Etiologic Study of Primary Congenital Hypothyroidism

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Abstract

The underlying causes of 35 children with primary congenital hypothyroidism at the Children's Hospital were studied. There were 21 girls and 14 boys. Serum T_4 and TSH level, 24 hours ^{131}I uptake, and technetium-99m thyroid scintigraphy were performed after discontinuation of synthetic thyroid hormone for 4-6 weeks. Athyrosis was the most common cause and accounted for forty-three per cent of the patients. Twenty per cent of the patients had thyroid hypoplasia. Ectopic thyroid was found in thirty-three per cent of the patients. Only a patient whose diagnosis was organification defect had slightly enlarged thyroid gland, high retention of ^{131}I and positive perchlorate discharge test. Onset of symptoms before 9 months of age may be helpful for distinguishing between lingual thyroid and the others. Serum T_4 level less than 2 μg/dL was observed to be more common in athyrosis and lingual thyroid groups than thyroid hypoplasia group.

Congenital hypothyroidism is one of the most common causes of endocrine disorders in childhood. Neonatal screening programs for congenital hypothyroidism (CH) from various countries has shown an incidence of approximately between 1:3,800 to 1:5,000[1-5]. In Thailand, its incidence from some studies is 1:1,792 to 1:3,900 [6,7]. Primary CH may be due to an absent or hypoplastic gland, an ectopic gland, or an inborn error of thyroid hormone metabolism[8].

In this report, we used ^{131}I thyroidal uptake and technetium-99m thyroid scintigraphy in determining the cause of CH. In addition, we determined which clinical or laboratory data is helpful for distinguishing the different causes of hypothyroidism.

MATERIAL AND METHOD

Thirty-five cases of CH were studied. They were 14 males and 21 females. Their mean age at

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the time of recall was 8.4 years (range 2 to 22 years). Their clinical and laboratory data were retrospectively analyzed. All patients had typical myxedema, low serum T_4, retarded skeletal age, and decreased 24 hours ^{131}I uptake. They had been on synthetic thyroid hormone until 4-6 weeks prior to the study. Determination of serum T_4, serum TSH, ^{131}I uptake at 24 hours and technetium-99m scanning of the thyroid gland were then performed on all children. Grouping was based primarily on the result of scintiscanning of the thyroid gland. The findings were then correlated with the clinical and laboratory data.

RESULTS

Most cases (71%) lived in the central part of Thailand. None had a history of hypothyroidism in other siblings or relatives. All mothers were healthy and denied taking any antithyroid drugs, radioactive iodine during the pregnancy.

The result of etiologic study of CH is shown in Table 1. Athyrosis was found in 15 patients (42.9%). They had 24 hours ^{131}I uptake between 0-9 per cent and negative thyroid scintiscanning. In 7 patients (20.0%) with thyroid hypoplasia, three had normal size of thyroid, and four had small thyroid glands. Their ^{131}I uptake at 24 hours varied between 0 to 20 per cent. Twelve patients (34.3%) had lingual thyroid and had 24 hours ^{131}I uptake between 0-9 per cent. The only patient who was suspected of organification defect had a slightly enlarged thyroid gland, her 3 hours and 24 hours ^{131}I uptake were 22.17 per cent and 8.27 per cent respectively. Perchlorate discharge test was positive. However, there was no family history of thyroid disease in this patient.

Table 2 shows comparison of age at onset between the 3 groups. No patient in the lingual thyroid group was diagnosed before 9 months of age. In athyrosis and thyroid hypoplasia groups, most of them were diagnosed before 9 months of age.

Table 3 shows comparison of clinical data at onset between the 3 groups. Most of them were females. About eighty per cent of lingual thyroid group presented with delayed development and failure to thrive. Symptoms that were found only in athyrosis and thyroid hypoplasia groups included hoarse voice, and lethargy whereas prolonged jaundice was found only in the athyrosis group. No clinical data were significantly different between these groups (P>0.05). One child with organifica-

Table 1. Grouping of the patients according to the result of 24 hours ^{131}I uptake and ^{99m}Tc scanning of thyroid gland.

Group	No.(%)	% 24 hours ^{131}I uptake (normal 20-50)				Thyroid scintiscanning			
		0-3 No.(%)	3-6 No.(%)	6-9 No.(%)	18-20 No.(%)	negative No.(%)	small No.(%)	normal No.(%)	enlarged No.(%)
1. Athyrosis	15(42.9)	12(80.0)	1(6.7)	2(13.3)	-	15(100)	-	-	-
2. Thyroid hypoplasia	7(20.0)	4(57.1)	1(14.3)	-	2(28.6)	-	4(57.1)	3(42.9)	-
3. Lingual thyroid	12(34.3)	4(33.3)	6(50.0)	2(16.7)	-	-	-	-	-
4. Organification defect	1(2.9)	-	-	1	-	-	-	-	1

Table 2. Comparison of age onset between 3 groups of cretins.

Age at onset (month)	No.(%)		
	Athyrosis	Thyroid hypoplasia	Lingual thyroid
0- <3	6 (40.0)	3 (42.9)	-
3- <6	2 (13.3)	1 (14.3)	-
6- <9	1 (6.7)	3 (42.9)	-
9- <12	2 (13.3)	-	3 (25.0)
>12	4 (26.7)	-	9 (75.0)
Total	15	7	12

Table 3. Comparison of clinical data at onset between 3 groups of cretins.

Clinical data	No.(%)			P value		
	Athyrosis[a] (n=15)	Thyroid[b] hypoplasia (n=7)	Lingual[c] thyroid (n=12)	(a) VS (b)	(a) VS (c)	(b) VS (c)
Female	8 (53.3)	3 (42.9)	9 (75.0)	1.00	0.42	0.32
Constipation	8 (53.3)	2 (28.6)	5 (41.7)	0.38	0.55	0.65
Delayed development	9 (60.0)	6 (85.7)	10 (83.3)	0.35	0.23	1.00
Failure to thrive	7 (46.7)	3 (42.9)	10 (83.3)	1.00	0.11	0.12
Distended abdomen	4 (26.7)	1 (14.3)	3 (25.0)	1.00	1.00	1.00
Dry skin	1 (6.7)	1 (14.3)	1 (8.3)	1.00	1.00	1.00
Hoarse voice	2 (13.3)	3 (42.9)	-	0.27		
Lethargy	2 (13.3)	1 (14.3)	-	1.00		
Umbilical hernia	1 (6.7)	-	2 (16.7)		0.57	
Prolonged jaundice	4 (26.7)	-	-			
Pale	1 (6.7)	-	-			

Table 4. Comparison of laboratory data after discontinuation of synthetic thyroid hormone between 3 groups of cretins.

Clinical data	No.(%)			P value		
	Athyrosis[a]	Thyroid[b] hypoplasia	Lingual[c] thyroid	(a) VS (b)	(a) VS (c)	(b) VS (c)
T4 <2	12/13 (92.3)	3/7 (42.9)	11/12 (91.7)	0.03	1.00	0.04
TSH >50	11/14 (78.6)	2/7 (28.6)	10/12 (83.3)	0.06	1.00	0.04
Delayed bone age	3/15 (20.0)	1/6 (16.7)	3/12 (25.0)	1.00	1.00	1.00

tion defect presented with seizure, jaundice, and typical myxedema but no other significant symptoms.

The laboratory data after discontinuation of synthetic thyroid hormone was compared between 3 groups (Table 4). A greater proportion of children with athyrosis and lingual thyroid had serum T_4 level less than 2 μg/dl when compared with those with thyroid hypoplasia ($P<0.05$). In addition, groups of children with athyrosis and lingual thyroid also had a higher serum TSH level than those with thyroid hypoplasia. The number of patients with delayed skeletal age was not different between the groups ($P>0.05$).

DISCUSSION

We found a significant number of patients with lingual thyroid in this study which was different from the study of Churesigaew S[9] which reported no case with ectopic thyroid gland. This might be the result of scintiscanning technique. In this study, we used technetium-99m scanning of thyroid gland instead of ^{131}I scanning because the former technique was considered to be superior than the latter by many authors[10-12]. In addition, technetium-99m is useful in evaluating the anatomy of a gland in patient who may have a low iodine uptake. In this study, we could demonstrate the ectopic thyroid as one of the common causes of primary CH which agreed with other studies[5,8].

As in other series[5,8,13-16], the primary CH was more common in girls than in boys, though the lingual thyroid group in this study was not. In various studies, between 37 and 57 per cent of the diagnosis of hypothyroidism due to ectopic thyroid tissue were made within the first year of life, and retardation of growth and development were common presentations. Depending upon the amount of thyroid hormone produced, the signs and symptoms of hypothyroidism may be masked causing delayed diagnosis[17]. Comparing this study with the others, our cases with lingual thyroid gland were diagnosed after late infancy period. There were only 25 per cent of our patients with lingual thyroid gland who were diagnosed before 12 months of age. Most of them were presented with failure to thrive and delayed development. Hoarse voice, lethargy and prolonged jaundice were found only in athyrosis and thyroid hypoplasia groups. In our opinion, the age at presentation might be helpful for differentiating the lingual thyroid group from the others groups. However, other factors were not helpful for distinguishing the different etiologies of primary CH.

Some laboratory data after discontinuation of synthetic thyroid hormone including serum T_4 and TSH levels were different between these groups. Since serum T_4 level less than 2 μg/dl was found in the majority of athyrosis and lingual thyroid groups compared to the thyroid hypoplasia group, it might reflect the wide range of thyroid function in the thyroid hypoplasia group.

In organification defect of thyroid hormone synthesis, the patients usually had goiter and most of them had a family history of this defect[18]. Due to the high risk of recurrent rate in the siblings, counseling to their parents is very important.

SUMMARY

We studied the underlying causes of 35 cases with primary congenital hypothyroidism. There were 21 girls and 14 boys with age at time of recall of 2 to 22 years. The technetium-99m thyroid scintigraphy had shown that most of them had athyrosis (42.9%) followed by lingual thyroid which accounted for 34.3 per cent of these patients. Thyroid hypoplasia was found in 20.0 per cent of cases. One case whose diagnosis was organification defect had a slightly enlarged thyroid gland, high retention of ^{131}I, and positive perchlorate discharge test. Onset of symptoms before 9 months of age may be helpful for distinguishing between lingual thyroid and the others. Serum T_4 less than 2 μg/dL was observed to be more common in athyrosis and lingual thyroid groups than in the thyroid hypoplasia group.

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การศึกษาสาเหตุในผู้ป่วยที่ขาดธัยรอยด์ฮอร์โมนแต่กำเนิดชนิดปฐมภูมิ

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ได้ศึกษาถึงสาเหตุของภาวะขาดธัยรอยด์ฮอร์โมนแต่กำเนิดชนิดปฐมภูมิที่โรงพยาบาลเด็กจำนวน 35 ราย เป็นเพศหญิง 21 ราย เพศชาย 14 ราย อายุตั้งแต่ 2.2 ถึง 22 ปี โดยหยุดยาฮอร์โมนธัยรอยด์ที่ใช้รักษาผู้ป่วยเหล่านี้เป็นเวลานาน 4 ถึง 6 สัปดาห์ แล้วตรวจระดับ serum T_4, TSH, skeletal age, วัดระดับ ^{131}I uptake ที่ 24 ชั่วโมง และทำ technetium-99m scanning of thyroid gland

พบว่าผู้ป่วยทุกรายมีระดับ serum T_4 ต่ำและ TSH สูง ส่วนใหญ่ skeletal age ปกติ จาก thyroid scan พบผู้ป่วยที่ไม่มีต่อมธัยรอยด์เลยมากที่สุด (ร้อยละ 42.9) โดยมีระดับ ^{131}I uptake ร้อยละ 0-9 ผู้ป่วยที่มีต่อมธัยรอยด์เล็กกว่าปกติ (ร้อยละ 20) มีค่า ^{131}I uptake ร้อยละ 0-20 พบผู้ป่วยมีต่อมธัยรอยด์อยู่ผิดที่ร้อยละ 34.3 โดยมีค่า ^{131}I uptake ร้อยละ 0-9 ผู้ป่วย 1 รายมีความผิดปกติของเอ็นซัยม์ที่ใช้ในการสังเคราะห์ธัยรอยด์ฮอร์โมน โดยมีต่อมธัยรอยด์โตและมี ^{131}I ค้างอยู่ในต่อมมากกว่าปกติ และ การทดสอบ perchlorate discharge test ให้ผลบวก ประวัติอายุของผู้ป่วยเมื่อเริ่มแสดงอาการขาดธัยรอยด์ฮอร์โมนอาจช่วยแยกกลุ่มได้ โดยถ้าผู้ป่วยเริ่มแสดงอาการก่อนอายุ 9 เดือน มักไม่ใช่ต่อมธัยรอยด์อยู่ผิดที่ ระดับ serum T_4 ต่ำกว่า 2 μg/dl พบในกลุ่มไม่มีต่อมธัยรอยด์และต่อมธัยรอยด์อยู่ผิดที่ได้บ่อยกว่ากลุ่มต่อมธัยรอยด์มีขนาดเล็กกว่าปกติอย่างมีนัยสำคัญทางสถิติ

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