

Acquired severe hypothyroidism in children – forgotten or unbelievable diagnosis in a time of large and easy availability of thyroid tests?

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Key words severe hypothyroidism, atrophic thyroiditis, children

Introduction:

In a time of widespread availability of thyroid lab tests plenty of patients are reported to endocrine clinics because of isolated slightly increased TSH value and many papers are dedicated disscussion of precautions to treatment in subclinical hypothyroidism. Simultaneously in the same places other patients develop severe hypothyroidism without proper diagnosis. What is the reason of missing diagnoses?

The Aim:

Clinical characteristics of severe hypothyroidism in children. Identification of the reason of delayed diagnosis of severe hypothyroidism.

Materials and methods:

Patients with severe acquired primary hypothyroidism were enrolled to the study. The basic criterion was elevated TSH above 100 mIU/L. We analysed the clinical symptoms, time of diagnosis, referral reason, kind of thyroid disease and results of laboratory tests.

Results:

In years 2007-2018 twenty one patients of our clinic (15 girls and 6 boys) met above criteria. Severe hypothyroidism was diagnosed in 20 patients with autoimmune atrophic thyroiditis and one patient with thyroid ectopy. The mean age at diagnosis was $10,32 \pm 3,53$ years. Female predominance was 5:2. None of patients had goiter. Reported symptoms in order of the most frequent: slow rate of growth (77%), weight gain (60%), anaemia (40%), dry skin (37%), myxoedema (33%), loss of appetite (33%), constipation (27%), weakness (27%), somnolence (25%), lower physical activity (20%), hair loss (20%), noticeable bradycardia (20%), feeling cold (13%), hypertrichosis (13%), pituitary hypertrophy (5%). The mean time from the occurrence of the symptoms to the moment of diagnosis ranged from 3 months to 6 years (the mean value $22,9 \pm 20,32$ months, median – 19 months). TSH level at the time of diagnosis was $499,02 \pm 234,55$ ulU/ml, (range: 171,22 - 921,66 ulU/ml) normal range of method: 0,58-3,59 µlU/ml. The mean level of fT4 – $0,348 \pm 0,11$ mg/dl (normal range 0,78-1,31mg/dl), the mean fT3 level – $1,33 \pm 0,79$ pg/ml, (normal range 2,17-3,77 pg/ml). Anti-TPO antibodies : the mean value $2165 \pm 2565,35$ IU/ml (normal range <5,6 IU/ml) and anti-Tg antibodies: the mean value $854,5 \pm 1189,65$ IU/ml (normal range <4,1 IU/ml) were detected. In one patient anti-TSH receptor antibodies were detected (ECLIA, Roche). The patients before the endocrine consultation were evaluated by specialists of dermatology, cardiology, alergology and haematology.



growth retardation sleepiness 43.75% weight gain 37,50% hair changes dry skin myxoedema 31,25% 31,25% constipations 25% loss of apetite 12.50% Hypertrichosis 12.50% anemia 12.50% cold intolerance abdominal pain 6.25% 6.25% joints pain methrorrages 6,25%

The main symptoms at the diagnosis of hypothyroidism

0% 10% 20% 30% 40% 50%

patients [%]

No	Initials	Sex	Age	TSH	fT4	fT3	Anti-TPO	Anti-Tg	Anti-TSHR
			(years)						
Reff	erence valu	es		0,58–3,59 ulU/ml	0,78–1,31 ng/dl	2,17–3,77 pg/ml	<5,6 IU/mI	<4,1 IU/mI	<1,22 IU/I
1	A.Z	F	4,59	279,64	0,43	2,37	9340,9	61,2	-
2	Z.M.	F	5,34	859,74	<0,4	<1	140	2630,6	-
3	M.O.	М	5,67	534,45	<0,4	<1	4899,6	143,6	-
4	Z.K.	F	6,75	332,4	0,4	1,6	>2000	1399	-
5	J.K.	F	8,59	171,22	0,5	2,52	7,7	250,9	-
6	K.G.	F	9,08	>1000	<0,4	<1	65,5	784,8	+ 1,98 IU/I
7	M.G.	М	9,67	278,37	0,45	2,5	2756,7	283,5	-
8	Z.H.	F	10	561,43	<0,4	<1	124,5	26,6	-
9	W.K.	F	10,17	355,78	<0,4	B.D.	1804,4	15,7	-
10	P.P	F	11,75	899	0,04	<0,26	1589,7	1761	-
11	A.G.	М	12,09	510,55	<0,4	1,02	B.D.	B.D.	-
12	B.Z.	М	12,17	447,21	<0,4	1,08	2806,2	739,4	-
13	P.K.	F	13,84	461,48	<0,4	B.D.	1584,7	3712	-
14	P.Z.	М	14,67	310,4	<0,4	<1	207,7	39,8	-
15	A.K.	F	14,67	561,98	0,38	B.D.	873,3	45,8	-
16	M.T.	М	14,85	921,66	0,22	0,74	1278,7	56,8	-
17	K.F.	Μ	10,6	362,1	0,51	<1,5	476,1	29,8	-
18	G.K.	F	11,8	876	0,045	1,1	1451,9	1340	-
19	A.H.	F	12,1	511,2	0,35	1,05	1678,0	267	
20	B.M.	F	13,2	473	<0,4	1,2	1579,2	1670,3	
21	J.F.	F	11,6	283,7	0,52	1,48	53,4	24,1	-
1	Maan value 10.24			520.06	0.22	1.00	2015.00	940 564	
	iviean value		10,24	000,90	0,33	1,29	2015,00	049,004	-
2	iviedian		10,09	486,02	<0,4	<1	1587,2	201,2	-
3	SD		3,43	260,12	0,12	0,75	2527,78	1143,13	-

Estimated disease duration before the diagnosis



Clinical and biochemical characteristic of patients with severe hypothyroidism

Conclusion:

Despite the patients presenting typical symptoms of hypothyroidism the diagnosis was delayed in majority of tchem more than 6 months. We presumed, that the lack of goiter can be the potential reason why thyroid disease was not considered at the beginning of diagnostic process. The anti TSHR antibodies are rarely detected in patients with atrophic thyroiditis.



