Case report

MRI features of lissencephaly with cerebellar hypoplasia

Nail Bulakbasi*, Murat Kocaoglu, Bahri Üstünsöz, Cem Tayfun, İbrahim Somuncu

Department of Radiology, Gülhane Military Medical School, Etlik 06018 Ankara, Turkey

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Abstract

Lissencephaly with cerebellar hypoplasia has been recently reported as different group of lissencephaly, which is not included in either classical or cobblestone types. We described magnetic resonance imaging findings of a 8-year-old boy with lissencephaly with cerebellar hypoplasia, to distinguish it from other forms of lissencephaly.

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1. Introduction

Lissencephaly with cerebellar hypoplasia (LCH) has been recently defined as different group of lissencephaly, which is not included in either classical or cobblestone types. It is characterized by cerebellar underdevelopment ranging from vermian hypoplasia to total aplasia with classical or cobblestone lissencephaly [1–5]. Ross et al. recognized six subtypes of LCH due to associated mutations in the LIS1, DCX and RELN genes [1]. Beside of these gene mutations, there are some imaging criterion distinguishing these subtypes, but there is also some overlap in imaging findings. We described magnetic resonance imaging (MRI) findings of a sibling with LCH, to distinguish it from other forms of lissencephaly.

2. Case report

He was single affected 8 year-old-boy in a family with no previous abnormal history. He was the second pregnancy born to a 23-year-old woman and 28 year-old man, both have Caucasian descent. Their first and third children were normal. The pregnancy history was unremarkable, but he had no prenatal ultrasonographic examination.

Affected child was born by normal delivery. Apgar scores were six and seven at 1 and 5 min, respectively. Birth weight was 2680 g (% 25–50 percentile) and length 48.5 cm (% 3–10 percentile). He had small head circumference with −2 standard deviation for age. He had continued growth and mental retardation beginning within postnatal period. His developmental stages of motor, social and verbal skills were 4–7 months of age. He developed mild scoliosis by 3 year of age, but no dysmorphic features. Hypotonia and spasticity were reviled on his physical examination.

He had generalized seizures since his first month of life. Electroencephalography (EEG) while awaked showed irregular alpha activity without paroxysmal activities. EEG while asleep showed single, diffuse, high-voltage slow activity and frequent focal spike like and wave complex discharges. Brainstem auditory evoked potential, visual evoked potential and short-latency somatosensory evoked potential were normal. There were no abnormal laboratory findings in renal and liver functions and serum electrolytes. Metabolic screening of urine did not show defects in the metabolism of amino acids, mucopolysaccharides, purines and pyrimidines. Serologic tests for toxoplasmosis, rubella, cytomegalovirus and herpes simplex virus yielded normal results. Chromosome analysis showed a normal male karyotype of 46. XY. Fluorescence in-situ hybridization for Miller–Dieker syndrome did not identify any deletion at 17p13.3 chromosome. His chest X-ray and abdominopelvic ultrasonography were normal.

He was examined by 1.5 Tesla superconducting MR scanner (Magnetom Vision Plus, Siemens, Erlangen, Germany) using a standard circularly polarized head coil. Axial, sagittal and coronal T1 weighted (650/14 ms, TR/TE) spin-echo (SE), axial T2 weighted (2000/80 ms, TR/TE)
Turbo SE and fast fluid attenuated inversion recovery (FLAIR) (9000/2500/110 ms, TR/TE/TI) images were obtained by using 5 mm slice thickness, 210 mm field of view (FOV) and 160 × 256 matrix size. Cranial MR images (Fig. 1) showed severe vermian and cerebellar hypoplasia with small posterior fossa and low-lying tentorium. Hypoplastic and dysplastic cerebellar peduncles were the only remnants of the cerebellar hemispheres. Fourth ventricle was replaced by large subarachnoid space. The brainstem appeared thin and flattened in the anteroposterior axis. The aqueduct was normally developed. Nasal septum was deviated but no cleft palate.

Moderate pachygyria representing with thickened and flattened cortical gyri were noted with no agyric areas. MR measurement of the cortical thickness was ranged from 4 to 12 mm. Anterior part of the cerebral hemispheres was affected more predominantly than the posterior. He had flattened Sylvian and central sulci. The splenium of the corpus callosum was hypogenetic. There were also mild malformation of both hippocampus and asymmetric dilatation of the third and lateral ventricles. Both olfactory and optic pathways and septum pellucidum were normal.

Fig. 1. (a), (b) T1 weighted axial and midsagittal images show dysplastic cerebellar peduncles with severe vermian and cerebellar hypoplasia, small posterior fossa and low-lying tentorium. Fourth ventricle is dilated and connects with enlarged retrocerebellar subarachnoid space. The brainstem appears thin and flattened. The splenium of the corpus callosum is hypogenetic. (c), (d) T1 weighted axial and coronal image show mild malformation of both hippocampal complex, pachygyria represents with thickened and flattened cortical gyri predominantly involves anterior cerebral hemispheres.
3. Discussion

Lissencephaly comprises a group of malformations caused by altered neuronal migration. It pathologically involves agyria (total loss of gyri) and pachygyria (fewer, broadened gyri). Lissencephaly is radiologically classified into six grades, depending on the relative amounts of agyria and pachygyria, and the presence or absence of heterotopy [6]. The most frequently used and revised classification of lissencephaly includes classical lissencephaly formerly called type I and cobblestone lissencephaly formerly called type II [6–8]. Classical lissencephaly is characterized by the presence of agyria and represents as Miller–Dieker and Norman–Roberts syndromes. Agyric regions of the cerebral cortex pathologically reveal a loosely organized four-layer cortex compared to normal six layers. It usually represents as absent or hypoplastic corpus callosum, decreased size of cerebellar hemispheres and specific craniofacial anomalies. Cobblestone lissencephaly includes a group of syndromes, Fukuyama congenital muscular dystrophy, Walker Warburg syndrome and muscle-eye-brain disease. It is characterized by an almost complete absence of cortical layer formation and associated with hydrocephalus, brain stem and cerebellum hypoplasia, congenital eye malformations and muscular dystrophy.

The term of formerly classified type IV lissencephaly is revised and divided into microlissencephaly and LCH [7–9]. LCH involves a heterogeneous group of cortical malformations without severe congenital microcephaly (> −3 SD), but some overlap between these two groups is also expected [1]. The major cause of this heterogeneity is different gene mutations, which are responsible for gross brain malformation involving both cerebral and cerebellar cortices [8–10]. LCH was classified into six subgroups due to phenotypic and genetic properties [1,9,11]. Although existence of some distinctive phenotypic features of these subgroups, there is also some overlap between them. Our patient has subtle microcephaly associated with severe cerebellar hypoplasia, hippocampal malformation and frontoparietal pachygyria with gray matter thickened to 4–12 mm. Although he has poor mental and motor skills and generalized seizures, he lives up to 8 year-old of age and is still alive. According to these findings our patient was classified as severe form of LCHb subgroup with RELN mutation.

LCHb is an autosomal recessively inherited disorder. Hippocampal malformation is a characteristic of LCHb subgroup and due to the marked disorganization of the CA regions and dentate gyrus with marked reduction in the anterior–posterior extent of the parahippocampal cortex [1]. This subgroup distinguished from LCHd subgroup by presence of milder microcephaly (~ −2 vs. −3 SD), and from LCHA reverse gradient of pachygyria [1]. According to Ross et al. presence of the large representation and more heterogeneity of this subgroup suggest that a number of genes, which are associated with neuronal migration in both cerebral and cerebellar cortices, will be found to be responsible for this group [1].

Although siblings who have severe forms of LCH usually die neonatally, most of them reach up to first decade of life, which allows MR examination of this group of patients. Careful MR examination with appropriate protocol, which includes multiplane T1, T2 and inversion recovery sequences, allows detailed anatomical description of all pathologies for diagnosis and subcategorization of LCH cases. Noninvasive MR examination is also very useful for these patients in whom autopsy cannot be performed on religious grounds and leads to genetic studies for the most relevant gene analysis.

4. Summary

Lissencephaly with cerebellar hypoplasia (LCH) is a subgroup of lissencephalies. We presented single affected 8 year-old-boy with small head circumference, growth and mental retardation, hypotonia and spasticity. MR imaging revealed dysplastic cerebellar peduncles with severe vermian and cerebellar hypoplasia, thin and flattened brainstem, hypogenesis of splenium of the corpus callosum, malformation of hippocampus, and pachygyria predominantly involving anterior cerebral hemispheres. He was classified as severe form of LCHb subgroup with RELN mutation.

References

Murat Kocağlu, MD was graduated from Medical Faculty of Gülhane Military Medical Academy in 1992. He has got his radiology fellowship in 1998. He has worked as associated professor of Radiology in Radiology Department of GMMA since 2000. He has six published articles about Radiology.

Bahri Üstünsoz, MD was graduated from Medical Faculty of Gülhane Military Medical Academy in 1986. He has got his radiology fellowship in 1992. He studied as research fellow in vascular intervention in University of North Carolina for one year. He is also studied in vascular intervention as fellow in University of New Orleans for 2 years. He has been worked as assistant professor of Radiology in Radiology Department of GMMA since 1993. He has 49 published articles and three chapters about Radiology.

Cem Tayfun, MD was graduated from Cerrahpasa Medical Faculty of Istanbul University in 1980. He has got his radiology fellowship from Radiology in Radiology Department of GMMA in 1987. He studied as neuroradiology research fellow in NIH, Clinical Center Radiology Department, Bethesda, Maryland for one year. He has worked as professor of Radiology in Radiology Department of GMMA since 1999. He has 60 published articles and one chapter about Radiology.

Ibrahim Somuncu, MD was graduated from Medical Faculty of Istanbul in 1972. He has got his radiology fellowship from Radiology in Radiology Department of GMMA in 1980. He has worked as professor of Radiology in Radiology Department of GMMA since 1991. He has 85 published articles about Radiology.