

Benign episodic unilateral mydriasis: case report, topographic and clinical approach



Midriasis unilateral episódica benigna: reporte de un caso y enfoque clínico-topográfico

Dear Editor:

Anisocoria is a pupillary disorder and occasionally a warning sign in the emergency department and outpatient clinics. Multiple aetiologies have been described, both severe and benign, and the condition represents a diagnostic challenge that generally requires further testing.^{1,2} Benign episodic unilateral mydriasis (BEUM) is an infrequent disease whose aetiology is poorly understood, and causes anisocoria secondary to autonomic nervous system dysfunction, frequently associated with migraine with aura.^{3,4} We present the case of a patient with BEUM in the absence of headache. We describe the clinical analysis prior to diagnosis, which may be very useful for avoiding unnecessary studies and establishing a diagnosis earlier.

Our patient was a 23-year-old woman with no relevant history, who presented sudden onset of photophobia and left pupillary dilation. The episode lasted approximately 5 minutes, but was repeated several times per day over the course of a week. She did not report headache, changes in visual acuity, eye pain, or double vision. Three months later, she noticed that her left pupil was dilated, with altered morphology and hyporeactivity to light stimuli. On this occasion, dilation lasted approximately 2 hours, was not accompanied by headache or other symptoms, and was not associated with any trigger factor.

The patient was assessed on numerous occasions at the emergency department and the outpatient neurology and neuro-ophthalmology clinics. She was asymptomatic at the time of the assessments, and no abnormalities were observed in the neurological examination. A non-contrast brain MRI study and MRI angiography yielded normal results. As no abnormalities were observed in the clinical examination or additional studies, we considered that the patient may present BEUM, requiring no treatment. [Fig. 1](#) shows a comparison between the patient's pupils in normal conditions and during an episode of left BEUM.

We present the case of a patient with episodes of left episodic mydriasis without associated headache. In the clinical assessment of pupillary disorders, we should evaluate the direct response when directing light at the pupil, the consensual response after directing light at the contralateral pupil, and accommodation.⁵ Pupillary control is regulated by the autonomic nervous system: pupillary contraction is mediated by parasympathetic activation of the sphincter muscle of the pupil and dilation by sympathetic activation of the iris dilator muscle.⁶ The accommodation reflex consists in pupillary contraction, accommodation of the ciliary muscle, and

eye convergence; it is activated by visual signs transmitted through the parasympathetic pathway to the visual cortex when looking at approaching objects.⁷

From a topographic perspective, pupillary anomalies may be caused by peripheral or central lesions, sympathetic or parasympathetic lesions, or alterations to the iris muscle or visual pathways.⁸ Pupillary anomalies may be bilateral or unilateral, in which case anisocoria or pupil asymmetry are observed, as in the case of our patient. In these cases, the light reflex of the affected pupil must be assessed. If the mydriatic pupil reacts poorly to light, anisocoria is less marked with low light, and the afferent visual system is normal, then it is likely that there is a defect in efferent parasympathetic innervation. If anisocoria is greater with low light or in darkness, then the defect involves the sympathetic innervation of the pupil. In cases of anisocoria with normal pupillary light reflex in both eyes, the patient probably presents physiological anisocoria.⁶ In these cases, the difference in pupil size is the same with bright or low light, and patients generally report the anomaly in the long term. Our patient reported sluggish pupillary light reflex during episodes of mydriasis.

Anisocoria due to sympathetic dysfunction manifests almost exclusively as Horner syndrome. It commonly presents as a triad of palpebral ptosis, miosis, and ipsilateral anhidrosis.⁵ Miosis is caused by loss of sympathetic innervation of the iris dilator muscle, which causes anisocoria that is more evident in the dark. Despite anisocoria, the patient did not present miosis, palpebral ptosis, or alterations in sweating function, which makes Horner syndrome unlikely.

Parasympathetic dysfunction may be associated with third nerve palsy, iris lesions, lesions to the ciliary ganglion or short ciliary nerves, or may be linked to the use of a drug.⁶ Third nerve palsy may manifest with lesions to the efferent parasympathetic pathway, resulting in unilateral mydriasis.⁸ Although we were aware of a decreased pupillary reaction to light during the patient's episodes of mydriasis, her neurological examination and neuroimaging studies yielded normal results, which ruled out left third cranial nerve palsy. Lesions to the ciliary ganglion and short ciliary nerves manifest as tonic pupil due to deficient or absent reaction to light stimulus, with slow contraction to prolonged near effort.⁸ This lesion has been associated with peripheral neuropathy, generalised dysautonomia, or Adie tonic pupil in healthy individuals.⁹ Our patient presented no history or examination findings suggesting neuropathy or dysautonomia.

Periodic pupillary phenomena are rare, and are mediated by abnormal sympathetic or parasympathetic activity.⁸ Excess parasympathetic activity may manifest with periodic pupillary contractions, such as cyclic oculomotor palsy, ocular neuromyotonia, and rhythmic pupillary oscillations. Intermittent unilateral mydriasis may manifest during or after a seizure, in association with migraine, in recurrent painful ophthalmoplegic neuropathy, in trigeminal autonomic cephalalgias, or as a transient phenomenon in healthy young adults.^{4,10–13} [Table 1](#) shows the possible causes of anisocoria according to the light reflex in the affected pupil.

In 1955, Jacobson described the clinical characteristics of the syndrome of neurologically isolated episodic unilateral mydriasis, which was not associated with neurological disorders.¹ Jacobson associated this entity with a parasymp-



Figure 1 Top: symmetrical pupils. Bottom: left pupil is mydriatic and dyscoric. Photographs were taken by the patient.

Table 1 Causes of anisocoria according to the light reflex in the affected pupil.

Greater anisocoria in low light	Greater anisocoria in bright light	Equal anisocoria in low and bright light	Episodic anisocoria
Horner syndrome Physiological anisocoria	Adie tonic pupil Third nerve palsy Pharmacological anisocoria	Physiological anisocoria	Cyclic sympathetic spasm Benign episodic unilateral mydriasis

pathetic insufficiency or sympathetic hyperactivity. A case series published in 2015 described the epidemiological and clinical characteristics of patients with episodic benign mydriasis at a Spanish hospital.¹⁴ Mydriasis manifested unilaterally in the majority of cases, and more than half of patients showed no associated symptoms, although the disorder is usually associated with episodes of migraine with aura or ophthalmoplegic migraine.^{4,15,16}

BEUM should be suspected in healthy young patients presenting no abnormalities in the neurological examination other than mydriatic pupil, or even no abnormalities at all. Comprehensive history-taking and neurological and ophthalmological examination are important, as well as additional studies to rule out other diseases when necessary. Once secondary causes have been ruled out, BEUM does not require further study or specific treatment.

References

1. Jacobson DM. Benign episodic unilateral mydriasis. *Ophthalmology*. 1995;102:1623–7.
2. Hallett M, Cogan DG. Episodic unilateral mydriasis in otherwise normal patients. *Arch Ophthalmol*. 1970;84:130–6.
3. Vera J, Lázaro MD, Vivo C. Migrañas acompañadas de midriasis unilateral benigna episódica. *Gac Optom Óftm Oftalm*. 2013;485.
4. Skeik N, Jabr F. Migraine with benign episodic unilateral mydriasis. *Int J Gen Med*. 2011;501.
5. Blumenfeld H. Neuroanatomy through clinical cases. In: *Sinauer Associates*. 2.a ed. Oxford University Press; 2010. p. 566–90.
6. McDougal DH, Gamlin PD. Autonomic control of the eye. In: *Comprehensive physiology*. Wiley; 2014. p. 439–73.
7. Saladin KS, Gan CA, Cushman HN. *Anatomy and physiology: the unity of form and function*. 9.a ed. New York: McGraw-Hill Education; 2021.

8. Brazis PW, Masdeu JC, Biller J. Localization in clinical neurology. 6.a ed. Lippincott Williams & Wilkins; 2011. p. 173–278.
9. Idiáquez CJ, Idiáquez RJF, Benarroch E. Evaluación clínica de las disautonomías. *Rev Chil Neuropsiquiatr.* 2020;58:324–36.
10. Schiemer A. Benign episodic unilateral mydriasis in a flight nurse. *Aerosp Med Hum Perform.* 2017;88:500–2.
11. García-Martín AM, Molina-Martínez FJ, Amer-Ferrer G, Sureda-Ramis B, Moreno-Rojas AJ, Barceló-Artigues I. Unilateral mydriasis during temporal lobe seizures, 10. *Epileptic Disorders;* 2008. p. 165–9.
12. Antonaci F, Sances G, Loi M, Sandrini G, Dumitrache C, Cuzconi M. SUNCT syndrome with paroxysmal mydriasis: clinical and pupillometric findings. *Cephalalgia.* 2010;30:987–90.
13. Li C, Huang X, Tan X, Fang Y, Yan J. A clinical retrospective study of recurrent painful ophthalmoplegic neuropathy in adults. *J Ophthalmol.* 2021;2021:1–5.
14. Martín-Santana I, González-Hernández A, Tándón-Cárdenes L, López-Méndez P. Midriasis benigna episódica. Experiencia en una consulta monográfica de neuro-oftalmología de un hospital terciario. *Neurología.* 2015;30:290–4.
15. Maggioni F, Mainardi F, Malvindi ML, Zanchin G. The borderland of migraine with aura: episodic unilateral mydriasis. *J Headache Pain.* 2011;12:105–7.
16. Edelson RN, Levy DE. Transient benign unilateral pupillary dilation in young adults. *Arch Neurol.* 1974;31:12.

Valeria Valencia-Cifuentes^{a,b,*}, Jairo A. Quiñones^{a,b}

^a *Departamento de Neurología, Fundación Valle del Lili, Cali, Colombia*

^b *Universidad Icesi, Cali, Colombia*

Corresponding author.

E-mail address: Valeriavc1209@gmail.com

(V. Valencia-Cifuentes).

<https://doi.org/10.1016/j.nrleng.2024.01.009>

2173-5808/ © 2024 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/>).

Osmotic demyelination syndrome amidst COVID-19: A case report with literature review



Síndrome de desmielinización osmótica en medio de COVID-19

Dear Editor,

Osmotic demyelination syndrome (ODS) is of the most feared rare brain complications that could lead to protracted neurological consequences or death. Its occurrence is strongly associated with rapid correction of chronic hyponatremia.

Hyponatremia is common in COVID-19 patients and is associated with poor prognosis.¹ However, few publications have described ODS in COVID-19 patients. As of May 2023, we found 12 papers in English, five case reports and seven retrospective studies, containing a total of 16 COVID-19 patients with certain ($n=14$) or presumable ($n=2$) ODS^{2–13} (Table 1).

Surprisingly, none of the case reports contain information about the 24-h change in serum sodium, which is of utmost importance in current guidelines.¹⁴

Herein, we present the case of a 44-year-old male, who was admitted to our intensive care unit (ICU) with altered consciousness, positive for COVID-19. His complaints started two weeks prior when he felt nauseous, vomited several times daily, had fever and cough. On day 10 of symptom onset, the patient experienced a single tonic–clonic seizure with loss of consciousness for the first time. The nationwide shortage of hospital beds due to the pandemic has restricted his immediate hospitalization. Subsequent blood tests at a laboratory revealed severe hyponatremia of 112 mmol/L.

On admission (three days later), repeated blood tests revealed hyponatremia of 122 mmol/L, or +10 mmol/L,

indicating that the patient had experienced sodium auto-correction, where the exact correction rate is unknown.

Notable features in the patient's medical history exist. He had managed hypertension with a thiazide diuretic. Thiazide diuretics are a well-known cause of hyponatremia. He also maintained a restrictive diet for a year. In addition, he lost appetite and had been eating less for a week. Finally, he had multiple episodes of vomiting prior to hospital admission. The loss of gastrointestinal fluid results in the release of antidiuretic hormone (ADH), which could cause hyponatremia.

The patient became comatose, and required intubation in early hospitalization days, which made adequate neurologic examination difficult, and magnetic resonance imaging (MRI) impossible. Initial and repeated CT scans of the brain on day 4 were normal. On day 13, his general condition allowed for better examination. Quadriplegia, extraocular muscle palsy, and bulbar syndrome were observed. We performed MRI of the head, which confirmed the diagnosis of ODS (Fig. 1).

Diagnosing ODS is difficult in ICU where encephalopathies are common, including during the COVID-19 era.³ The gold standard is using MRI. However, the need for intensive care limits its feasibility. CT of the brain, while being more accessible and performed under these circumstances, is not sufficiently sensitive.

The question arises whether ODS is underdiagnosed and underreported in COVID-19 patients. Existing studies on COVID-19 patients indicate that ODS may not be rare, particularly in severely ill. In a study by Chougar et al., among 35 COVID-19 patients hospitalized in the ICU with neurological symptoms, three (8.6%) were identified with ODS.⁴ Fitsiori et al. found one ODS case among nine ICU patients (11.1%),⁵ Neumann et al. identified one case among 30 COVID-19 patients (3.3%), with the patient being in a critical condition,⁶ and Jensen-Kondering et al. reported one case of ODS in 12 patients (8.3%), with the patient being severely