Clinical Presentation of Primary Congenital Hypothyroidism: Experience Before Mass Screening

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Abstract

Primary congenital hypothyroidism is a common preventable cause of mental retardation. Neonatal thyroid screening is highly successful in early diagnosis and the improvement of developmental prognosis in the hypothyroid neonate. However, rarely cases could be missed, so doctors must be aware of the earl symptoms and signs of hypothyroidism. Therefore, the purpose of this study was to emphasize the presenting clinical features of primary congenital hypothyroidism at the age of diagnosis. The study population included 17 children with primary congenital hypothyroidism who attended the Department of Pediatrics, University Clinical Center Tuzla between 1986 and 1999. The diagnosis of all patients was confirmed by serum thyroid function tests (T4 and TSH). Of the 17 patients 10 (58.8%) were diagnosed in the first three months of life and 3 of them (17.6%) between fourth and sixth month of life. Four children (23.5%) were diagnosed after the age of six months. In the first three months of life hypothermia, constipation, jaundice, poor feeding, hoarse cry, macroglossia and hypoactivity were the moste common symptoms. Among the 17 patients with primary congenital hypothyroidism 5 of them (29.4 %) were diagnosed to have disgenetic thyroid tissue and 12 (70.6%) as having dyshormonogenesis. TSH and T4 levels were higher in patients in whom thyroid tissue was dysgenetic as comapared with those with dyshormonogenesis but the difference was not statistically significant ($p>0.05$). Now it is expected that neonatal screening program in Bosnia and Herzegovina Federation will contribute to the detection of primary congenital hypothyroidism in early days of life. However, until an effective screening test is not yet routine in whole country, paediatricians should consider the diagnosis of hypothyroidism whenever it is clinically suggested.

KEY WORDS: primary congenital hypothyroidism, clinical presentation

Introduction

Primary congenital hypothyroidism (PCH) is a common preventable cause of mental retardation. The overall incidence is approximately 1:3500 to 1:4000, females are affected about twice as often as males (1). The incidence for our country is unknown. Approximately 85% of cases are sporadic, while 15% are hereditary. The most common sporadic etiology is thyroid dysgenesis, with ectopic glands more common than aplasia or hypoplasia. The most common hereditary etiology is the inborn errors of thyroxine (T4) synthesis which characterized by normal-sized or enlarged thyroid gland in the normal position (2,3). Approximately 5% to 10% of infants identified by the newborn screening program have transient form of congenital hypothyroidism which the causes remain incomplete understood (4). Neonatal thyroid screening is highly successful in early diagnosis and the improvement of developmental prognosis in the hypothyroid neonate. However, rarely cases could be missed, so doctors must be aware of the early symptoms and signs of hypothyroidism. An improperly collected and labeled specimen, the absence of a specimen, laboratory error, and various physiologic and pathophysiologic conditions are responsible for missed cases (1). In addition, in the territory like Bosnia and Herzegovina Federation that has not tradition of neonatal screening some percent of neonates is not tested in spite of implemented neonatal screening program. Therefore, the purpose of this study was to emphasize the presenting clinical features of PCH at the age of diagnosis.

Patients and Methods

The study population included 17 children with PCH who attended the Department of Pediatrics, University Clinical Center Tuzla betwen 1986 and 1999. The diagnosis of all patients was confirmed by serum thyroid function tests (T4 and TSH). Recording data included gestational age, age at diagnosis, clinical manifestations, laboratory investigations and etiology. Thyroid ultrasound included a survey of the pathway of the thyroglossal tract and evaluation of the location, size and echogenicity. The subjects were examiend in the supine position with the neck hyperextended. Imagines were obtained in the transverse and longitudinal planes. Thyroid scintigraphy with pertechnetate Tc 99m was performed using gamma camera equipped. Thyroid function was assessed using comercial kits for fluoroimmunoassay measurements of Total T4, and TSH (Delphia-Wallac, Turku, Finland). Statistical analysis was performed using the Arcus Quic statistical package for personal computers.

Results

Of the 17 patients diagnosed as PCH 8 are females and 9 are males. Seven (41.2 %) patients had gestational ages > 41 wk and 4 (23.5 %) body weight at birth > 4 kg. The mean age (± SD) of the children at the time of diagnosis was 4.5 months ±5.38 (range 3 day to18 months). Prevalence of symptoms and signs according to the age of diagnosis is shown in Table 1.

OBSERVED SYMPTOMS AND SIGNS	AGE AT DIAGNOSIS (MONTHS)							
	0-3 (n= 10;58,8%)		4-6 (n=3;17,6%)		7-12 (n=2;11,6%)		>12 (n=2;11,6%)	
	n	%	n	%	n	%	n	%
HYPOTHERMIA <36,5°	9	90,0	3	100,0	2	100,0	2	100,0
CONSTIPATION	5	50,0	2	66,7	2	100,0	2	100,0
JAUNDICE	5	50,0	-	100,0	-	-	-	-
POOR FEEDING	8	80,0	3	100,0	2	100,0	2	100,0
DRY OR MOTTLED SKIN	3	30,0	2	66,7	2	100,0	2	100,0
HOARSE CRY	6	60,0	3	100,0	2	100,0	2	100,0
PUFFY FACE	4	40,0	2	66,7	2	100,0	2	100,0
MACROGLOSSIA	6	60,0	3	100,0	2	100,0	2	100,0
HYPOACTIVITY	8	80,0	3	100,0	2	100,0	2	100,0
ABDOMINAL DISTENSION	4	40,0	3	100,0	2	100,0	2	100,0
UMBILICAL HERNIA	4	40,0	3	100,0	2	100,0	2	100,0

TABLE 1. Prevalence of symptoms and signs according to the age of diagnosis

Of the 17 patients 10 (58,8%) were diagnosed in the first three months of life and 3 (17,6%) between fourth and sixth month of life. Four children (23,5%) were diagnosed after the age of 6 months. In the first three months of life hypothermia, constipation, jaundice, poor feeding, hoarse cry macroglossia and hypoactivity were the moste common symptoms. Between fourth and sixth month of life constipation and dry or mottled skin were present in 66,7% cases and other symptomes and signes listed in Table 1 were present in 100,0% cases. As expected, after the 6th month of age all signs and symptoms of hypothyroidism listed in Table 1 with the exception of jaundice were present in all children. Characteristics of the patients with primary congenital hypothyroidism (at the time of diagnosis) with respect to etiology assessed by ultrasonography and/or thyroid scanning findings are shown in the Table 2. Among the 17 patients with PCH 5 of them (29,4 %) were diagnosed to have dysgenetic thyroid tissue and 12 (70,6%) as having dyshormonogenesis. Initial results of TSH and T4 in patients with dysgenetic thyroid tissue and dyshormonogenesis are presented in Table 3. Serum TSH and T4 levels were higher in patients in whom thyroid tissue was dysgenetic as comapared with those with dyshormonogenesis but the difference was not statistically significant (p>0,05)

Discussion

Our study showed that congenital hypothyroidism was detected in 10 patients (58,8%) before a 3 months period has elapsed. In similar study (5) only 27% patients were diagnosed in the first three months of life. Hypothermia, constipation, poor feeding, hoarse cry, macroglossia, prolongate neonatal jaundice and hypoactivity were the most common symptoms in CH within 3 months of life. The presence of initial signs and symptoms in CH is similar to that of other studies (5,6). Early diagnosis and treatment is extremely important in patients with CH to prevent mental and somatic retardation (7) because late diagnosis in neonates with congenital hypothyroidism results in brain damage with the clinical consequence of irreversible mental and somatic retardation. In countries where neonatal screening for CH is not yet routine general practitice and paediatricians should try to diagnose congenital hypothyroidism early, so that treatment can be initiated as soon as possible. Early postnatal signes of hypothyroidism such as those listed in Table 1 need to be the major basis for detection of CH (6). To explore etiological diagnosis of CH we used ultrasonography and/or thyroid scanning findings and found 5 patients to be disgenetic thyroid tissue and 12 patients with normal location. This is not the usual etiological distribution and may reflect sampling bias. Among the patients with normal location eight of them have goiter and the patients with dysgenetic thyroid tissue 3 have ectopic thyroid gland and 2 have global hypoplasia of the gland. Tests to determinate the underlying etiology are important to proven a hereditary form of PCH. They guide counseling regarding futures pregnancies (2, 8). Thyroid ultrasound assessment is noninvasive and may also be informative for

ETIOLOGY	NUMBER OF CASES		
	F	M	Total
DYSGENESIS			
Hypoplasio	2	-	2
Ectopic	-	3	3
DYSHORMONOGENESIS	6	6	12
TOTAL	8	9	17

TABLE 2. Etiology of primary congenital hypothyroidism

CONGENITAL HYPOTHYROIDISM	RESULTS OF THYROID FUNCTION TESTS (X±SD)	
	TSH (mIU/L)	Total T_4 (nmol/L)
DYSGENESIS (N=5)	191,1±45,8*	13,8±11,7*
DYSHORMONOGENESIS (N=12)	(127,6 - 237,0)	(2,1-30,0)
	179±108,4	9,6±18,2
	(60,0-404,0)	(0,04-66,0)

P >0,05 compared to dyshormonogenesis.

TABLE 3. Compariason of initial TSH and T4 results among two groups of patients with primary congenital hypothyroidism

etiologic diagnosis of PCH (9). However, it is generally accepted that thyroid ultrasonography for etiologic diagnosis can not replace thyroid scanning (9,10). TSH and T_4 levels were higher in patients in whom thyroid tissue was dysgenetic as comapared with those with dyshormonogenesis but the difference was not statistically significant ($p>0,05$). The mean age of our patients at the time of diagnosis was 4,5 months. Someone of them were detected beyond 3 months when the prognosis for normal intelectual and neurological function and linear growth is poor.

Now it is expected that neonatal screening program for congenital hypothyroidism in Bosnia and Hercegovina Federation can improve such situation. However, until an effective screening test is generally not yet routine in whole country, the early postnatal signes of hypothyroidism such as those listed in Table 1 need to be the basis for detection of CH. In addition, any infant can be missed in the screening program, so that family doctors and paediatricians should consider the diagnosis of hypothyroidism whenever it is clinically findings suggested, regardless of whether or not screening is done at birth.

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