

3. Mori M, Kuwabara S, Fukutake T, Yuki N, Hattori T. Clinical features and prognosis of Miller Fisher syndrome. *Neurology*. 2001;56:1104–6, <http://dx.doi.org/10.1212/wnl.56.8.1104>.
4. Koga M, Gilbert M, Takahashi M, Li J, Hirata K, Kanda T, et al. GQ1b-seronegative Fisher syndrome: clinical features and new serological markers. *J Neurol*. 2012;259:1366–74, <http://dx.doi.org/10.1007/s00415-011-6360-y>.
5. Yuki N. Ganglioside mimicry and peripheral nerve disease. *Muscle Nerve*. 2007;35:691–711, <http://dx.doi.org/10.1002/mus.20762>.
6. Chiba A, Kusunoki S, Obata H, Machinami R, Kanazawa I. Ganglioside composition of the human cranial nerves, with special reference to pathophysiology of Miller Fisher syndrome. *Brain Res*. 1997;745:32–6, [http://dx.doi.org/10.1016/S0006-8993\(96\)01123-7](http://dx.doi.org/10.1016/S0006-8993(96)01123-7).
7. Fukami Y, Wong AH, Funakoshi K, Safri AY, Shahrizaila N, Yuki N. Anti-GQ1b antibody syndrome: anti-ganglioside complex reactivity determines clinical spectrum. *Eur J Neurol*. 2016;23:320–6, <http://dx.doi.org/10.1111/ene.12769>.
8. Wong AHY, Umapathi T, Nishimoto Y, Wang YZ, Chan YC, Yuki N. Cytoalbuminologic dissociation in Asian patients with Guillain-Barré and Miller Fisher syndromes. *J Peripher Nerv Syst*. 2015;20:47–51, <http://dx.doi.org/10.1111/jns.12104>.
9. Zhang Y, Zhao Y, Wang Y. Prognostic factors of Guillain-Barré syndrome: a 111-case retrospective review. *Chin Neurosurg J*. 2018;4:14, <http://dx.doi.org/10.1186/s41016-018-0122-y>.
10. Bai HX, Wang ZL, Tan LM, Xiao B, Goldstein JM, Yang L. The effectiveness of immunomodulating treatment on Miller Fisher syndrome: a retrospective analysis of 65 Chinese patients. *J Peripher Nerv Syst*. 2013;18:195–6, <http://dx.doi.org/10.1111/jns.12030>.
11. Mori M, Kuwabara S, Miyake M, Noda M, Kuroki H, Kanno H, et al. *Haemophilus influenzae* infection and Guillain-Barré syndrome. *Brain*. 2000;123:2171–8, <http://dx.doi.org/10.1093/brain/123.10.2171>.
12. Odaka M, Yuki N, Hirata K. Anti-GQ1b IgG antibody syndrome: clinical and immunological range. *J Neurol Neurosurg Psychiatry*. 2001;70:50–5, <http://dx.doi.org/10.1136/jnnp.70.1.50>.
13. Rodríguez Uranga JJ, Delgado López F, Franco Macías E, Sánchez Arjona MB, Martínez Quesada C, Palomino García A. Síndrome de Miller-Fisher: hallazgos clínicos, infecciones asociadas y evolución en 8 pacientes [Miller-Fisher syndrome: clinical features, associated infections and clinical course in 8 cases]. *Med Clin (Barc)*. 2004;122:223–6, <http://dx.doi.org/10.1157/13058172> [Spanish].
14. Blasetti A, Cerruto M, Cutarella R, Tocco A, Caporale MC, Chiarelli F, et al. Miller Fisher syndrome and *Escherichia coli* infection: is it a novel association? *J Child Neurol*. 2007;22:71–3, <http://dx.doi.org/10.1177/0883073807299969>.
15. Kono Y, Nishitarumizu K, Higashi T, Funakoshi K, Odaka M. Rapidly progressive Guillain-Barré syndrome following *Escherichia coli* infection. *Intern Med*. 2007;46:589–91, <http://dx.doi.org/10.2169/internalmedicine.46.6330>.
16. Jo YS, Choi JY, Chung H, Kim Y, Na SJ. Recurrent Guillain-Barré syndrome following urinary tract infection by *Escherichia coli*. *J Korean Med Sci*. 2018;33, <http://dx.doi.org/10.3346/jkms.2018.33.e29>, e29.

J.H. Bejarano-Ferreira^{a,*}, W. Aguirre-Quispe^{a,*},
E. Guevara-Silva^b, L. Torres-Ramírez^c, M. Flores-Mendoza^c

^a Instituto Nacional de Ciencias Neurológicas, Lima, Peru

^b Centro Básico de Investigación en Demencia y Enfermedades Desmielinizantes del Sistema Nervioso, Instituto Nacional de Ciencias Neurológicas, Lima, Peru

^c Centro de Investigación de Enfermedades Neurodegenerativas, Instituto Nacional de Ciencias Neurológicas, Lima, Peru

* Corresponding author.

E-mail address: Wilfor.aguirre.q@upch.pe
(W. Aguirre-Quispe).

<https://doi.org/10.1016/j.nrl.2021.09.001>

0213-4853/ © 2021 Sociedad Española de Neurología. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Mild head trauma: Acute encephalopathy trigger in children with RHOTB2 de novo mutation

Traumatismo craneoencefálico leve: desencadenante de encefalopatía aguda en niños con mutación de novo en RHOTB2

Dear Editor,

We present a 6 year old girl with microcephaly and epileptic seizures associated with a RHOTB2 pathogenic variant, who consulted the Pediatric Emergency Department for low consciousness after a mild head traumatism 40 min earlier. The patient had fallen from her own height, neither having presented nausea, vomits, seizures nor immediate conscience loss. Around 10 min after the head trauma, the patient suffered medium disconnection, hypotonia and tendency

to fall asleep. At her arrival to the Pediatric Emergency department, the patient had bilateral arreactive and mydriatic pupils as well as a non-sustainable airway. Glasgow scored 3 points. No other signs of intracranial hypertension were present. Orotracheal intubation was conducted and a unique hypertonic saline bolus was administered. Computed tomography (CT) was performed, which did not show structural traumatic injury. Blood tests were normal. Our patient was admitted in the Pediatric Intensive Care Unit, where she remained intubated with propofol perfusion for 24 h. Programmed extubation was performed, with complete neurological recuperation without focal deficits and Glasgow 15 score. Usual treatment was resumed (valproic acid and lacosamide) and the patient was transferred to the general pediatric hospitalization unit, being discharged after 48 h of monitorization and observation.

Rho-related BTB domain-containing protein 2 (RHOTB2) belongs to an atypical Rho GTPase family whose mRNA levels are high in humans' nervous system. Hence, the important role of normal regulation levels of RHOTB2 in



adequate brain function.¹ *De novo* missense variants in RHOTB2 have been related to developmental and epileptic encephalopathy.^{2,3} Increased levels of RHOTB2 lead to epileptic encephalopathy, however, the pathogenic mechanism remains unknown.¹ Clinical presentation is common to other genetic disorders such as FOXG1 encephalopathy, Rett syndrome or GLUT1 deficiency syndrome-1, hence RHOTB2-related developmental and epileptic encephalopathy diagnosis usually relies on exome sequencing.² Clinical spectrum includes early-onset seizures (mostly within the first 3 years of life), postnatal encephalopathy, movement disorders and intellectual disabilities.^{2,4} Acute encephalopathy and febrile epileptic status have been previously described in patients with RHOTB2 *de novo* mutation, however there is only another reported case of acute encephalopathy triggered by head trauma in a patient with this genetic mutation.⁴

Knijnenburg et al.⁴ describe a patient with RHOTB2 who suffered a mild head trauma (against his bicycle) maintaining consciousness until minutes after, when he stopped answering to verbal orders and started vomiting. On admission, anisocoria was detected and endovenous midazolam was administered under the suspicion of a non-convulsive epileptic status. CT scan was performed and no signs of traumatic injury were detected. Additionally, the electroencephalogram (EEG) showed signs of severe encephalopathy; a non-continuous pattern with slow activity without epileptic activity. Magnetic resonance imaging (MRI) showed reduced diffusion in some areas and hippocampal atrophy. Similar findings were observed by Belal et al.,¹ in all three patients analysed during an acute encephalopathy episode secondary to febrile epileptic status. Neither EEG nor MRI were performed in our patient, therefore we cannot compare these findings. Unlike the early clinical recovery observed in our patient, the child described by Knijnenburg et al.⁴ did not recover completely until day 11 of admission. It is known that encephalopathy episodes are long lasting in children with this mutation as well as the fact that long-term symptoms and MRI findings can worsen after these episodes.^{2,4}

In conclusion, this is the second case report published describing an acute encephalopathy episode secondary to a mild trauma in a child with RHOTB2 *de novo* mutation, providing further evidence about this disease and possible encephalopathy episodes' trigger factors. More studies are needed to determine the consequences of these episodes.

Financial disclosure

All authors have indicated they have no financial relationships relevant to this article to disclose.

Conflict of interest

None.

References

1. Belal H, Nakashima M, Matsumoto H, Yokochi K, Taniguchi-Ikeda M, Aoto K, et al. *De novo* variants in RHOTB2, an atypical Rho GTPase gene, cause epileptic encephalopathy. *Hum Mutat.* 2018;39:1070–5.
2. Straub J, Konrad EDH, Grüner J, Toutain A, Bok LA, Cho MT, et al. Missense variants in RHOTB2 cause developmental and epileptic encephalopathy in humans, and altered levels cause neurological defects in *Drosophila*. *Am J Hum Genet.* 2018;102:44–57.
3. Deciphering Developmental Disorders Study. Prevalence and architecture of *de novo* mutations in developmental disorders. *Nature.* 2017;542:433–8, <http://dx.doi.org/10.1038/nature21062>.
4. Knijnenburg A, Nicolai J, Bok LA, Bay A, Stegmann A, Sinnema M, et al. Acute encephalopathy after head trauma in a patient with a RHOTB2 mutation. *Neurol Genet.* 2020;6:e418, <http://dx.doi.org/10.1212/NXG.0000000000000418>.

A. Jové Blanco^a, J. Lorente Romero^{a,*},
E. Barredo Valderrama^b, P. Castro de Castro^c

^a *Pediatric Emergency Department, Hospital Infantil Gregorio Marañón, Madrid, Spain*

^b *Pediatric Neurology Department, Hospital Infantil Gregorio Marañón, Madrid, Spain*

^c *Head of the Pediatric Neurology Department, Hospital Infantil Gregorio Marañón, Madrid, Spain*

* Corresponding author.

E-mail address: jllorente083@hotmail.com (J. Lorente Romero).

<https://doi.org/10.1016/j.nrl.2021.10.001>

0213-4853/ Published by Elsevier España, S.L.U. on behalf of Sociedad Española de Neurología. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).