The complementary role of Ultrasound and MRI in the evaluation of Lissencephaly type 1. Poster 10

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Abstract

Introduction

Lissencephaly type 1 results from the impaired ability of neurons to migrate to their correct destination in the cerebral cortex.

Case study

We report a 6 months old infant who presented with lack of acquired milestones and epilepsy. Cranial ultrasound showed ventriculomegaly with paucity of gyri, a shallow calcarine fissure without calcar avis, a shallow cingulate gyrus and a rudimentary insula. Previously undescribed findings included 1. cortical thickening 3 identifiable cortical layers (a. an anechoic superficial dense layer rich in neurons, b. a striped echogenic middle layer with sparse columnar neurons [Figure A,1] and c. a radially organized less echogenic deeper layer with thick columns of neurons [Figure A,2] and 2. a prominent radial distribution of medullary veins highlighting the radial organization of cortical layers on power Doppler imaging [Figure B]. Brain MRI showed a tigroid pattern of the glia [Figure D] associated with a similar arrangement of cortical layers best recognized on T2 weighted images The radial columnar organization of the deep cortex and the striped middle cortical layer of the cortex were easily identified [Figure C and E].

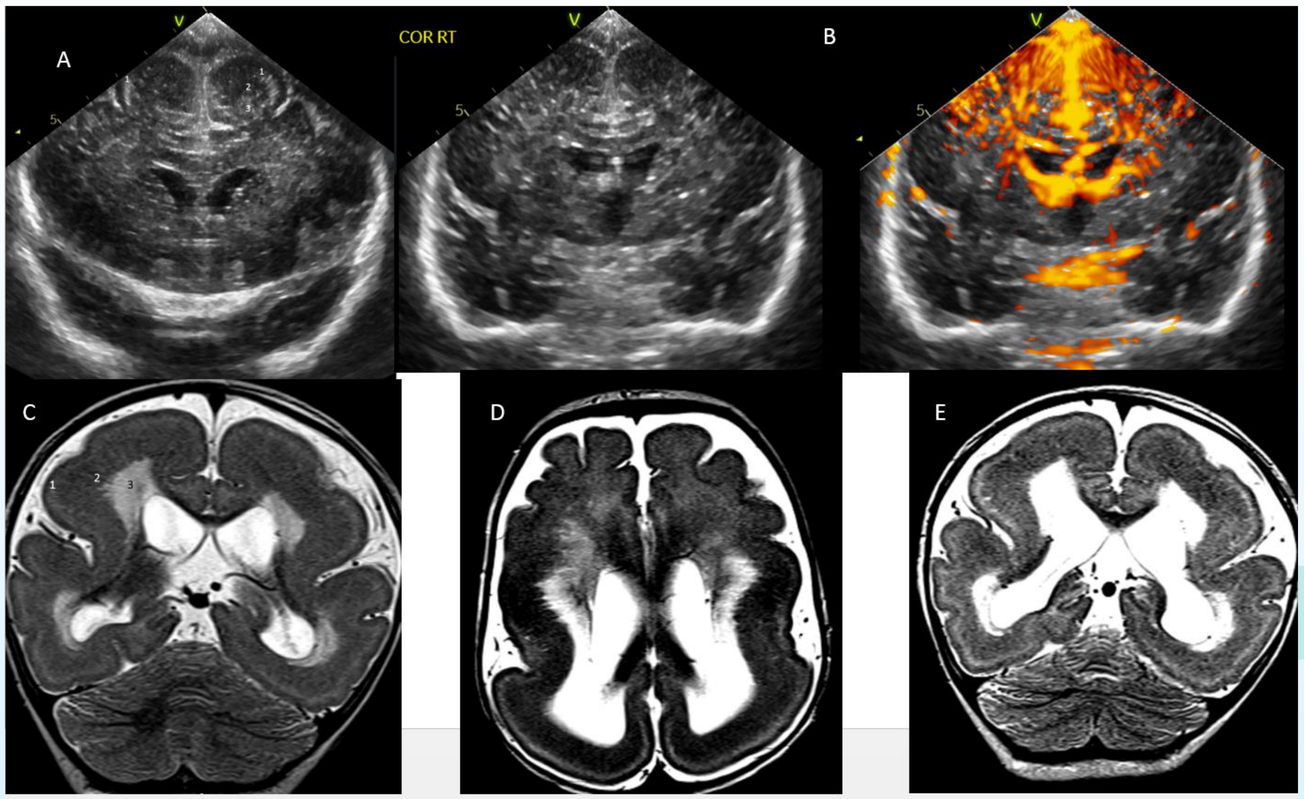
Discussion

This case report illustrates the importance of comparing neuroimaging features using ultrasound and MRI and illustrates the complementary value of each procedure. Our review of the literature bears no mention of these previously unreported neuroimaging characteristic of the cortex in lissencephaly type 1

Background

Lissencephaly (LIS), literally meaning smooth brain, is characterized by smooth or nearly smooth cerebral surface and a paucity of fissures, gyri and sulci. The absence of interhemispheric fissure is usually not described as a form of LIS, instead it is called holoprosencephaly. Abnormal cortical development is the main manifestation of LIS although other associated cranial and extracranial abnormalities may be present. LIS have been divided into three groups based on clinicopathologic type. In type I or classic LIS, many neurons fail to reach the cortical plate and the normal six-layer cortex seen at histologic analysis is replaced by an abnormally thick and poorly organized cortex with four primitive layers. Type II LIS, also known as cobblestone complex, is pathologically distinct from type I as it results from hypoglycosylation of α-dystroglycans receptors in astrocytic endfeet forming glia limitans. On histologic analysis, it is characterized by a disorganized unlayered cortex with many neurons moving too far into the subpial space resulting into a granular surface with effacement of gyri. Microphthalmia, a common feature of type II LIS is rare in type I Lis. Congenital muscular dystrophy is an additional feature common in LIS type II. Type III LIS is associated with severe microcephaly and is a neurodegenerative process with abnormal apoptosis. Prenatal neurosonographic features of LIS type I and type II have been described [1,2]. In this paper, we describe postnatal diagnosis of LIS type I using cranial ultrasound in an infant with isolated lissencephaly sequence (LIS).

Figure 1:Cranial ultrasound and brain MRI



Case Report

We report a 6 months old female infant who presented with lack of acquired milestones and epilepsy. She never rolled but had acquired some head control. She was not reaching or grasping food/toys. She responded to sounds around her, but does not always to her name. Two to three weeks prior to admission she started having staring spells lasting seconds and myoclonic jerks. On day of admission, patient started having longer episodes lasting 1-2 minutes, with vacant look and occasional eye deviation to the right. Mother denied vomiting or feeding difficulties. Family history and past medical history were otherwise non-contributory. On exam child was 6.46 kg (20%) and normocephalic (head circumference of 43 cm @60%). Dysplasia survey was negative.

Cranial ultrasound showed ventriculomegaly with paucity of gyri, a shallow calcarine fissure without calcar avis, a shallow cingulate gyrus and a rudimentary insula. Previously undescribed findings included 1. cortical thickening with 3 identifiable cortical layers (a. an anechoic superficial dense layer rich in neurons, b. a striped echogenic middle layer with sparse columnar neurons [Figure A,1] and c. a radially organized less echogenic deeper layer with thick columns of neurons [Figure A,2] and 2. a prominent radial distribution of medullary veins highlighting the radial organization of cortical layers on power Doppler imaging [Figure B]. Brain MRI showed a tigroid pattern of the glia [Figure D] associated with a similar arrangement of cortical layers best recognized on T2 weighted images The radial columnar organization of the deep cortex and the striped middle cortical layer of the cortex were easily identified [Figure C and E].

Testing of PAFAG1B1 gene showed a heterozygous, pathogenic deletion in exon 4 (c.162del), creating a premature translational stop signal (p.Lys54Asnfs*15) in the PAFAH1B1 gene. Such mutation resulting in an absent or disrupted protein product with loss-of-function has been observed in individuals with isolated LIS type I.

Discussion

The location and type of mutation predict malformation severity in **isolated lissencephaly sequence (**ILS) caused by abnormalities within the LIS1 gene [3] **The degree of agyria may vary and has been stratified by Dobyns into six different grades of severity. [4.5] Grade 1, or complete agyria, is typically seen in MDS. Grade 2 has some minimal gyration in the frontal region usually due to early truncating mutation in LIS 1 gene. Our patient corresponds to this phenotype. The remaining grades have decreasing extent agyria and increased pachygyria or abnormally broad gyri. Such patients may have late truncating mutations or missense mutations in LIS 1 gene. Other gene defects may present a similar phenotype with additional findings.**

In all types of LIS, there is a paucity or lack of normal sulcation. In most LIS cerebral hypoplasia is suggested by ventriculomegaly with or without prominent subarachnoid space. Corpus callosum is hypoplastic. Previously described features of LIS type 1 include shallow Sylvian fissure and lack of opercularization of the insula which is typically seen in ILS and MDS, but this can also occur in other forms of LIS. Shallow calcarine fissure without calcar avis is another common feature of but ILS and MDS. In MDS cingulate gyrus and parieto-occipital fissure are absent while in ILS they are shallow [6]. In both ILS and MDS cerebral cortex is thickened measuring 5 mm instead of 3 mm. Cerebellar vermis hypoplasia can be seen in all forms of LIS, while cerebellar hemisphere hypoplasia suggests type 2 and type 3 LIS or less frequently RELN mutation in type 1 LIS [4].

In this paper new describe the unique features of LIS type 1. More than 75 % of classic LIS can be attributed to mutations in LIS1 gene (PAFAH1B1) or DBX (in boys only). **Miller-Dieker syndrome (MDS) is a rare disorder which consists of classical or type I LIS, characteristic facial appearance, and often other abnormalities. Typical facial changes may include prominent forehead, bitemporal hollowing, short nose with upturned nares, prominent upper lip and small jaw. Many other abnormalities, especially heart defects, hypoplastic male external genitalia and growth deficiency, also occur. Facial dysmorphism and other anomalies in MDS patients appear to be the consequence of deletion of additional genes distal to** LIS1 gene (PAFAH1B1). [8] **MDS must be differentiated from ILS, which consists of lissencephaly and relatively normal facial appearance. Our patient did not have features of MDS.**

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