Case Report

A Case of Recurrent Benign Episodic Unilateral Mydriasis and Decreased Visual Acuity and Review of the Literature

Jane T. Caty, MD;[1] Michael Kogan, MD, PhD;[2] J. James Reidy, MD;[3] Adnan H Siddiqui, MD, PhD;[2,5,6] Osman Farooq, MD;[4] Ping Li, MD, MSc[4]*

[1] *University Hospitals Eye Institute at Case Western Reserve University School of Medicine, Cleveland, OH*
[2] *Departments of Neurosurgery,[2] School of Medicine and Biomedical Sciences, University at Buffalo, State University of New York, Buffalo, NY*
[3] *Departments of Ophthalmology, School of Medicine and Biomedical Sciences, University at Buffalo, State University of New York, Buffalo, NY*
[4] *Departments of Neurology, School of Medicine and Biomedical Sciences, University at Buffalo, State University of New York, Buffalo, NY*
[5] *Toshiba Stroke and Vascular Research Center, University at Buffalo, State University of New York, Buffalo, NY*
[6] *Jacobs Institute, Buffalo, NY*

Unilateral mydriasis has a variety of causes, some of which are life-threatening. Migraine with benign episodic unilateral mydriasis is a nonsurgical cause of anisocoria, with unknown underlying pathophysiology. This disorder is thought to be caused by an Adie's pupil triggered by migraine due to overactivation of the sympathetic nervous system or hypoactivity of the parasympathetic nervous system. We present the case of a 47-year-old patient who had recurrent benign episodic unilateral mydriasis associated with migraine headaches. Other vascular causes of mydriasis were investigated and excluded. Ultimately, the patient's symptoms of blurred vision and pupillary dilation resolved over the 2 weeks after onset. We reviewed all 50 cases of benign episodic unilateral mydriasis reported in the literature and summarized common presentations of this disorder. The case presented here is typical in its progression and associated symptom of blurred vision, which is reported in 56% of cases in the literature.
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INTRODUCTION

An association between migraine headache and benign episodic unilateral mydriasis has been reported. The cause is unknown but speculated to be secondary to hyperactivity of the sympathetic nervous system or hypoactivity of the parasympathetic nervous system. We report a case of benign episodic unilateral mydriasis during a migraine headache and provide a literature review of the association.

CASE REPORT

A 47-year-old patient with a past medical history remarkable for migraine headaches, bilateral keratoconus, penetrating keratoplasty in the right eye, hypothyroidism, aortic valve replacement, and thoracic aortic aneurysm stent placement was referred to a tertiary medical center emergency room by an ophthalmologist to exclude the presence of cerebral infarction or aneurysm because of a 2-day history of left eye mydriasis and decreased vision. The outpatient ophthalmologic examination immediately before presentation had demonstrated light sensitivity, normal anterior chamber pressures, full visual fields, and normal extraocular movements, with no ptosis bilaterally. Vision in the right eye was unchanged from the most recent examination; and the best corrected vision in the left eye was 20/50, with a baseline of 20/20. The left pupil was 6 mm and nonreactive to light, with a normal pupillary response on the right. Anterior segment and fundoscopic examinations were unchanged from baseline. A review of systems in the emergency room was positive for a dull headache, stiff neck, and mydriasis and blurry vision in the left eye.

A computed tomographic (CT) scan of the head and CT perfusion imaging of the head and neck did not reveal any signs for intracranial hemorrhage, ischemic stroke, mass lesion, or herniation (**Figure 1A/1B**). A magnetic resonance imaging study could not be obtained because of the presumed implant in the patient's right eye. Due to the medical history of thoracic aortic aneurysm, keratoconus, and a family history of keratoconus, there was suspicion of systemic collagen vascular disease and cerebral aneurysm. After obtaining consent from the patient, a cerebral angiogram was

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***Corresponding Author:** Department of Neurology, Buffalo General Medical Center, 100 High Street, Buffalo, NY 14203.
Tel: 01-716-859-7540; Fax: 01-716-869-2430.
(Email: pli6@buffalo.edu)

performed to exclude the presence of dissection, thrombus, or occlusion of the ophthalmic artery, or a posterior communicating artery, posterior cerebral artery, or superior cerebellar artery aneurysm, all of which were found to be absent (**Figure 2A-2C**).

A neurology consultation was obtained on hospital day 1, and the left mydriasis was confirmed, with slight reactivity to light at the time. The remainder of the physical and neurologic examinations was unremarkable. Complete blood count, coagulation studies, urinalysis, and basic metabolic panel were within normal limits. Upon further questioning, the patient recounted a similar episode approximately 10 years ago that resolved spontaneously after several weeks. Due to the negative evaluation, history of migraine headache, and previous episode of mydriasis, the patient was discharged home with the diagnosis of benign episodic unilateral mydriasis and with instructions to follow up with the ophthalmologist. During a telephone conversation, the patient reported that the left mydriasis and visual acuity resolved over the 2 weeks after discharge, and no a recurrence was experienced as of 5 months later.

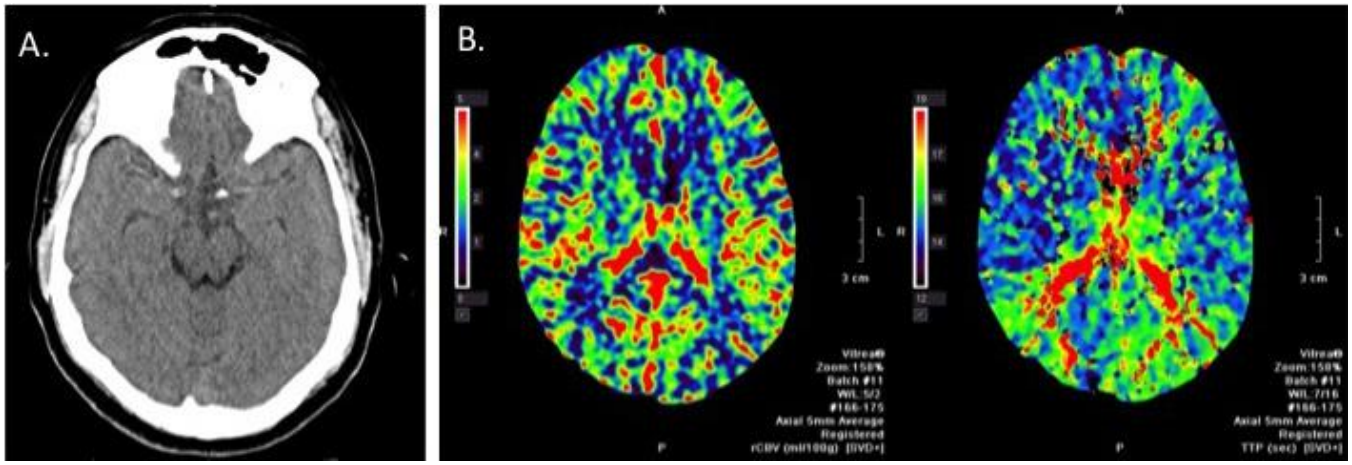

Figure 1. CT Head and CT perfusion. **A**. CT scan at the time of admission shows no sign of ischemia, mass, or herniation. B. CT perfusion study shows no volume voids (left) or perfusion differences (right), suggesting that no acute ischemic event has occurred. A, anterior. P, posterior.

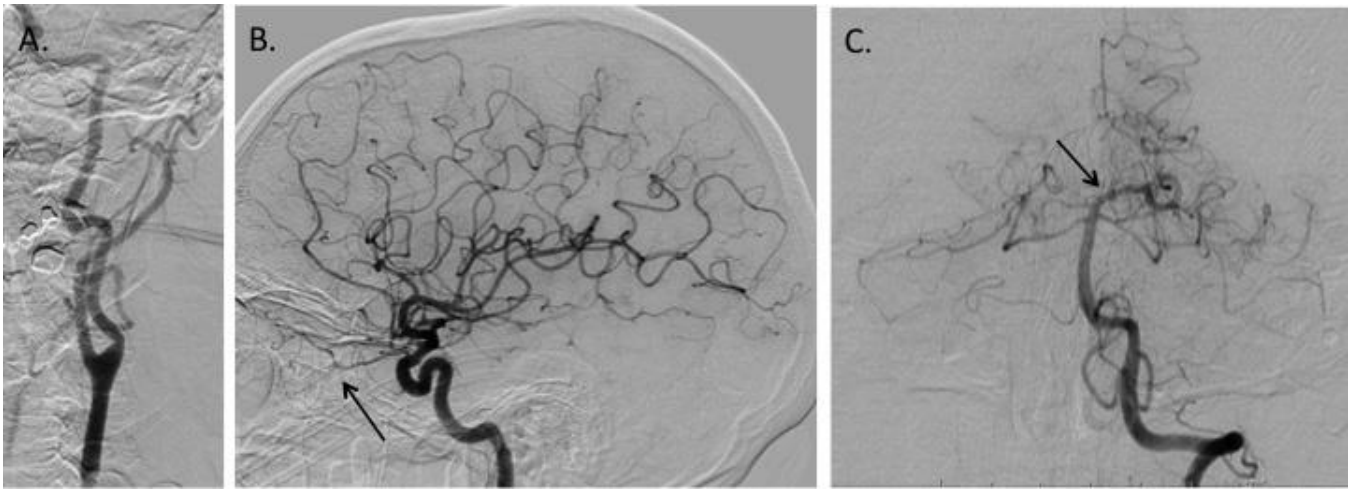

Figure 2. Cerebral Angiogram. **A.** Left common carotid angiogram shows no dissection, stenosis, or thrombus. **B.** Lateral view left common carotid angiogram demonstrates that the anterior circulation on the left side is intact, including a well-perfused ophthalmic artery (*black arrow*). The posterior communicating artery is shown (*white arrow*), with no sign of aneurysm. **C.** Anterior view of left vertebral artery angiogram shows no sign of an aneurysm of the posterior cerebral artery (*black arrow*) or superior cerebellar artery (*white arrow*).

DISCUSSION

Pupil asymmetry, or anisocoria, can be caused by ophthalmic medications, topical medications applied to the face, orbital cellulitis, third cranial nerve palsy causing inhibition of the parasympathetic short ciliary nerves that cause pupillary constriction, trauma to the orbit damaging the iris sphincter muscle, and angle closure glaucoma.[1,2] Cerebral aneurysms are also a common cause of third cranial nerve palsy, of which posterior communicating artery aneurysms are the

most common cause; however, numerous other vascular causes, including superior cerebellar artery and posterior cerebral artery aneurysms may be involved.[3,4] Unilateral mydriasis may be also seen in association with migraine headaches, as presented in our case above.

Table 1. Reports of benign episodic unilateral mydriasis and migraine.

Authors, y	Age (y), Sex	Temporal factors	Associated symptoms
Ault, 2011[5]	32, F	Yearly migraines lasting 12-48 h with 2 episodes of R eye mydriasis	Nausea, neck pain, phonophobia, photophobia, vertigo
Barriga et al., 2011[6]	9 patients: 7 women, mean age 33.8 (range 19-52)	Migraine with mydriasis persisting for mean of 3 mo	Not described
Blaik and Hiremagular, 1998[7]	17, F	3 d migraine with intermittent mydriasis	Blurred vision, dizziness, nausea, photophobia, near-syncopal episode
Evans and Jacobson, 2003[8]	43, F	Mydriasis followed by migraine 6 h later; mydriasis resolved after 10 h	None
Ishikawa et al., 2000[9]	4, F	Drowsiness after vomiting every 2 mo with recurrent mydriasis	Diplopia, ptosis, third nerve palsy
Jacobsen, 1995[10]	24 patients: 19 F, median age 31.5 y (range 14-50)	Median duration 12 h, median frequency once every 3-4 mo	15/24 Blurred vision, 5/24 orbital pain, 4/24 photophobia, 4/24 red eye, 2/24 diplopia
Leone et al., 1994[11]	23, F	Two episodes migraine with persistent mydriasis (48 h and 4 mo)	Nausea, phonophobia, photophobia
Maggioni et al., 2011[12]	24, M	3 y of monthly transient left eye blurred vision and mydriasis followed by migraine	Nausea, phonophobia, photophobia
Purvin[13]	46, F	Transient mydriasis during migraine, then second episode 1 wk later lasting 1 mo	Photophobia, scotoma
Simonetto et al.[14]	23, F	6-8 attacks per month of headache with 48 h nonreactive R eye mydriasis that became bilateral after 4 mo	None
Skeik and Jabr, 2011[15]	30, F	1 y intermittent migraine with occasional unilateral mydriasis	Confusion, lower-extremity weakness
Sobreira et al., 2013[16]	15, F	6 y persistent mydriasis with intermittent migraines	Diplopia, nausea, ptosis, nausea, vertigo, vomiting
Woods et al.[17]	5, 27, 28, 37, 46, 48, 53; all 7 pts F	15 min-24 h mydriasis during migraine	7 of 7 blurred vision, 2 of 7 orbital pain, 1 of 7 photophobia, 1 of 7 ptosis, 1 of 7 third nerve palsy

Abbreviations: h, hours; d, day; F, female; M, male; min, minutes; mo, months; pts, patients; R, right; wk, week; y, years

We reviewed all 50 reported cases written in English of benign episodic unilateral mydriasis associated with migraine headache identified through a PubMed search. Our search revealed a female predominance of this condition in 45 of 50 published cases, with an age range of 5 to 53 years (**Table 1**[5-17]). Episodes are reported to last from 10 minutes to 6 years, with a mean duration of 12 hours.[10,16,17] Multiple reports in the literature describe an association between mydriasis and migraine (summarized in **Table 1**). The most frequently associated symptoms during migraine-related pupil dilation include blurred vision in 56.1%, photophobia in 24.4%, and orbital pain in 17.0% (**Table 2**). Less commonly associated symptoms include red eye, confusion, neck pain, third nerve palsy, and scotoma (**Table 2**). Family history of migraine is common.[17] Mydriasis may precede the migraine as an aura rather than an associated symptom or have a similar time of onset.[12] Several cases of mydriasis persisting after resolution of the associated migraine are reported,[6,11,13,16] as seen in our patient after resolution of the migraine.

The mechanism of mydriasis during migraine is thought to be decreased activity of parasympathetic fibers.[13] One study tested reaction to pilocarpine, a nonselective parasympathetic nervous system agonist, in patients with residual pupil dilation for a mean of 3 months after resolution of migraine and found hypersensitivity to the drug in all patients.[6] The parasympathetic fibers in the third cranial nerve rather than sympathetic overactivity, possibly occurring as a response to pain.[6,10] Another patient had no response to tyramine (4-

Table 2. Symptoms associated with migraine and nilateral mydriasis (not including Barriga et al.[6] as associated symptoms were not described).

Associated Symptom	No. of Patients	Percentage
Blurred vision	23/41	56.1%
Photophobia	10/41	24.4%
Orbital pain	7/41	17.0%
Nausea	5/41	12.2%
Diplopia	4/41	9.8%
Red eye	4/41	9.8%
Phonophobia	3/41	7.3%
Ptosis	3/41	7.3%
Third nerve palsy	2/41	4.9%
Vertigo	2/41	4.9%
Confusion	1/41	2.4%
Dizziness	1/41	2.4%
Lower extremity weakness	1/41	2.4%
Near-syncopal episode	1/41	2.4%
Neck pain	1/41	2.4%
Scotoma	1/41	2.4%
Vomiting	1/41	2.4%

authors concluded that this reaction was due to dysfunctional hydroxyphenethylamine), which releases norepinephrine to stimulate the sympathetic nervous system, further supporting the hypothesis that mydriasis in this patient population is due to parasympathetic hypoactivity.[11]

Patients presenting with unilateral mydriasis of an unknown cause need a thorough medical evaluation, including review of eye drops and other medications they are using, recent trauma, and associated neurological symptoms. Ophthalmic and neurological examinations may reveal a need for neuroimaging, such as the cerebral angiogram performed in this patient. Optic neuritis and giant cell arteritis should be considered in patients with headache and visual disturbance. As our patient had a known thoracic aortic aneurysm, thereby having risk factors for atherosclerosis and vessel tortuosity, an extensive evaluation was conducted for other vascular causes for the mydriasis. Many patients with unilateral mydriasis have a benign underlying cause, but each case merits individualized medical decision making.[15,18]

CONFLICT OF INTEREST
The authors have no conflict of interest to disclose.

ETHICAL APPROVAL
This work meets all the ethical guidelines.

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CONTRIBUTORS
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REFERENCES

1. Alkhalil M, Lewis S, Hawker M, et al. Persistent unilateral mydriasis and headache (doi: 10.1136/bcr.11.2008.1260). BMJ Case Rep. 2009;2009 epub March 17.
2. Caglayan HZ, Colpak IA, Kansu T. A diagnostic challenge: dilated pupil. Curr Opin Ophthalmol. 2013;24:550-557.
3. Kerr FW, Hollowell OW. Location of pupillomotor and accommodation fibres in the oculomotor nerve: experimental observations on paralytic mydriasis. J Neurol Neurosurg Psychiatry. 1964;27:473-481.
4. Nam KH, Choi CH, Lee JI, et al. Unruptured intracranial aneurysms with oculomotor nerve palsy : clinical outcome between surgical clipping and coil embolization. J Korean Neurosurg Soc. 2010;48:109-114.
5. Ault J. Teaching case: migraine and pupil dilation. Headache. 2011;51:324-326.
6. Barriga FJ, Lopez de Silanes C, Gili P, et al. Ciliary ganglioplegic migraine: migraine-related prolonged mydriasis. Cephalalgia. 2011;31:291-295.
7. Blaik Z, Hiremagular S. Episodic unilateral mydriasis and headaches. Tenn Med. 1998;91:107-108.
8. Evans RW, Jacobson DM. Transient anisocoria in a migraineur. Headache. 2003;43:416-418.
9. Ishikawa H, Yoshihara M, Mizuki K, et al. A pediatric case of ophthalmoplegic migraine with recurrent oculomotor nerve palsy. Jpn J Ophthalmol. 2000;44:576.
10. Jacobson DM. Benign episodic unilateral mydriasis. Clinical characteristics. Ophthalmology. 1995;102:1623-1627.
11. Leone M, Grazzi L, Moschiano F, et al. Internal ophthalmoplegia associated with migraine attacks. Cephalalgia. 1994;14:461-462.
12. Maggioni F, Mainardi F, Malvindi ML, et al. The borderland of migraine with aura: episodic unilateral mydriasis. J Headache Pain. 2011;12:105-107.
13. Purvin VA. Adie's tonic pupil secondary to migraine. J Neuroophthalmol. 1995;15:43-44.
14. Simonetto M, Zanet L, Capozzoli F, et al. Unilateral headache with bilateral internal ophthalmoplegia. Neurol Sci. 2012;33:1185-1187.
15. Skeik N, Jabr FI. Migraine with benign episodic unilateral mydriasis. Int J Gen Med. 2011;4:501-503.
16. Sobreira I, Sousa C, Raposo A, et al. Ophthalmoplegic migraine with persistent dilated pupil. J Child Neurol. 2013;28:275-276.
17. Woods D, O'Connor PS, Fleming R. Episodic unilateral mydriasis and migraine. Am J Ophthalmol. 1984;98:229-234.
18. Tomsak RL. Ophthalmologic aspects of headache. Med Clin North Am. 1991;75:693-706.