

# Giant bilateral open-lip schizencephaly

## *Esquizencefalia bilateral gigante de labio abierto*

Karina Sarango-Amay,<sup>1</sup> Alberth Muñoz-Gualan<sup>2</sup>

### Abstract

Schizencephaly is a rare congenital brain malformation characterized by clefts in the cerebral cortex, it is classified in Type I (open lip) and Type II (close-lip). Patients with schizencephaly present seizures, hydrocephalus, motor and mental deficits. Ultrasound is used for in-utero and newborns patients' diagnosis, and MRI or CT for already born patients. The management of schizencephaly is conservative, with rehabilitation in motor or mental deficits, medication or surgery for seizures and shunt in hydrocephalus with increased intracranial pressure. In the literature, only few giant bilateral cases have been reported. We report a case of giant bilateral open lip schizencephaly, in a 10-day old male patient, presenting with mild hypotonia and no seizures. This case is rare because the relatively benign features compared to other reported cases.

**Keywords:** brain malformation, CT; giant cleft, bilateral schizencephaly, pediatrics

### Resumen

La esquizencefalia es una malformación cerebral congénita caracterizada por hendiduras en la corteza cerebral, se clasifica en Tipo I (labio abierto) y tipo II (labio cerrado). Los pacientes con esquizencefalia presentan convulsiones, hidrocefalia, déficit motor y mental. La ecografía se utiliza para el diagnóstico intra útero y recién nacidos, y la resonancia magnética o tomografía computarizada en pacientes ya nacidos. El manejo de la esquizencefalia es conservador, con rehabilitación de los déficits motores o mentales, medicación o cirugía para convulsiones y derivación en hidrocefalia con aumento de la presión intraacraeal. En la literatura, solo se han informado unos pocos casos bilaterales gigantes. Presentamos un caso de esquizencefalia gigante bilateral de labio abierto, en un paciente masculino de 10 días, que se presenta con hipotonía leve y sin convulsiones. Este caso es raro debido a las características relativamente benignas en comparación con otros casos notificados.

**Palabras clave:** malformación cerebral, TAC, hendidura gigante, esquizencefalia bilateral, pediatría

Rev. Ecuat. Neurol. Vol. 30, N° 3, 2021

### Introduction

Richard Heschl in 1859 described “porencephaly” as a disorder characterized by cavities through the full thickness of the brain parenchyma, that directly communicates the ventricular cavity with subarachnoid space.<sup>1</sup> In 1946, Yakovlev and Wadsworth described the term “schizencephaly” as a specific group of brain cavities, with unknown origin or development, usually with bilateral and symmetrical clefts in the parenchyma. The cavities described as schizencephaly are an expansion of the ventricle so they don't show vascular remnants and are separated in two groups: fused lips, in which the cleft doesn't allow free flow of cerebrospinal fluid (CSF); and separated lips or open lips, in which the CSF flows between the ventricular cavity and subarachnoid

space. This latter group is associated with other abnormalities such as absence of the corpus callosum and septum pellucidum.<sup>2,3</sup>

Schizencephaly is considered a lesion in the cortex, with several associated neurological and mental disturbances, caused by abnormalities in neuroblast migration in fetal life no later than the beginning of the third month of gestation.<sup>4-6</sup> It is considered to have a prevalence of 1.5/100,000,<sup>7</sup> with no clear gender predilection.<sup>8</sup> Cases of schizencephaly are considered sporadic with some familial cases described, the causes of schizencephaly are poorly understood,<sup>9-11</sup> but some authors have mentioned etiologies such as maternal infections and drug abuse,<sup>7,12</sup> maternal young age and lack of prenatal care,<sup>13</sup> vascular defects during early neuro embryogenesis (like thrombotic occlu-

<sup>1</sup>Department of Pediatrics, Pediatric Hospital, Tuxtla Gutierrez, Chiapas, Mexico.

<sup>2</sup>Department of Nervous Diseases and Neurosurgery, Peoples' Friendship University of Russia, Moscow, Russia.

Correspondencia:  
Alberth Muñoz-Gualan  
E-mail: albmu93@gmail.com

sion, ischemia and arteriovenous malformations) with a direct relationship between the vascular defect and the severity of the cleft,<sup>14-16</sup> and genetic mutations in the EMX2 gene in more than 70% of the patients.<sup>17,18</sup>

These malformations are best visualized on magnetic resonance imaging (MRI), where it is possible to observe the lining of the lips, and other accompanying anomalies. Although MRI is more sensitive than computer tomography (CT), the latter can be used if the malformations are pronounced.<sup>19,20</sup> The use of ultrasound can be helpful in newborns 14 and in utero patients after the 24th week.<sup>21</sup>

Clinical presentation of schizencephaly is variable and related to the location and amount of brain involved. The symptoms can start in infancy or adulthood, with the most common symptoms being seizures, hemiparesis, developmental deficits, motor delay, and hydrocephalus. The open lip and bilateral cases have worse symptomatology.<sup>22,23</sup>

Seizures occur in 36-65% of schizencephaly cases, of which between 9-38% are drug resistant.<sup>24</sup> Patients with open-lip schizencephaly have more difficult to treat seizures.<sup>23</sup> In medically intractable epilepsy, it is possible to use neurosurgical techniques because the cleft tissue can be epileptogenic.<sup>25</sup>

The therapeutic management of schizencephaly is usually conservative, with rehabilitation in case of motor or mental deficits, epilepsy treatment using medication or surgery, and shunt in cases of hydrocephalus with increased intracranial pressure.<sup>26</sup>

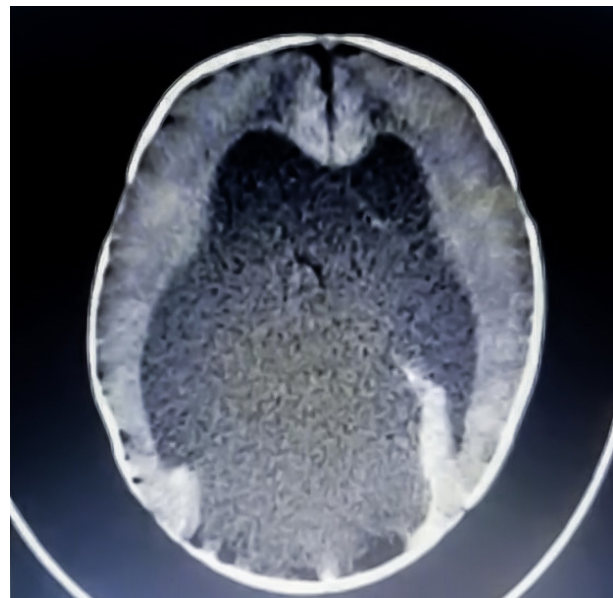
Herein, we report a rare case of bilateral giant open lip schizencephaly.

### Case report

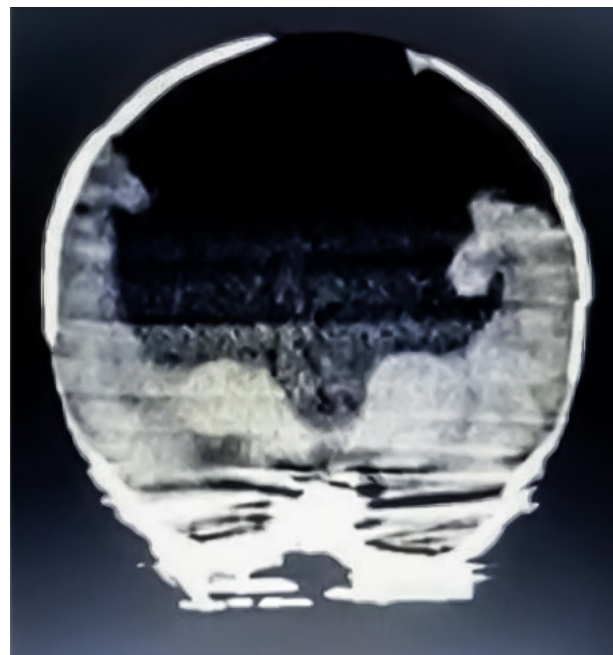
The mother of the patient is 27 years old without pathologic antecedents and primigravida. The mother received all prenatal care (including folic acid and iron supplements), was not exposed to any possible risk factor, and has no family history of schizencephaly. During pregnancy, 4 ultrasounds were performed: the first in the second month of pregnancy without any abnormal result, the second at 5th month with a report of hydrocephalus, then at 8th month with a report of holoprocencephaly, and at the 9th month with a report of probable open-lip schizencephaly.

After delivery at 38 week of gestation, the male newborn presented with ideal weight for age, spontaneous breathing and crying, without antecedent of perinatal asphyxia, APGAR 9 – 9, Silverman at 10 min with a score of 0, hypotonic – Grade 1 according to Campbell scale-, macrocephaly with increase suture width in the cranium, ear pinna of low implantation, setting sun eyes present, retrognathia is evident, respiratory function is normal, no other relevant physical finding. Trans fontanelle ultrasound showed bilateral clefts in both hemispheres with possible diagnosis of porencephaly. A CT

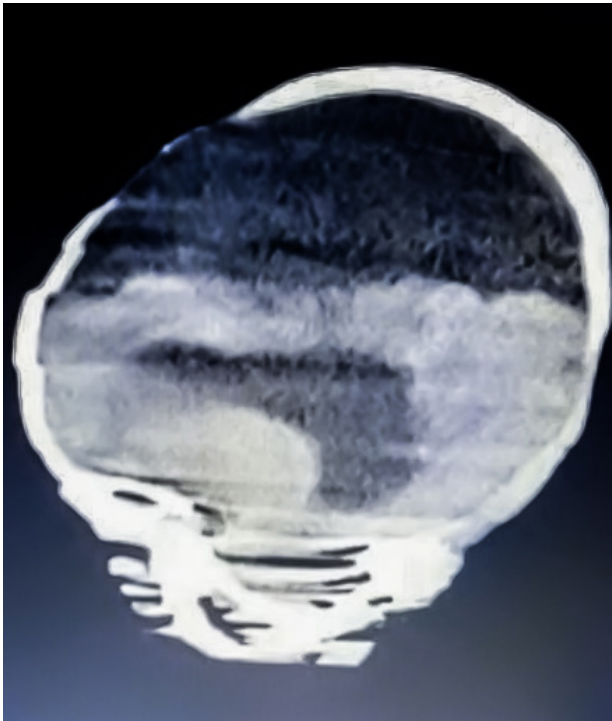
revealed bilateral open-lip schizencephaly, associated with compensatory hydrocephalus, absent septum pellucidum and corpus callosum, and no further imaging studies were done. After 10 days in observation in the ward, no further symptoms were observed and no symptomatic increase in intracranial pressure; therefore, conservative treatment was chosen, with periodic follow-ups.



**Figure 1.** Axial brain CT. Cerebral cortex with a thin layer of subcortical tissue, additionally monoventricle is observed.



**Figure 2.** Coronal brain CT. Cerebral cortex present at the base near the diencephalon, there is no cortex near the vertex, additionally it is not possible to differentiate lateral ventricles and third ventricle, creating a single monoventricle.



**Figure 3.** Sagittal brain CT. Thin cerebral cortex surrounding a monoventricle near the diencephalon. Hydrocephalus is notable superior to the cerebral cortex.

### Discussion

Schizencephaly is a rare development condition, its diagnosis is possible with prenatal ultrasound or MRI, the latter more specific; most severe cases can be seen in utero, thus open-lip malformations are more commonly diagnosed.<sup>20</sup> In our case, there was a possible diagnosis of schizencephaly using ultrasound in prenatal care, but it was confirmed using CT in the newborn, so it was not considered necessary to use MRI.

In some cases, the diagnosis of schizencephaly is not made until adulthood, with late onset symptoms being mainly seizures. Other symptoms such as borderline personality disorder, bipolar disorders, or psychotic phenotype of schizophrenia do occur, and the symptoms depend on the site and size of the lesion.<sup>27-30</sup>

The prevalence of seizures in schizencephaly is high, with several reports about their predilection according to the type of cleft present.<sup>31</sup> Our patient presented with giant bilateral open-lip schizencephaly with no seizures or other major symptoms, in contrast with a similar case report of giant bilateral schizencephaly in a 15 day old female, who had poor breastfeeding since birth, spasticity, seizures, and use of antiepileptic drugs.<sup>32</sup> Although the onset of seizures occurs mainly in childhood for patients with bilateral schizencephaly,<sup>33</sup> our patient is seizure-free (but there is the possibility he develops seizures later in life).

Some reports state that schizencephaly is due to a functional brain reorganization in these patients; thus, the hemispherectomy used for intractable epilepsy in patients with cortical development malformations has good results, with minimal secondary effects.<sup>34,35</sup>

The conservative treatment in these patients is associated with a similar cognitive and motor development in comparison with children of the same age when the malformation is minor, but in wide and bilateral cases there is a poor outcome; at the moment our patient's treatment is conservative, with physiotherapy and periodic follow ups for recognizing new symptoms.<sup>36,37</sup>

### Conclusions

Schizencephaly is a rare condition with unknown etiology that can be diagnosed in utero if the disease is severe; on the other hand, it can be underdiagnosed when the disease is minor. It is important to treat conservatively all patients with schizencephaly, regardless of the severity in the imaging studies, because it is proven to be associated with a good outcome in mental and motor development.

### References

1. Heschl R. Gehirndefect und Hydrocephalus. *Prakt Helkd.* 1859;61:59–74.
2. Yakovlev P, Wadsworth R. Schizencephalies; a study of the congenital clefts in the cerebral mantle; I clefts with fused lips. *J Neuropathol Exp Neurol.* 1946;5:116–30. <https://doi.org/10.1097/00005072-194604000-00003>
3. Yakovlev P, Wadsworth R. Schizencephalies; a study of the congenital clefts in the cerebral mantle; II clefts with hydrocephalus and lips separated. *J Neuropathol Exp Neurol.* 1946;5(3):169–206.
4. Barkovich J, Gressens P, Evrard P. Formation, Maturation, and Disorders of Brain Neocortex. *AJNR* [Internet]. 1992;13:423–46. Available from: <http://www.ajnr.org/content/ajnr/13/2/423.full.pdf>
5. Volpe J. *Neurology of the newborn.* Third. Philadelphia: W.B Saunders; 1995.
6. Miller G, Stears J, Guggenheim M, Wilkening G. Schizencephaly: a clinical and CT study. *Neurology.* 1984;34(8):997–1001.
7. Curry C, Lammer E, Nelson V, Shaw G. Schizencephaly: Heterogeneous etiologies in a population of 4 million California births. *Am J Med Genet.* 2005;137(2):181–9. <https://doi.org/10.1002/ajmg.a.30862>
8. Stopa J, Kucharska-Miasik I, Dziurzynska-Bialek E, Kostkiewicz A, Solinska A, Zajac-Mnich M, et al. Diagnostic Imaging and Problems of Schizencephaly. *Polish J Radiol.* 2014;79:444–9. <https://doi.org/10.12659/PJR.890540>
9. Howe D, Rankin J, Draper E. Schizencephaly pre-

- valence, prenatal diagnosis and clues to etiology: a register-based study. *Ultrasound Obstet Gynecol.* 2012;39(1):75–82. <https://doi.org/10.1002/uog.9069>
10. Sarnat H, Curatolo P. *Malformation of the Nervous System.* First. Elsevier; 2007. 235 p.
  11. Merello E, Swanson E, De Marco P, Akther M, Striano P, Rossi A, et al. No major role for the EMX2 gene in schizencephaly. *Am J Med Genet.* 2008;146(9):1142–50. <https://doi.org/10.1002/ajmg.a.32264>
  12. Friede R, Mikolasek J. Postencephalitic porencephaly, hydranencephaly or polymicrogyria, A review. *Acta Neuropathol.* 1978;43:161–8. <https://doi.org/10.1007/BF00685011>
  13. Dies K, Bodell A, Hisama F, Guo C, Barry B, Chang B, et al. Schizencephaly: Association with young maternal age, alcohol use, and lack of prenatal care. *J Child Neurol.* 2012;28(2):198–203. <https://doi.org/10.1177/0883073812467850>
  14. Denis D, Chateil J, Brun M, Brissaud O, Lacombe D, Fontan D, et al. Schizencephaly: clinical and imaging features in 30 infantile cases. *Brain Dev.* 2000;22(8):475–83. [https://doi.org/10.1016/S0387-7604\(00\)00173-X](https://doi.org/10.1016/S0387-7604(00)00173-X)
  15. Komarniski C, Cyr D, Mack L, Weinberger E. Prenatal Diagnosis of Schizencephaly. *J ultrasound Med.* 1990;9(5):305–7. <https://doi.org/10.7863/jum.1990.9.5.305>
  16. Van der Knaap M, Valk J. Classification of congenital abnormalities of the CNS. *Am J Neuroradiol.* 1988;9(2):315–26.
  17. Brunelli S, Faiella A, Capra V, Nigro V, Simeone A, Cama A, et al. Germline mutations in the homeobox gene EMX2 in patients with severe schizencephaly. *Nat Genet.* 1996;12(1):94–6. <https://doi.org/10.1038/ng0196-94>
  18. Granata T, Farina L, Faiella A, Cardini R, D'Incerti L, Boncinelli E, et al. Familial schizencephaly associated with EMX2 mutation. *Neurology.* 1997;48(5):1403–6. <https://doi.org/10.1212/wnl.48.5.1403>
  19. Barkovich A, Norman D. MR imaging of schizencephaly. *Am J Roentgenol.* 1988;150(6):1391–6. <https://doi.org/10.2214/ajr.150.6.1391>
  20. Oh K, Kennedy A, Frias A, Byrne J. Fetal Schizencephaly: Pre- and Postnatal Imaging with a Review of the Clinical Manifestations. *RadioGraphics.* 2005;25(3):647–57. <https://doi.org/10.1148/rg.253045103>
  21. Klingensmith W, Cioffi-Ragan D. Schizencephaly: diagnosis and progression in utero. *Radiology.* 1986;159(3):617–8. <https://doi.org/10.1148/radiology.159.3.3517949>
  22. Kopyta I, Jamroz E, Marszał E, Kluczevska E. Schizencephaly - clinical and radiological presentation of pediatrics patients. *Wiad Lek.* 2006;59:471–6.
  23. Packard A, Miller V, Delgado M. Schizencephaly: correlations of clinical and radiologic features. *Neurology.* 1997;448(5):1427–34. <https://doi.org/10.1212/wnl.48.5.1427>
  24. Heuer G, Hardesty D, Zaghoul K, Simon E, Foley R, Storm P. Anatomic hemispherectomy for intractable epilepsy in a patient with unilateral schizencephaly. *J Neurosurg Pediatr.* 2008;2(2). <https://doi.org/10.3171/PED/2008/2/8/146>
  25. Silbergeld D, Miller J. Resective Surgery for medically intractable epilepsy associated with schizencephaly. *J Neurosurg.* 1994;80(5):820–5. <https://doi.org/10.3171/jns.1994.80.5.820>
  26. Halabuda A, Klasa L, Kwiatkowski S, Wyrobek L, Milczarek O, Gergont A. Schizencephaly - diagnostic and clinical dilemmas. *Child's Nerv Syst.* 2015;31:551–6.
  27. Kamble V, Madanlal A, Dhok A, Taori A, Pajnigara N. A rare case of schizencephaly in an adult with late presentation. *J Fam Med Prim Care.* 2017;6(2):450–2. [https://doi.org/10.4103/jfmpc.jfmpc\\_43\\_17](https://doi.org/10.4103/jfmpc.jfmpc_43_17)
  28. Filardi F, Molloy-Diniz L, Alves K, Cano H, Correa H, Teixeira A. Borderline personality features possible related to cingulate and orbitofrontal cortices dysfunction due to schizencephaly. *Clin Neurol Neurosurg.* 2008;110(4):396–9. <https://doi.org/10.1016/j.clin-neuro.2007.12.009>
  29. Comparelli A, Ambrosi E, De Carolis A, Kotzalidis G, Maneschi M, Simonetti A, et al. Open-Lip Schizencephaly Associated with Bipolar Disorder in a Young Man Exposed in Utero to the Chernobyl Disaster. *J Neuropsychiatr.* 2012;24(1):E34–5.
  30. Tyls F, Brunovsky M, Sulcova K, Kohutova B, Ryznarova Z, Kopecek M. Latent Schizencephaly with Psychotic Phenotype or Schizophrenia with Schizencephaly? A case report and Review of the Literature. *Clin EEG Neurosci.* 2019;50(1):13–9. <https://doi.org/10.1177/1550059418781119>
  31. Kopyta I, Skrzypek M, Raczkiwicz D, Bojar I, Sarecka-Hujar B. Epilepsy in paediatric patients with schizencephaly. *Ann Agric Environ Med.* 2020;27(2):279–83. <https://doi.org/10.26444/aaem/122796>
  32. Rege S, Patil H. Bilateral giant open-lip schizencephaly: A rare case report. *J Pediatr Neurosci.* 2016;11(2):128–30. <https://doi.org/10.4103/1817-1745.187638>
  33. Hung P, Wang H, Chou M, Lin K, Hsieh M, Chou I, et al. Schizencephaly in children: a single medical center retrospective study. *Pediatr Neonatol.* 2018;59(6):573–80. <https://doi.org/10.1016/j.pedneo.2018.01.009>
  34. Vossler D, Wilkus R, Pilcher W, Farwell J. Epilepsy in schizencephaly: abnormal cortical organization studied by somatosensory evoked potentials. *Epilepsia.* 1992;33(3):487–94. <https://doi.org/10.1111/j.1528-1157.1992.tb01697.x>
  35. Gonzalez-Martinez J, Gupta A, Kotagal P, Lachhwani D, Wyllie E, Luders H, et al. Hemispherectomy for Catastrophic Epilepsy in Infants. *Epilepsia.*

2005;46(9):1518–25. <https://doi.org/10.1111/j.1528-1167.2005.53704.x>

36. Ortega V, Arango L, Pineda L, Suarez J. Integridad cognitiva y motora-sensorial en un niño con esquizencefalia de labio abierto unilateral derecho: reporte de un caso. *Acta Neurol Colomb*. 2018;34(1):59–63. <https://doi.org/10.22379/24224022180>
37. Pascual-Castroviejo I, Pascual-Pascual S, Velazquez-Fragua R, Viaño J, Quiñones D. Esquizencefalia. Estudio de 16 pacientes. *Neurología*. 2012;27(8):491–9. <https://doi.org/10.1016/j.nrl.2011.06.005>

**Funding:** *This research did not receive any specific grant from funding agencies in the public, commercial, or not profit sectors.*

**Conflict of interest:** *The authors declare there is no conflict of interest.*