

## CASE REPORT

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# Pachygyria with cerebellar hypoplasia and tigroid pattern of the white matter secondary to neuronal migration disorders

Jihane El Houssni, Siham El Haddad, Latifa Chat, Nazik Allali

## ABSTRACT

**Introduction:** Pachygyria is a subtype of the lissencephaly spectrum that is secondary to neuronal migration disorders during embryogenesis, it may be associated with other extracortical anomalies such as cerebellar hypoplasia. Lissencephaly with cerebellar hypoplasia is a very rare malformation. In this form we can also observe a tigroid pattern of the white matter.

**Case Report:** We report a very rare case of an infant with pachygyria with cerebellar hypoplasia and a tigroid appearance of the substance secondary to a neuronal migration disorder.

**Conclusion:** Lissencephaly with hypoplasia of the cerebellum is a very rare malformation. The tigroid pattern of the white matter can be observed in neuronal migration disorders. Magnetic resonance imaging (MRI) of the brain is the key examination in the exploration of lissencephaly.

**Keywords:** Cerebellar hypoplasia, Pachygyria, MRI, Tigroid pattern

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## INTRODUCTION

The anomalies of neuronal migration during embryogenesis are at the origin of severe cerebral malformations of which we distinguish lissencephaly [1], which manifests itself by a smooth and thickened cerebral surface, it regroups two entities, agyria which refers to a thick cortex, without detectable furrows and pachygyria which is characterized by the presence of some cortical furrows wider than in the normal cortex [2]. Lissencephaly may be associated with extracortical anomalies such as cerebellar hypoplasia [3]. Magnetic resonance imaging (MRI) of the brain is the key examination in the exploration of lissencephaly. The tigroid pattern is often seen on MRI in disorders of myelin formation such as metachromatic leukodystrophy [4]. We report a very rare case of an infant with pachygyria with cerebellar hypoplasia and a tigroid appearance of the substance secondary to a neuronal migration disorder.

## CASE REPORT

A 1-year-old, male infant, born at term, from a consanguineous marriage, who was admitted for microcephaly with delayed psychomotor acquisitions. An MRI was performed.

The MRI of our patient showed diffuse pachygyria in the frontal, parietal, temporal, and occipital lobes, more marked anteriorly, with a thickness of the cortex measured at 6 mm, bilateral and symmetrical signal abnormalities of the periventricular white matter, in T2 and Flair hyperintensity, associated with radial stripes signal abnormalities, in hyperintensity T2, of subcortical, fronto-parieto-temporal and periventricular location,

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bilateral and symmetrical, realizing a tigroid aspect of the white matter (Figure 1A–C), suggesting an abnormality of myelination, this MRI also showed a dysplasia of the cerebellar hemispheres, a partial aplasia of the vermis (Figure 1F), with a smooth aspect of the cerebellum (Figure 1A), a moderate passive quadrivertricular hydrocephalus and an enlargement of the great cistern communicating with the fourth ventricle (Figure 1D).

There are also signal abnormalities in the cerebellar hemispheres in T2 and Flair hyperintensity (Figure 1E).

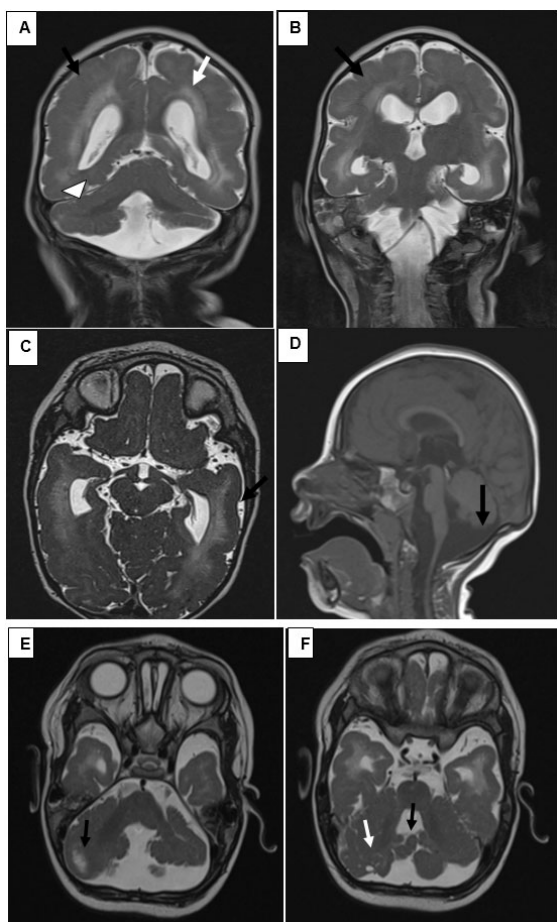


Figure 1: Brain MRI: Coronal (A, B) and 3D axial (C) T2-weighted sequences showing abnormalities of the periventricular white matter (white arrow) with subcortical radial bands in T2 weighted with hypersignal “tigroid pattern” (black arrow), pachygyria (B) and a smooth aspect of the cerebellum (head arrow in (A)). Sagittal T1-weighted sequence showing in (D) enlargement of the great cistern communicating with the fourth ventricle. Axial T2-weighted sequence (E, F) showing dysplasia of the cerebellar hemispheres (white arrow) and of the vermis (black arrow in (F)) with hypersignal of the right cerebellar hemisphere (E).

## DISCUSSION

The development of the cerebral cortex takes place in three successive steps. During the first step, stem cells proliferate and transform into neuroblasts or glial cells all along the ventricular and periventricular wall [5]. In the second step, after the last mitotic divisions, cortical

neurons migrate to the pial surface, a large number of neurons, especially pyramidal neurons migrate radially from their production site within the germinal zone to the cortex, guided by radial glial cells or fibers that extend from the ventricular surface to the pial membrane. A significant proportion of migratory neurons initially adopt a tangential trajectory at the periventricular germinal zone before taking a radial trajectory along the glial guides to the forming cortical plate [3, 5]. The third step is the six-layered cortical organization, associated with the processes of synaptogenesis and apoptosis [5].

According to the classification of Dobyns and Barkovich (2005), there are three groups of cortical malformations: disorders of proliferation, disorders of migration of postmitotic neurons to the cortical plate, and disorders of cortical organization of neurons and the establishment of dendritic and axonal arborizations [5].

Neuronal migration disorders are the cause of severe brain malformations including lissencephaly [1].

Clinically, lissencephaly may manifest itself as mild microcephaly, frequently observed in patients with pachygyria, delayed development of psychomotor acquisitions, focal or generalized convulsions or infantile spasms [4].

Our patient presents with mild microcephaly, with delayed psychomotor acquisitions. Imaging plays a very important role in the management of patients with lissencephaly. Prenatal diagnosis of severe lissencephaly is possible thanks to prenatal ultrasound [5]. The development of MRI has allowed a more precise analysis of the cortical plate and a better characterization of the different forms of lissencephaly [2].

According to the aspect of the cortex and the associated malformations found on MRI and the nature of the chromosomal damage, we distinguish between classic lissencephalies (type 1) and its variants, squamous or cobaltoid lissencephalies (type 2), and a third type of more recent discovery [3].

Classical lissencephalies result from an abnormality of neuronal migration [6]. The term “variant” refers to the existence of agenesis of the corpus callosum and/or cerebellar hypoplasia [3]. Pavement lissencephaly (type 2) (congenital muscular dystrophy) characterized by a nodular brain surface, ocular abnormalities, and congenital muscle disorders [3]. Lissencephaly (type 3) is characterized by severe microcephaly, agyria, agenesis of the corpus callosum, hypoplasia of the cerebellum, and basal ganglia [3].

The neuroradiological manifestations of classic lissencephalies are highly variable, the main radiological aspects revealed on MRI are agyria and pachygyria [3]. On MRI, the cortex appears thickened by 5–20 mm, whereas the normal thickness is 2.5–4 mm [3]. Dobyns proposed a radiological severity score: Grade 1 includes diffuse agyria, grade 2 includes diffuse agyria with some frontal or occipital relief, grade 3 includes mixed agyria and pachygyria, grade 4 includes only pachygyria, grade 5 comprises mixed pachygyria and heterotopias of the

subcortical band, and grade 6 includes only subcortical band heterotopia [4].

In our case, we have a pachygyria without agyria or heterotopia of the white matter, thus it was a grade 4 lissencephaly.

Lissencephaly with cerebellar hypoplasia (LCH) is a very rare form of lissencephaly [7], characterized by cerebellar hypoplasia, predominantly on the vermis [3]. The main difference between classical lissencephaly and LCH is the absence of a cell-sparse zone in LCH [7]. According to the Ross et al. (2001) classification, there are six types lissencephaly: type A: severe form of lissencephaly, characterized by a thick cortex, a mild cerebellar hypoplasia with a furrowed aspect of the cerebellum [3, 5]. Type B is characterized by severe cerebellar hypoplasia and pachygyria (grade 4) with a relatively thin cortex (5–10 mm) and an anterior predominance of abnormalities (antero-posterior gradient). The cerebellum has a smooth appearance, small size of both hemispheres and vermis, without visible lobulation, foliation or fissures [5]. Type C has a cleft palate [3]. Type D has massive hypoplasia of the brain, cerebellum, and corticospinal bundles. The cortex is very thick (10–20 mm) [3]. Type E is similar to type A, but with a marked gradient between frontal agyria and occipital pachygyria [3]. Type F has an additional agenesis of the corpus callosum [3].

Our case involves pachygyria (grade 4) with a thin cortex measured at 6 mm, predominantly anterior with absence of cell-sparse zone and a smooth appearance of the cerebellum which is hypoplastic. This is consistent with cerebellar lissencephaly-hypoplasia type B. The tigroid appearance of white matter on MRI corresponds to the presence of linear areas of normal white matter interspersed with linear demyelinated bands in T2 hypersignal [8]. This aspect is classically described in myelin formation disorders [4], it results from a preservation of the white matter from the demyelination process [8], the main etiologies are:

Metachromatic leukodystrophy is characterized by symmetrical demyelinating damage to the periventricular white matter and the oval centers; the U-shaped subcortical fibers and the subcortical white matter are spared [4, 9].

Pelizaeus–Merzbacher disease affects both the U-shaped subcortical fibers and the periventricular white matter, associated with damage to the cerebellum and brainstem and a rarefaction of the white matter [4, 10].

The tigroid appearance has also been reported in Lowe's syndrome, which is an X-linked recessive oculo-cerebro-renal syndrome characterized by the presence of congenital cataract, glaucoma, mental retardation, and Fanconi syndrome [8].

The tigroid appearance has been described in other hereditary diseases, such as Globoid cell leukodystrophy or Krabbe disease, an autosomal recessive disorder in which the tigroid appearance is secondary to the presence of perivenular clusters of globoid cells [11].

In Alexander's disease, due to mutations in the gene coding for glial fibrillary protein, the tigroid appearance is secondary in this case to perivascular deposits of Rosenthal fibers [11].

A tigroid appearance of the white matter can also be seen in acute disseminated encephalomyelitis (ADEM) [11], which is an acquired demyelinating disease in which non-specific activation of autoreactive T cells by bacterial and viral antigens can lead to demyelination of the white matter and infiltration of mononuclear cells along the venules, which is manifested on MRI as linear bands in T2 hypersignal [11]. The perivenular inflammatory response and demyelination may result in alternating bands of T2 hypersignal and hyposignal and thus a tigroid appearance of the white matter on T2-weighted sequences [11].

The tigroid appearance can also be found in neuronal migration disorders, it can be observed in patients with LCH [7]. This is the case of our patient. In LCH, this appearance is due to a mutation of the RELN gene, which codes for reelin, an extracellular glycoprotein, secreted in particular by Cajal–Retzius cells in the marginal zone of the cortex. It is involved in signaling the radial migration of neurons [3, 4].

## CONCLUSION

Lissencephaly with hypoplasia of the cerebellum is a very rare malformation. The tigroid pattern of the white matter can be observed in neuronal migration disorders. Magnetic resonance imaging is the key examination, it has a diagnostic, prognostic, and therapeutic interest, and it allows a better management of patients with lissencephaly.

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**Author Contributions**

Jihane El Houssni – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Siham El Haddad – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Authors declare no conflict of interest.

**Data Availability**

All relevant data are within the paper and its Supporting Information files.

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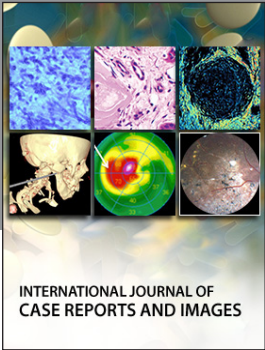
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