

# Extreme Microcephaly, Diffuse Agyria, Agenesis of Corpus Callosum, Cerebellar Hypoplasia with Dandy-Walker Malformation: Is This A Severe Form (Barth Syndrome) or A New Variant of Microlissencephaly

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**Article ID:** WMC00600

**Article Type:** Case Report

**Submitted on:** 18-Sep-2010, 02:06:01 PM GMT **Published on:** 18-Sep-2010, 03:21:03 PM GMT

**Article URL:** [http://www.webmedcentral.com/article\\_view/600](http://www.webmedcentral.com/article_view/600)

**Subject Categories:** NEURORADIOLOGY

**Keywords:** Microlissencephaly, Lissencephaly Cerebellar Hypoplasia (LCH) Syndrome, Agenesis of Corpus Callosum, Dandy-Walker Malformation

**How to cite the article:** Aneja H , Saikia B , Patel A , Sural A . Extreme Microcephaly, Diffuse Agyria, Agenesis of Corpus Callosum, Cerebellar Hypoplasia with Dandy-Walker Malformation: Is This A Severe Form (Barth Syndrome) or A New Variant of Microlissencephaly . WebmedCentral NEURORADIOLOGY 2010;1(9):WMC00600

**Source(s) of Funding:**

None

**Competing Interests:**

None

# Extreme Microcephaly, Diffuse Agyria, Agenesis of Corpus Callosum, Cerebellar Hypoplasia with Dandy-Walker Malformation: Is This A Severe Form (Barth Syndrome) or A New Variant of Microlissencephaly

**Author(s):** Aneja H , Saikia B , Patel A , Sural A

## Abstract

A five month girl with extreme microcephaly and complex brain malformation is reported. Magnetic resonance imaging (MRI) revealed bilateral thickened smooth cortex with diffuse agyria-pachygyria spectrum, agenesis of corpus callosum, bilateral hypoplastic cerebellar hemispheres and ventriculomegaly with Dandy-Walker malformation. By adding our case in the list of similar case reports by László Sztrihá [1] and Mitsuhiro Kato [2], we suggest a possible classification of a new variant of microlissencephaly.

## Introduction

Lissencephaly refers to rare malformations that share the absence of normal circumvolutions of the cerebral cortex. Has several subtypes as described by Dobyns and Leventer and the classification is based on associated malformations and etiologies. [3]

Out of the five different subtypes [i.e. classic lissencephaly, lissencephaly X-linked with agenesis of corpus callosum (ARX gene), lissencephaly with cerebellar hypoplasia (LCH), microlissencephaly and cobblestone lissencephaly], microlissencephaly and LCH syndrome shares some overlapping features, major cause of heterogeneity being different gene mutations responsible for gross brain malformations in both cerebral and cerebellar cortices. [4]

We report a case of microcephaly with diffuse agyria and pachygyria, agenesis of corpus callosum, bilateral hypoplastic cerebellar hemispheres and ventriculomegaly with Dandy-Walker malformation. With almost similar case reports by László [1] and Mitsuhiro [2] but with interesting associated finding of Dandy-Walker malformation, this could well be a distinct variant of microlissencephaly (like Type A and Type B) with a possible classification among the lissencephaly syndromes.

## Case Report(s)

Five month female child, born to nonconsanguineous parents presented with multiple episodes of seizures for past one month. Born at full term by cesarean section, indication being fetal distress; baby cried immediately after birth with good APGAR score. Antenatal ultrasound was suggestive of microcephaly. Perinatal period was uneventful. Weight (4.5 kgs) and length (56 cms) were rdpercentile for age. Head circumference was 32cms (rdpercentile for age). There was no history of hypothyroidism, inborn error of metabolism (sensorial alteration, recurrent episodes of poor feeding, lethargy and tone abnormalities) or congenital malformations. There was no family history of seizures.

On examination, the child had bitemporal hollowing, anteverted nostrils with broad nasal bridge, receding forehead, thin vermilion border of upper lips, retrognathia and posteriorly angulated auricles. There were no skeletal deformities and neurocutaneous markers. There was generalized hypotonia with global developmenatal delay. Other systemic examination including ophthalmological examination was normal. Child was having refractory seizures inspite on being phenytoin 8mg/kg/day, valproate 40 mg/kg/day and clobazam 0.5mg/kg/day.

Magnetic resonance imaging (MRI) of brain revealed thickened smooth cortex with absent sulcations and shallow vertically oriented sylvian fissures giving 'figure of eight' configuration to the cerebrum suggestive of lissencephaly. There was associated agenesis of corpus callosum, ventriculomegaly and fourth ventricle communicating with posterior fossa cyst suggestive of Dandy-Walker malformation. There was hypoplasia of bilateral cerebellar hemispheres. [Illustrations 1-5] X-ray chest and spine, abdominopelvic ultrasound scan and Echocardiography was normal. Thyroid profile, creatine phosphokinase (CPK), liver and renal function tests were normal.

## Discussion

Lissencephaly describes a smooth brain; it refers to rare malformations that share the absence of normal circumvolutions of the cerebral cortex. There are several types and classification (Dobyns and Leventer, 2003), based on associated malformations and etiologies. Five major groups of lissencephalies can be recognized. [3]

This rare brain formation disorder is caused by defective neuronal migration during the 12th to 24th weeks of gestation, resulting in a lack of development of brain folds (gyri) and grooves (sulci). It is a form of cephalic disorder. Children with lissencephaly are severely neurologically impaired and often die within several months of birth. [5]

Microlissencephaly differs from classical lissencephaly and other variants by the presence of severe microcephaly, resulting from an abnormal neuronal proliferation or survival combined to neuronal migration disorders. Two main types are recognized: Type A (previously called the Norman-Roberts syndrome with no infratentorial anomalies) and Type B (or Barth syndrome) which is associated with severe hypoplasia of cerebellum and corpus callosum. [3]

László Sztriha has described a case of extreme microcephaly with agyria-pachygyria, partial agenesis of the corpus callosum and pontocerebellar dysplasia [1]. Whereas Mitsuhiro Kato reports two families with diffuse pachygyria and cerebellar hypoplasia and proposed it to be a milder form of microlissencephaly. [2] Similar cases have been reported by Miyata [6] and Farah [7] respectively with the possibility of new lissencephaly syndrome. There have been only two case reports of lissencephaly (and not microlissencephaly) from India prior to this. [8] Our case has similar findings to that of László Sztriha and Mitsuhiro Kato with interesting finding of Dandy Walker malformation. By reporting this case, we are adding one more in the list of microlissencephaly syndrome. Therefore, we propose it to be a genetically distinct variant of microlissencephaly with a possible classification among the lissencephaly syndromes.

## Acknowledgement(s)

Dr. Zubair Ahmed Lone and Dr. Pompa Dutta, Department of Pediatrics, St Stephens Hospital, Delhi-54

## Authors contribution(s)

Dr Himanshu Aneja and Dr Aneet Patel are involved in the work-up of the case.

Dr Bedangshu Saikia has contributed in finding out the references and writing the discussion.

Dr Anuradha Sural, a consultant in Radiology, has contributed in the radiology part

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## Description of Illustrations

**Illustration 1 and 2** are Magnetic Resonance Images of Brain (Axial T1 and T2 respectively) showing thickened smooth cortex with absence of sulcations and 'figure of eight' configuration to the cerebrum suggestive of lissencephaly associated with agenesis of corpus callosum.

**Illustration 3 and 4** Magnetic Resonance Images of

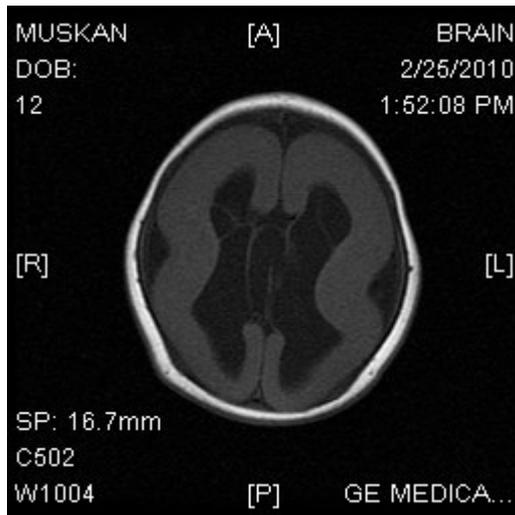
Brain (Sagittal T1 and T2 respectively) showing associated agenesis of the cerebellar vermis and the fourth ventricle communicating with posterior fossa cyst suggestive of Dandy walker malformation. There was hypoplasia of bilateral cerebellar hemisphere.

**Illustration 5** Magnetic Resonance Diffusion Weighted Image of Brain showing thickened smooth cortex with absence of sulcations and 'figure of eight' configuration to the cerebrum suggestive of lissencephaly associated with agenesis of corpus callosum.

## Illustrations

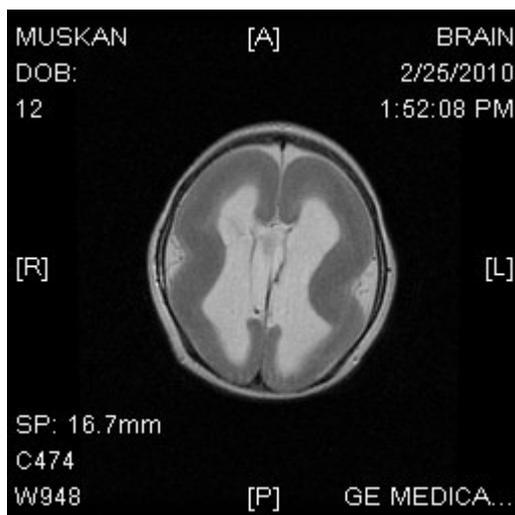
### Illustration 1

MRI Brain (Axial T1)



### Illustration 2

MRI Brain (Axial T2)



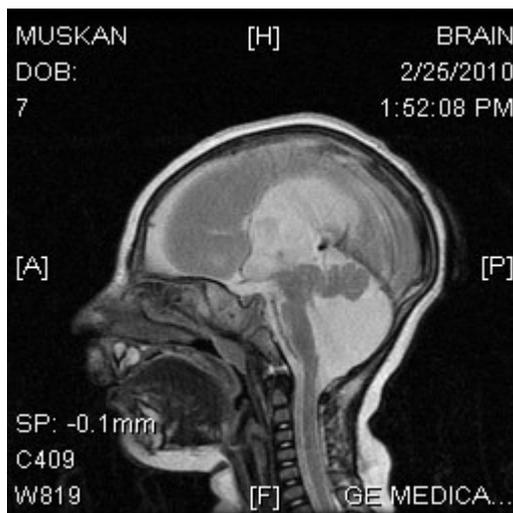
### Illustration 3

MRI Brain (Sagittal T1)



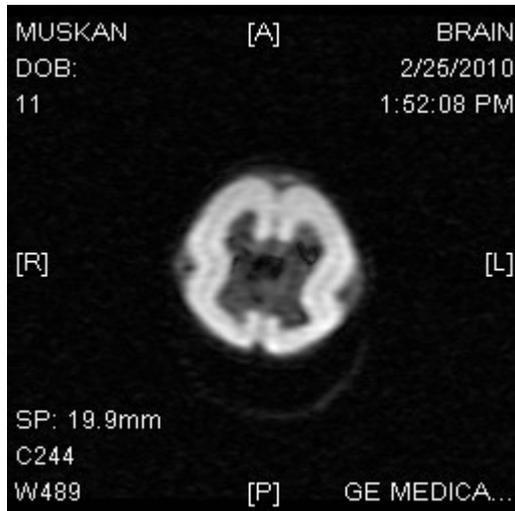
### Illustration 4

MRI Brain (Sagittal T2)



## Illustration 5

MRI Brain (DWI)



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