CONGENITAL PRIMARY HYPOTHYROIDISM DIAGNOSED AT ADVANCED AGES

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ABSTRACT

• ***Objective:*** *Aim of this study was to investigate that clinical and laboratory findings of sixteen cases who were referred to our endocrinology outpatient clinic due to a complaint of growth and developmental delay and who were diagnosed with primary congenital hypothyroidism at advanced ages.*

• ***Material and Method:*** *Sixteen cases of which the youngest was minimum six and the oldest was 23 years old were enrolled into the study. Anthropometrical measures, chrono-logical, height and bone ages of the patients were recorded.*

Hypothyroidism was diagnosed by the decrease in free thyroxin (sT4) levels and the elevated in serum thyroid stimulating hormone (TSH) levels. To clarify the etiology, thyroglobulin (TG) level and thyroid ultrasonography were studied from the patient. Also thyroid scintigraphy was performed to the patients without a thyroid tissue at a normal anatomical localization.

• ***Results:*** *The mean diagnostic age in our cases was 12.6±4.3 years and female were predominant was present (female/male: 4/1). Height, weights and bone ages of patients were severely retarded. Ectopia was determined in two patients while in twelve patients the thyroid gland was hypoplastic. The thyroid gland was within normal borders in one patient for age and gender and hyperplasic in another case.*

• ***Conclusion:*** *We wanted to emphasize that congenital hypothyroidism should be kept in mind in cases with developmental delay and mental retardation as these may be non-diagnosed congenital hypothyroidism also infant or early childhood outside. It must be remember, diagnose of these patients may delay until the pre-adolescence and even prior the adulthood. We wish attract attention to the national screening program for congenital hypothyroidism by this study.*

• ***Key Words:*** *Congenital hypothyroidism diagnosed at advanced age, children, adolescent.* **Nobel Med 2010; 6(1): 74-77**

İLERİ YAŞLARDA TANI ALAN KONJENİTAL PRİMER HİPOTİRODİ

ÖZET

• **Amaç:** Bu çalışmanın amacı, çocuk endokrinolojisi polikliniğimize, gelişme geriliği yakınması ile gönderilen ve konjenital primer hipotiroidi tanısı alan ileri yaşlarda on altı vakanın klinik ve laboratuvar bulgularını incelemekti.

• **Materyal ve Metod:** Bu çalışmaya; en küçüğü 6 en büyüğü 23 yaşında olan on altı vaka kabul edildi. Hastaların antropometrik ölçümleri, takvim, boy ve kemik yaşları kaydedildi. Hipotiroidi tanısı, düşük serbest (sT4) düzeyi ve yükselmiş tiroit uyarıcı hormon düzeyi (TSH) ile konuldu. Etiyolojiyi aydınlatmak için tiroglobulin (TG) düzeyine bakıldı ve tiroit ultrasonografisi yapıldı. Normal anatomik lokalizasyonunda izlenemeyen vakalara ise tiroit sintigrafisi uygulandı.

• **Bulgular:** Vakalarımızda ortalama tanı yaşı 12,6±4,3 yıldı ve kız predominansı vardı (kız/erkek; 4/1). Hastaların boy, vücut ağırlığı ve kemik yaşları ileri derecede geri kalmıştı. İki hastada ektopik tiroit dokusu saptanırken 12 hastada tiroit bezi hipoplazikti. Bir hastada tiroit bezi yaşa ve cinsiyete göre normal büyüklükte iken, diğer bir hastada hiperplazikti.

• **Sonuç:** Gelişme geriliği ve zeka geriliği olan vakaların etyolojisinde, süt çocuğu veya erken çocukluk dönemi dışında da, konjenital primer hipotiroidiyi akılda bulundurmak gerektiğini vurgulamak istedik. Bu hastaların konjenital hipotiroidi tanısı almalarının, ergenlik öncesi hatta genç erişkin döneme kadar gecikebileceği hatırlanmalıdır. Ulusal yeni doğan hipotiroidi taramasının önemine bu vakalarla tekrar dikkat çekilmiştir.

• **Anahtar Kelimeler:** Konjenital hipotiroidi, gecikmiş tanı, çocuk, ergen. **Nobel Med 2010; 6(1): 74-77**

Table 1: Clinical and laboratory findings of cases.

CASE NO	GENDER	CALENDAR AGE (YEAR)	HEIGHT SDS	BONE AGE (YEAR)	BODY WEIGHT (SDS)	TOTAL T4 (mg/ml)	FREE T4 (ng/dl)	TSH (mu/ml)	THYROGLOBULIN (n g/ml)	THYROID USG	WALKING AGE (MO)	SPEAKING AGE (MO)	MENTAL RETARDATION
1	Male	13	-9.1	0.5	-2.5	<1	0.56	62.6	<0.2	Hypoplasia	12	None	Severe
2	Male	12	-7.8	0.5	-2.5	<1	0.56	>75.0	<0.2	Hypoplasia	48	None	Severe
3	Female	23	-10	8.5	-4.1	<1	0.57	>75	1.1	Hypoplasia	?	?	Severe
4	Female	15	-12.5	2	-6.1	<1	0.57	>75	<0.2	Hypoplasia	None	None	Severe
5	Female	14	-7.7	1.5	-5.1	<1	0.57	>75	<0.2	Normal	12	12	Severe
6	Female	12	-6	1.8	-4.2	<1	<0.30	>75	1.55	Hypoplasia	36	36	Moderate
7	Female	12	-2.3	8.5	0.9	6.4	1.07	36.1	150	Ectopic thyroid gland	12	12	None
8	Female	9	-13.9	2.5	-3.5	<1	0.36	>75	0.77	Hypoplasia	None	None	Severe
9	Female	18	-11.8	0.9	-6.3	<1	<0.30	30	1.36	Nodular hyperplasia.	None	None	Severe
10	Female	6	-4.1	2	-2.2	<1	0.57	>75	20	Hypoplasia	None	60	Moderate
11	Female	13	-8.8	1.3	-4.3	<1	<0.30	>75	30.6	Hypoplasia	?	?	Moderate
12	Female	7.3	-4.1	2.5	-1.8	3.5	0.6	>75	1.21	Hypoplasia	?	?	mild
13	Male	6.3	-2.8	2.3	-1.5	1.54	0.29	>75	20	Hypoplasia	24	24	Moderate
14	Female	13	-8.8	1.3	-3.5	<1	<0.3	>75	30	Hypoplasia	?	None	Severe
15	Female	15.4	-9	1.8	-5.2	<1	<0.3	>75	24.5	Ectopic thyroid	18	24	Moderate
16	Male	12.8	-3.7	6.5	-1.7	3.7	0.6	>75	22	Hypoplasia	12	?	mild

SDS: Standart Deviation of Statistical, USG: Ultrasonography, MO: Month

INTRODUCTION

Congenital hypothyroidism is one of the most frequent causes of growth and developmental delays and preventable mental retardation that may occur due to an anatomical defect of the thyroid gland, inadequate production of thyroid hormones that source from a disorder in the thyroid metabolism or iodine deficiency.[1] The morbidity of congenital hypothyroidism can be reduced to a minimum by early diagnosis and therapy. Unfortunately, usually the disease may become evident after many symptoms of the condition leads to an irreversible brain damage. It was reported that, during the first month of birth, only 10% of the congenital hypothyroidism cases were diagnosed by clinical findings while 35% were diagnosed within 3 months after birth and 70% within a year and 100% only within 3-4 years of age, before screening for hypothyroidism.[2] Unfortunately a national screening for this condition in our country has initiated only two years ago.

In the present case series, we introduced sixteen cases who were referred to our endocrinology outpatient clinic with developmental delay and who were diagnosed with primary congenital hypothyroidism at an advanced age.

MATERIAL and METHOD

Newly diagnosed sixteen cases, of which the youngest was minimum six and the oldest was 23 years old were enrolled into the study. Anthropometrical measures, calendar, length and bone ages of the patients were recorded. The height of the patients was measured by a Holtain limited crymch, dyfed (Britain) stadiometry. Turkish children percentile growth curves reported by Neyzi et al were used to evaluate of the height and body weight percentiles and the height ages of patients.[3] Bone ages were assessed by the means of the Greulich and Pyle atlas.[4] Hypothyroidism was diagnosed by the decrease in free thyroxin (sT4) and total thyroxin (TT4) levels and the increase in serum TSH levels. According to the etiological aspect, thyroglobulin (TG) level and thyroid ultrasonography were studied from the patient. Also thyroid scintigraphy was performed to the patients without a thyroid tissue at a normal anatomical localization. Serum sT4, TSH and TG levels were measured with an Immulite 2000 (DPC, Los Angeles, USA) brand hormone analyzer by using a chemiluminance method and Immulite kits. Thyroid gland ultrasonography was performed in using a 7.5 mHz linear transducer by the means of a Toshiba SSA 270A (Japan) brand ultrasound device.

RESULTS

The mean diagnostic age in our cases was 12.6±4.3 years and as female predominance was present (female/male: 4/1). Common findings were a course facial appearance, macro glossy, short neck, thick and dry hair; cold and pale skin and short height (cases 1-6, 8-11). Seven of the patients were able to walk without→

aid. However walking started at very advanced ages in all patients (Table 1). Only four of the patients were able to speak; however, speaking began at a delayed age and was not sufficient to maintain a cooperative level. Except for only one case (case 7), mental status of the patients were grossly. The height of the patients according to age and gender (mean 7.6 SDS) and body weights (mean 2.6 SDS) and bone ages (mean 3.5 years of age) were severely delayed. The thyroid glands in two patients (figure 1) were minimally enlarged by palpation while in one patient (figure 3, 4) it was large enough to cause suppressive symptoms. One of the patients (figure 2) displayed a thoracal kyphoscoliosis and an increased lordosis. An eight years old girl (figure 6) presented with thick, harsh and dark color hair on the back. Signs of puberty were delayed in 7 patients. One patient was pubertal (Tanner stage III, in case 3). We noticed that thyroglobulin levels were low which were due to hypoplasia or aplasia of thyroid gland (Table 1). Na L-thyroxin was administered to all patients 15 µg/kg/day. During follow up we observed that the height of the patients increased, firstly after a weight loss of an average 1-2 kg patient began to gain weight, and that their facial expression improved and their motion increased. Total mass excision was applied to patient 9 with a suppression symptom at the neck. Histopathological study revealed a diagnosis of nodular hyperplasia.

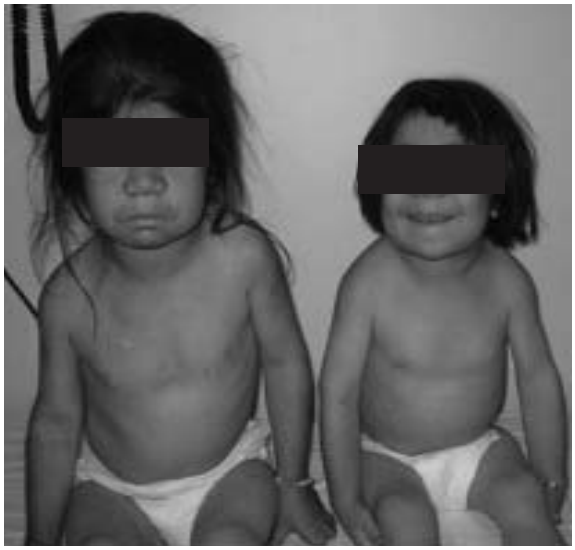

Fig 1. The thyroid gland is palpable of Cases 4-5 who are siblings

DISCUSSION and CONCLUSION

Congenital hypothyroidism is a frequently observed endocrinologycal disorder of childhood. Incidence of congenital hypothyroidism according to data obtained from countries where neonates are screened routinely was found to be 1: 3000-1: 4000. 5 Recently in some countries higher incidences such as 1/1800, 1/2759 were also reported.[6, 7] Although new born babies are screening for congenital hypothyroidism at birth in our country for the last two years, routine screening was not yet available at the time of diagnosis of our cases.

Based upon the results obtained from the neonatal screening process, it is reported that the most frequent etiological cause of congenital hypothyroidism is thyroid dysgenesis.[6-8] In a pilot study carried out in Turkey the incidence of congenital hypothyroidism was found to be 1/2730 and atresia of thyroid gland was reported to be the most frequent etiological cause.[9] In the present study, ectopia was determined in two patients while in twelve patients the thyroid gland was hypoplastic. However, the thyroid gland was hyperplastic only in one patient (case 9) and within normal limits in another case (case 5). It is necessary to do scintigraphic examination in all cases of hyphoplastic thyroid gland to exclude athyrosis but we couldn't do it (exception of two cases that had not observed thyroid gland with US) due to the fact that low economic status of our patients.→

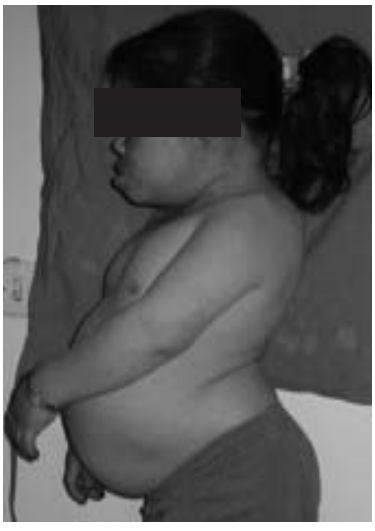

Fig 2. Lateral view of case 3

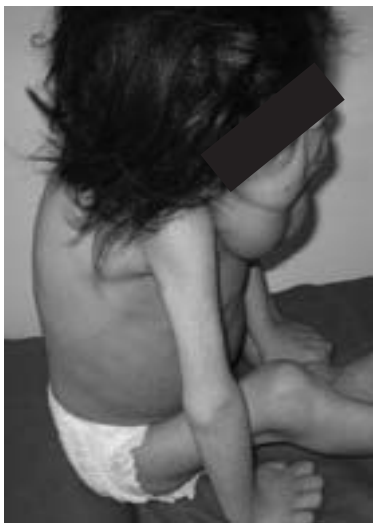

Fig 3. Lateral view of case 9

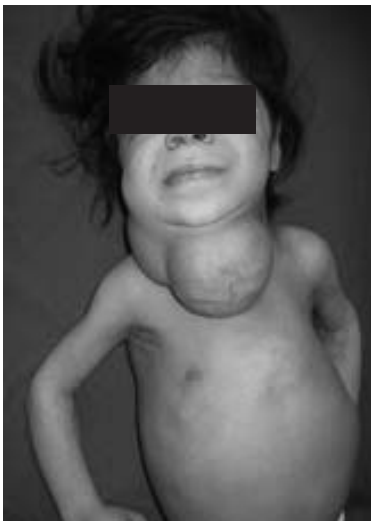

Fig 4. Front view of case 9

In many studies, female to male ratio was reported as 2/1, but Devos et al reported this ratio as 3/1 in Hispanic individuals.[10] In our series female predominance was present (4/1). Congenital hypothyroidism is usually diagnosed during the neonatal period or early infancy. Children diagnosed with hypothyroidism at two years of age or older may refer to hospitals due to uncertain growth and developmental retardation. Untreated congenital hypothyroidism cases may display different levels of mental retardation and delayed linear growth and bone maturation.[11]

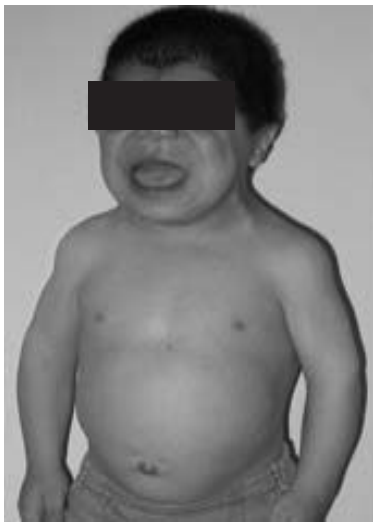

Fig 5. Front view of case 2

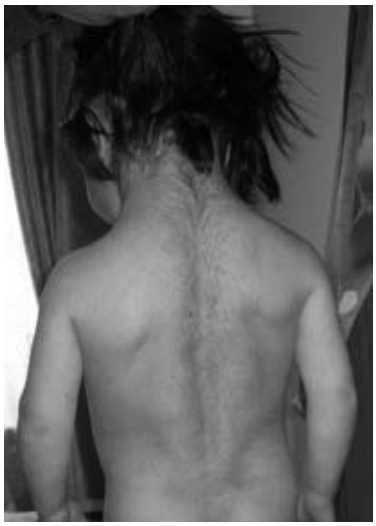

Fig 6. View of dark color hair on the back of case 6

Infants with delayed treatment may demonstrate neurological disorders such as spasticity and corrupted walking patterns, dysarthia or mutism and autistic behavior. According to age and gender the height of our patients, their mean height SDS; - 7.6 SDS (the highest-2.3 and the lowest -13.9) and body weights (mean - 2.6 SDS) and bone ages of mean - 2.7 years of age (the youngest 0.5 and the oldest 8.5 years of age) were severely delayed. Except for one patient (case 7), we diagnosed mental retardations in all of the patients. Twelve of the patients were able to walk, but walking started very lately than it is expected. Only six of the patients were able to speak. Three of these patients talked at a very late age and are not yet adequate to maintain a full cooperation. Patients were followed mean of 18.3 months (maximum 2 and minimum 33 months) and it was observed during follow up controls that the length of the patients extended (mean 5.9 cm/year), and after a mean weight loss of 1-2 kg at the beginning, patients began to gain weight, and their face expression and glances were more meaningful and there was an increase in their motion.

Most patients were staying in rural areas while some stayed in urban areas. Although sanitary services is easily available and free of charege, our patients were not taken to the doctor and they were accepted as a disables. Their parents were had low education and socio-cultural levels. In spite of improvement in their health, they were not brought to hospital for regular controls after one year from diagnose (except two patients).

In this study, we found that there were many congenital hypothyroidism cases which were not diagnosed through out the pre-adolescence, adolescence periods and even at adult ages, and therefore we wish to emphasize that it is important to consider congenital hypothyroidism in patients who display significant delay in growth and development. Otherwise, we want to underline importance of screening test for hypothyroid in new born period.

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✔ **DELIVERING DATE:** 15/ 11 / 2008 • **ACCEPTED DATE:** 14 / 07 / 2009

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