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A case of congenital hypothyroidism presented with dysmyelination findings

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ABSTRACT

The central nervous system is one of the most crucial targeted systems of hypothyroidism where tissues undergo various broad developmental processes such as neuronal and glial cellular differentiation, migration and myelination. However brain images are mainly normal. In this article we present findings related to a 1-year-old girl who has been referred to our outpatient clinic with complaints of slowing of movement and lack of interest. She was diagnosed with hypothyroidism. Her brain magnetic resonance image obtained during diagnosis displayed dysmyelination. It showed improvement after Na-L thyroxin therapy during follow up.

1. Introduction

Thyroid hormones have an important impact on the development, physiology and activity of many tissues. The central nervous system is one of the most targeted systems where tissues undergo various broad developmental processes such as neuronal and glial cellular differentiation, migration and myelination and are affected by the regulatory activity of the mentioned hormones[1]. Brain atrophy, cerebellar atrophy, cerebellar hypoplasia, abnormality in the globus pallidus and substantia nigra, severe hypoplasia of the right cerebellar hemisphere and vermis pathologies determined in the cranial images of patients with congenital hypothyroidism[2–7] while in some studies the above said conditions were found entirely normal[8].

In this study, findings related to a 1-year-old girl with quite a normal physical development are given, however later she was presented with delayed motor development and retarded motor functions, hypotonia, lack of interest, poor sucking, poor appetite, sluggishness, oversleep and constipation. At this time, her magnetic resonance image (MRI) showed delayed myelination and that finding was improved at the end of therapy.

2. Case report

The patient is a 1-year-old girl who was received with complaints of lack of interest, and decrease muscle tone and activity. She was born during the 42nd week of gestation weighing 3 500 g after an uneventful labor and delivery; her mother was 24-year-old and had her first pregnancy she had no history of gestational hypothyroid. Her weight was 6 500 g (3 percentile), height 65 cm (3–10 percentile), and occipito-frontal circumference was 43 cm (3 percentile). She had hypotonia, lack of interest, poor sucking, poor appetites, sluggishness, oversleep and constipation. She

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had no head control, sitting with aid, umbilical hernia, constipation, prolonged jaundice and large tongue. Hematological and biochemical investigations were normal. Thyroid antibodies of the patients and her mother were negative, and her mother's thyroid hormone and thyroid-stimulating hormone level were normal.

Anti cytomegalovirus IgG and IgM, parainfluenza virus antigen, parvovirus B19 IgG and IgM, respiratory syncytial virus, anti toxoplasma IgG and IgM and anti rubella IgG and IgM tests were negative.

Thyroid function tests disclosed the following values: thyroid-stimulating hormone 10.7 mIU/mL (0.7–6.5 mIU/mL), free T4 1.32 ng/dL (0.87–2.1 ng/dL), total T4 8.11 ng/dL (6.8–13.5 ng/dL). Thus thyrotropin releasing hormone perform stimulation test and peak thyroid-stimulating hormone value attained by thyrotropin releasing hormone stimulation test was 61 mIU/mL. Based on these findings, a diagnosis of congenital hypothyroidism was made, and treatment with L-thyroxin was initiated. The thyroid gland was at its normal location and its size appeared to be normal for the age group in thyroid ultrasound examination.

Brain MRI showed bilateral hiperintensity peri-supraventricular white matter, basal ganglia, capsule interna, tractus pyramydalis and thalamus (Figure 1). There was bifrontal atrophy and smoothing in gyruses in computed tomography of head. Cardiac evaluations, electromyography, auditory brainstem response, electroencephalography and ophthalmological findings including fundi were unremarkable. Tandem-MASS metabolic screening test was normal. Nine months after thyroxin treatment, her motor and mental developments were normal, and there was outcome of dysmyelinization findings in MRI after one year (Figure 2).

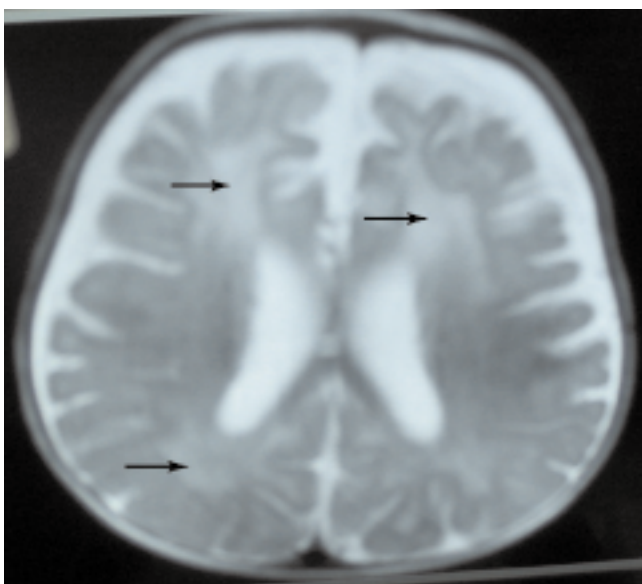


Figure 1. T2 axial rection of brain MRI shows bilateral hiperintensity peri-supraventricular white matter, basal ganglia, capsule interna, tractus pyramydalis and thalamus.

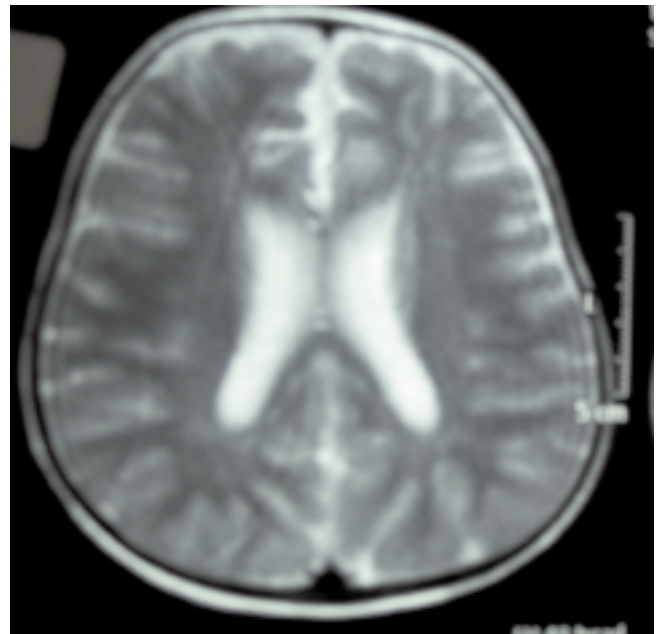


Figure 2. T2 axial rection of brain MRI shows outcome of bilateral hiperintensity.

3. Discussion

In a developing organism, lack of thyroid hormones may cause serious outcomes such as irreversible mental retardation and neurological deficits[9]. Since of thyroid hormones have an important impact on the brain system; during a broad developmental process where impaired synaptic transmission and decreased myelinization are present, the central nervous system is affected by the regulator activity of the mentioned hormones[1,10]. Delayed diagnosis and therapy in children may lead to neurological defects such as mental retardation and poor motor development, ataxia, spastic diplegia, muscular hypotonia, strabismus, learning difficulties and decreased in attention[11]. In our patient head control was delayed during the 6th month and the child had complaints of hypotonisity, lack of interest, poor sucking, poor appetites, sluggishness, oversleep and constipation. At the 9th month of therapy, patient gained head control and was able to sit without support and stand up. She was more interested in the environment and was able to speak a few words.

Ma *et al*[4] report the clinical and magnetic resonance imaging brain scan findings for 3 adult Chinese cretins. All show an apparent magnetic resonance imaging abnormality in the globus pallidus and substantia nigra, with hyperintensity on T1-weighted images and hypointensity on T2-weighted images. Tajima *et al*[5] report a Japanese baby of congenital hypothyroidism with cerebellar atrophy. They showed MRI demonstrated marked cereballar atrophy. They state that the atrophy did not worsen despite adequate

treatment. Jung *et al*[6] reported two patients who had facial anomalies, anterior chamber–cleavage disorder in addition to congenital hypothyroidism and cerebellar hypoplasia. Mauceri *et al*[7] described a patient with congenital hypothyroidism, craniofacial anomalies, bacycephay, large ears, pectus carinatum, and severe hypoplasia of the right cerebellar hemispere and vermis. Cranial images obtained from congenital hypothyroidism cases showed brain atrophy was reported[2]. For our patients, brain MRI showed bilateral hiperintensity peri–supraventricular white matter, basal ganglia, capsule interna, tractus pyramydalis and thalamus. There was bifrontal atrophy and smoothing in gyruses in computed tomography of head.

In a recent study, comparing the MRI findings of neonates with congenital hypothyroidism prior to treatment during neonatal scanning program and MRI findings of normal neonates revealed a totally normal state; especially according to myelinization pattern, no difference was found between patients with and without hypothyroidism and therefore it was suggested that perinatal hypothyroidism did not have an impact on the central nervous system[8]. Sella was normal in the MRI of our patient while an increased signal was observed at the U fibers of the bilateral periventricular and supra ventricular white matter, bilateral basal ganglia, posterior part of capsule interna, pyramidal tracts and thalamus. An increase in signals was monitored in diffusion images of these areas while low signal areas diffusion images were observed in apparent diffusion coefficients (ADC) mapping images.

Brain MRI before treatment is reportedly normal, however proton magnetic resonance spectroscopy shows high levels of choline–containing compounds, which may reflect blocks in myelin maturation[12,13]. We evaluated etiology of leucopathy and did not find any pathological conditions that cause metabolic diseases and intrauterin or postnatal infectious were considered. Experimentally, it was shown that hypothyroidism caused delayed reversible myelinization[14]. In our patient a progression was noticed at the end of one year therapy in motor and mental development and the myelinization defect displayed in the control MRI was regressed.

Consequently, sings of demyelination were determined in MRI images as it should be noted that congenital hypothyroidism must be considered during differentiating diagnosis and in congenital primary hypothyroidism. Likewise, we want to emphasize that if we obtain improvement in motor and mental status by appropriate therapy regression in cranial lesions can be obtained.

Conflict of interest statement

We declare that we have no conflict of interest

References

- [1] Bernal J. Thyroid hormones and brain development. *Vitam Horm* 2005; **71**: 95–122.
- [2] Tomei E, Francone A, Salabè GB, Diacinti D, Gentile F, De Martinis C. Magnetic resonance imaging studies of brain atrophy in hypothyroidism. *Rays* 1988; **13**: 43–47.
- [3] Yakolev PI, Lecours AR. The myelogenic cycles of regional maturation of the brain. In: Minowski A. *Regional Development of the Brain in Early Life*. Oxford: Blackwell; 1967, p. 3–70.
- [4] Ma T, Lian ZC, Qi SP, Heinz ER, DeLong GR. Magnetic resonance imaging of brain and the neuromotor disorder in endemic cretinism. *Ann Neurol* 1993; **34**: 91–94.
- [5] Tajima T, Fujiwara F, Sudo A, Saito S, Fujieda K. A Japanese patient of congenital hypothyroidism with cerebellar atrophy. *Endocr J* 2007; **54**: 941–944.
- [6] Jung C, Wolff G, Back E, Stahl M. Two unrelated children with developmental delay, short stature and anterior chamber cleavage disorder, cerebellar hypoplasia, endocrine disturbances and tracheostenosis: a new entity? *Clin Dysmorphol* 1995; **4**: 44–51.
- [7] Mauceri L, Ruggieri M, Pavone V, Rizzo R, Sorge G. Craniofacial anomalies, severe cerebellar hypoplasia, psychomotor and growth delay in a child with congenital hypothyroidism. *Clin Dysmorphol* 1997; **6**: 375–378.
- [8] Siragusa V, Boffelli S, Weber G, Triulzi F, Orezzi S, Scotti G, Chiumello G. Brain magnetic resonance imaging in congenital hypothyroid infants at diagnosis. *Thyroid* 1997; **7**: 761–764.
- [9] Joffe RT, Sokolov ST. Thyroid hormones, the brain, and affective disorders. *Crit Rev Neurobiol* 1994; **8**: 45–63.
- [10] Gilbert ME, Paczkowski C. Propylthiouracil (PTU)–induced hypothyroidism in the developing rat impairs synaptic transmission and plasticity in the dentate gyrus of the adult hippocampus. *Brain Res Dev Brain Res* 2003; **145**: 19–29.
- [11] Oatridge A, Barnard ML, Puri BK, Taylor SD, Hajnal JV, Saeed N, et al. Changes in brain size with treatment in patients with hyper or hypothyroidism. *Am J Neuroradiol* 2002; **23**: 1539–1544.
- [12] Gupta RK, Bhatia V, Poptani H, Gujral RB. Brain metabolite changes on *in vivo* proton magnetic resonance spectroscopy in children with congenital hypothyroidism. *J Pediatr* 1995; **126**: 389–392.
- [13] Jagannathan NR, Tandon N, Raghunathan P, Kochupillai N. Reversal of abnormalities of myelination by thyroxine therapy in congenital hypothyroidism: localized *in vivo* proton magnetic resonance spectroscopy (MRS) study. *Brain Res Dev Brain Res* 1998; **109**: 179–186.
- [14] Rosman NP, Malone MJ, Szoke M. Reversible of delayed myelinogenesis in experimental hypothyroidism. *J Neurol Sci* 1975; **26**: 159–566.