-resolution transducer were obtained in 204 healthy infants aged from newborn to 12 months (Group A), and 174 infants suspected of having CH detected by neonatal mass screening (Group B). The thyroid gland was imaged by transverse scanning at the anatomic site of the thyroid gland. The maximal width of thyroid on the transverse section in the normal location was measured. By comparing with the normal thyroid gland size and location obtained from Group A, 174 infants of Group B were divided into four subgroups: 1) Normal in size (n = 117), 2) Enlarged (n = 33), 3) Small (n = 1) and 4) Invisible in the normal location (n = 23). They were compared with the final diagnoses based on the results of chemical laboratory data and scintigraphic findings. The sensitivity and the specificity for the presence or absence of the thyroid gland in the normal location were 96% (22/23) and 99% (150/151), respectively. Both subgroups of normal and enlarged sized gland included healthy infants (false positive), transient hyperthyrotropinaemia, transient hypothyroidism and CH due to dyshormonogenesis. We conclude that ultrasonography is useful for determining the presence or absence of the thyroid gland in the normal location, whereas normal and enlarged sized glands require further examination to complete the diagnosis.

Key words: Thyroid ultrasonography, Congenital hypothyroidism, Newborn screening
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DURING the last twenty years newborn screening for CH has become an important health activity in most developed countries [1]. Determining the cause of congenital hypothyroidism is important since there are both differences in inheritance and prognosis [2]. Radionuclide scanning is presently the best diagnostic technique for delineating thyroid anatomy in CH infants [3, 4], however, in neonates, the oncogenic risk of the relatively increased total body effective dose of γ-irradiation is considered to be high [5]. It still remains controversial whether ultrasonography is a reliable substitute to radionuclide scanning [3, 6–8]. Since the quality of the scanner may determine the detection sensitivity, different scanners performed may be one of the factor. Only a few studies report the application of ultrasonography in hypothyroid infants before initiation of therapy [9]. Our study assesses the diagnostic usefulness of thyroid ultrasonography with a high-resolution transducer by comparing their findings with radionuclide scanning and thyroid function tests in infants detected by neonatal screening program for CH in early life

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before initiation of therapy.

Subjects and Methods

This study consisted of 204 healthy infants (Group A: 102 males and 102 females, aged from newborn to 12 months, weight and height, from 2.5 kg to 11.8 kg and 46.0 cm to 83.5 cm, respectively) [10] and 174 infants (Group B: 98 males and 76 females, mean age and mean weight, 19.6 days and 3693 g, respectively) with elevated thyrotropin concentrations of blood filter paper at neonatal mass screening from July 1989 to September 1998 in Chiba who were suspected of having CH. In all of them, thyroid ultrasonography was performed at the time of their initial hospital visit for further examination. On the basis of the normal thyroid gland size obtained from Group A [10], Group B were divided into four subgroups according to the findings of thyroid ultrasound performed at initial hospital visit:

1) Normal in size (n = 117): the maximal width of thyroid on the transverse section in the normal location was within normal range (within ± 2SD).
2) Enlarged (n = 33): the maximal width of thyroid showed more than 2 standard deviations of the mean in appropriate body weight.
3) Small (n = 1): the maximal width of thyroid showed less than −2 standard deviations of the mean in appropriate body weight.
4) Invisible in the normal location (n = 23): the thyroid gland was not found.

The ultrasound findings were compared with the final diagnoses based on the results of chemical laboratory data and scintigraphic findings. Hormones were measured by commercial kits. Radionuclide scanning with ^{99m}Tc-pertechnetate or ^{123}I-sodium iodine was performed in infants of all in small and invisible subgroups and some cases in normal and enlarged subgroups after sonographic evaluation.

Sonographic procedures

Every infant was examined without sedation and in the supine position with the neck extended. An examination of neck area was performed to visualize thyroid tissue. Transverse image of thyroid gland was evaluated. Using a real-time mechanical sector scanner (SSD-650, ALOKA Co. Ltd., Japan) with digital scan-converter and high-frequency (7.5 MHz or 10 MHz) transducer, the maximal width of thyroid, the distance between the outer edges of each lobe, on the transverse image was measured (Fig. 1). Each ultrasonography examination was performed by ultrasonographers in each hospital "blinded" to the result of the radionuclide scanning.

Transient infantile hyperthyrotropinaemia was defined as elevated thyrotropin levels and normal thyroid hormone levels in a newborn with spontaneous recovery of thyrotropine levels within 1 year after birth [11]. Transient hypothyroidism was defined as high thyrotropine levels and low thyroxine in a newborn with spontaneous recovery within 1 year after birth [12]. Infants with persistent elevated thyrotropin that endured more than 1 year after birth were excluded because of undefined diagnosis.

Statistical significance was determined using the Student's *t* test. The data were expressed as mean ± SD.

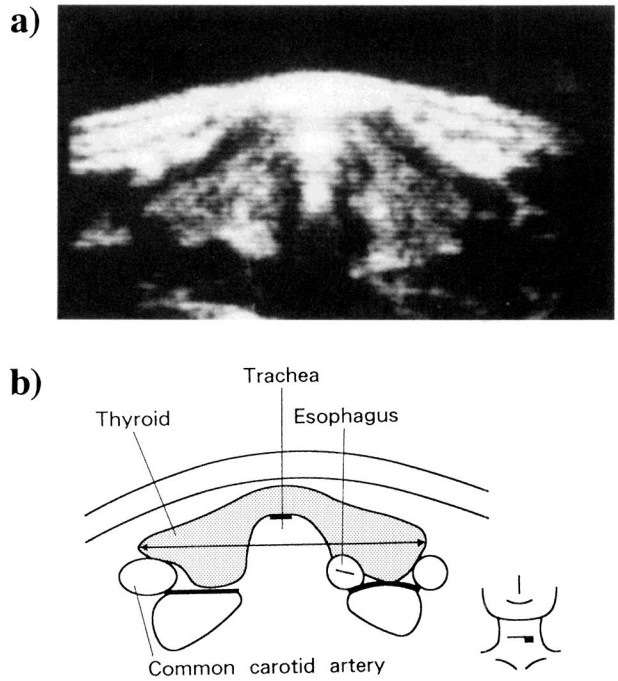

Fig. 1. Sonographic image of normal thyroid in a healthy infant and method of measurement of thyroid gland size.
a) Thyroid ultrasonography on transverse section in the normal location
b) Method of measurement of the maximal width of thyroid (arrow)

Result

1. Group A

The transverse views of the thyroid gland detected by ultrasound in all the healthy subjects were clearly obtained, in which the maximal transverse width was increasing with age and well correlated to body height, body weight and body surface area (Fig. 2, r = 0.874–0.887) [10].

2. Group B

Transverse views of the enlarged and invisible subgroups detected by ultrasound are showed in Fig. 3. Of the invisible subgroup, the hyperechogenic findings located laterally on both sides of the trachea may be contributed to remnants of the ultimobranchial body [13]. The final diagnoses based on the results of chemical laboratory data and scintigraphic findings in each subgroup are showed in Table 1.

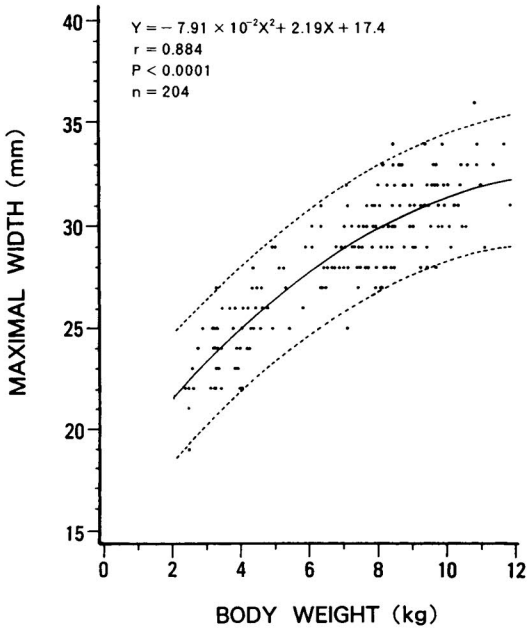

Fig. 2. Relationship between body weight and the maximal width of thyroid on transverse section in healthy infants. The curved area shows the 95% confidence limit of the maximal width in healthy infants.

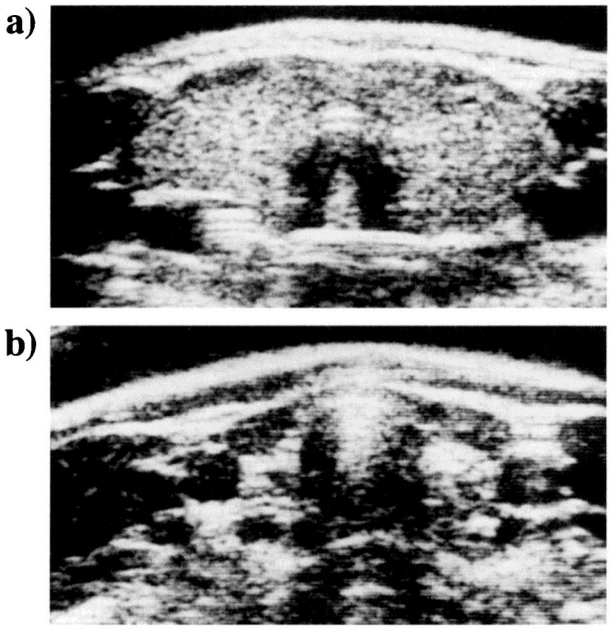

Fig. 3. Ultrasonogram of thyroid obtained on transverse section in the normal location. a): Enlarged b): Invisible

Table 1. Correlation of thyroid ultrasonography (US) with clinical diagnoses.

US Group	No. of Individuals	Healthy	IH	TH	CH		
					A	E	D
Normal	117	93	13	9	0	0	2
Enlarged	33	11	3	13	0	0	6
Small	1	0	0	0	0	1	0
Invisible	23	1	0	0	6	16	0

IH, transient infantile hyperthyrotropinaemia; TH, transient hypothyroidism; CH, congenital hypothyroidism; A, agenesis; E, ectopia; D, dyshormonogenesis.

1) Normal in size

In 117 infants with normal sized gland demonstrated by ultrasonography, 93 of infants were found to have a normal thyroid function; however, of the remaining 24 infants 2 were subsequently diagnosed as hypothyroid due to an inborn error of thyroid hormone metabolism (dyshormonogenesis) and 22 were revealed to have transient thyroid disorders (transient infantile hyperthyrotoropinaemia in 13 and transient hypothyroidism in 9).

2) Enlarged in size

In 33 infants with enlarged sized gland demonstrated by ultrasonography, 6 infants were found to be hypothyroid due to an inborn error of thyroid hormone metabolism. Of the remaining 27 infants, 16 were finally diagnosed as having thyroid disorders; however, 11 were revealed to be normal in thyroid function.

3) Small in size

The only case of small sized gland found by ultrasonography was revealed to have a lingual thyroid gland on radionuclide scanning.

4) Invisible in the normal location

Of the 23 infants with invisible gland in the normal location detected by ultrasonography, 16 and 6 were revealed to have ectopic (lingual or sublingual) and invisible thyroid glands on radionuclide scanning, respectively. The remaining one was found to have a normal thyroid function and thyroid gland size and shape, in the normal location, on radionuclide scanning.

Discussion

It is important to define the causes of congenital hypothyroidism since there are known differences in inheritance and prognosis. Agenesis, hypoplasia, and ectopia of thyroid are sporadic events, whereas inborn errors of thyroid hormone metabolism are inherited, usually in an autosomal recessive fashion. Genetic counseling, therefore, is required for patients with this disorder. Determining the presence or absence of functioning thyroid tissues is clinically important, because patients with functioning thyroid tissues have better neuropsychologic prognoses than those with none [2].

Pöyhönen and Lenko showed that the correlation between thyroid ultrasonography and radioisotope scintigraphy was poor in patients in whom there was no cervical thyroid tissue [6]. Muir *et al.* reported that neither thyroid ultrasonography nor serum level of thyrogrobulin were reliable alternatives to radionuclide scanning [3]. However, their study was performed with a static B scanner equipped with a 5- or 7 MHz transducer.

Our study was performed with a high-resolution transducer (7.5 MHz or 10 MHz) by the collaboration of ultrasonographers. Ultrasonography misinterpreted, for unknown reason, one ectopia (lingual) as dysplasia (small thyroid gland in the normal location). Perhaps the nearby soft tissue (for example, remnants of the ultimobranchial body or the sternocleidomastoid muscle) was misinterpreted as the thyroid gland [13]. Ultrasonography also misinterpreted one case with normally sited thyroid gland as invisible. The case may have had to be excluded from this study because of the subject's restlessness during the examination. A second examination of ultrasonography concluded that the case had normally sited thyroid gland.

In our study, ultrasound detection sensitivity and specificity for the presence or absence of the thyroid gland in the normal location were 96% (22/23) and 99% (150/151), respectively. The concordance between ultrasound examination and final diagnosis for the presence of the thyroid gland in the normal location is better in our study, compared with that of some previous studies [3, 6–8]. This may be due to the use of a high-resolution transducer and the larger number of patients we studied.

Since those with normal and enlarged sized gland may be healthy or having transient infantile hyperthyrotropinaemia, transient hypothyroidism and CH due to dyshormonogenesis, they need to have further examination to complete the diagnosis.

We conclude that the sonographically invisible images of thyroid gland in the normal location indicate thyroid agenesis or thyroid ectopia and the replacement therapy with full dose of L-thyroxine should immediately be started for them without waiting for the results of serum examination, whereas those with sonographically normal and enlarged gland require further examination to complete the diagnosis. Thyroid ultrasonography is a useful diagnostic imaging

technique and may be adopted as the first line image examination for patients with suspected CH. However, as a substitute for radionuclide scanning, more experience with thyroid ultrasonography is necessary before a decision can be reached.

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