

## Benign Episodic Unilateral Mydriasis in a Flight Nurse

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- BACKGROUND:** Benign episodic unilateral mydriasis is one cause of anisocoria. This phenomenon is thought to be related to an imbalance between the sympathetic and parasympathetic nervous systems. There is a documented association with migraines, but asymptomatic cases have also been reported. A challenge with all cases is the level of investigation required to exclude more sinister causes of nervous system dysfunction. In a dynamic flight environment, additional considerations need to be made, such as varying light levels and use of night vision devices.
- CASE REPORT:** A 27-yr-old woman on deployment to Afghanistan as a flight nurse presented to the role one clinic with right-sided mydriasis. The patient denied headache or any history of migraines. A dilated right pupil that was reactive to light was found on exam. Symptoms and exam findings resolved shortly after initial presentation. We consulted an ophthalmologist who requested patient transfer for review. He made a diagnosis of benign episodic unilateral mydriasis.
- DISCUSSION:** There are a variety of causes for anisocoria. A thorough history and examination are required to avoid unnecessary investigations that may not be locally available in the more austere deployed military settings. From an operational perspective, the decision needs to be made regarding the maintenance of flight status. Consideration needs to be given to patient care capability when treating a flight nurse. In cases of rapid resolution such as this, removal from operational status is not reasonable should a clinician be confident of the diagnosis.
- KEYWORDS:** anisocoria, military flight medicine, ophthalmology.

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Anisocoria, or pupil asymmetry, provides a diagnostic challenge for physicians due to the variety of possible causes. It is a cause of multiple presentations to family medicine physicians, emergency departments, and neurologists, with varying onset and symptomatology. The cause of such presentations can be benign or particularly sinister, requiring extensive investigation and management.

Benign episodic unilateral mydriasis (BEUM) is one such cause of anisocoria that is thought to be due to either a hyperactive sympathetic nervous system or, conversely, hypoactivity of the parasympathetic nervous system<sup>3</sup> (one of several theories). Overall, the condition is not well understood.

Awareness of the condition known as simple or physiological anisocoria is important for the clinician, as it potentially informs the presentation of many patients, particularly those with incidental findings. This is a condition affecting nearly 20% of the population, in that a difference of  $\leq 1$  mm diameter of the pupils in the dark is considered normal.<sup>12</sup> Nevertheless, there are many case reports discussing medication, toxin, and surgically induced anisocoria that make investigation of such patients a challenging proposition.

Predominantly, however, existing literature identifies multiple cases of BEUM associated with migraines.<sup>2,3,18</sup> The purpose of this case report is to add to the literature that identifies asymptomatic presentations with minimal or no other relevant neurological findings. This may potentially aid in earlier diagnosis and prevent unnecessary investigations for those patients presenting in this fashion. This report is of relevance to those working in the aviation environment and in military flight medicine, where maintenance of flight and/or operational status is a critical consideration. Additionally, knowledge of the condition and knowing when to refer and/or investigate further is useful to those medical professionals deployed in a more austere military environment, where more advanced investigative measures may not be readily available.

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## CASE REPORT

A 27-yr-old woman on deployment to Afghanistan as a flight nurse presented to a multinational Role 1 clinic with right-sided mydriasis. This was the second occurrence that week, with the initial episode several days prior resolving spontaneously within minutes. No medical attention was sought for the first episode and there were no described associated symptoms. As the patient was also nearly completely asymptomatic for the second episode (see below), the time of onset was not known—the phenomenon was noted by the patient upon looking into a mirror several minutes prior to her presentation. Her background was unremarkable in that she did not currently have, nor had previously suffered from, any chronic or relevant medical conditions, took no medications beyond the oral contraceptive pill (long term with no recent changes), and was not aware of any allergies. The patient denied any current tobacco use. There was no recollection of neurological or ophthalmological conditions or issues in the past, beyond myopia for which the patient used spectacles and contact lenses. Again, she denied headache at the time or any history of migraines, or any neck stiffness or photophobia. The only relevant symptom that the patient could describe was a mild visual deterioration, described as a slight ‘fuzziness,’ around the visual peripheries when looking out of the right eye. This was comparable to symptoms experienced during previous visits to the optometrist, where the pupil had been dilated via pharmacological means. A neurological exam was conducted within minutes of the presentation. Visual acuity testing was included as part of this assessment, as was tonometry, with neither test identifying any abnormalities.

A dilated right pupil that was mildly reactive to light was found on examination (**Fig. 1**), with no other relevant findings noted. Specifically, no ophthalmoplegia was noted, and accommodation and consensual reflexes remained intact and reacting normally in the context of anisocoria. We consulted an ophthalmologist via phone who requested patient transfer for review. This was conducted within 2 h of the initial presentation, by which point the presenting sign and symptom had resolved (approximately 1 h post-presentation). The specialist performed no neuro-radiological imaging and made a diagnosis of benign episodic unilateral mydriasis based on his clinical findings. No follow-up was recommended and the patient was returned to operational status following her return to base. No further episodes were described by the patient in the days following the initial presentation.



**Fig. 1.** Photo of the case patient showing a dilated right pupil.

## DISCUSSION

A literature review noted multiple documented cases of benign episodic mydriasis in the patient presenting with anisocoria. The majority, however, presented with at least one additional complaint, commonly migraine.<sup>3</sup> Prior studies have reviewed cases of BEUM associated with migraine,<sup>2,3,18</sup> with summarized common presentations of the disorder. A complaint of blurred vision, a category in which our case may fit, depending on the symptom interpretation, was identified in 56% of cases.<sup>3</sup> Other more common associated symptoms from the same study included photophobia (24.1%) and orbital pain (7.0%).<sup>3</sup> Given the review looked at the association between anisocoria and migraine, these results are not surprising. The number of documented cases of BEUM in the absence of migraine symptoms are significantly fewer. A 2013 study<sup>14</sup> published in the Spanish Neurology Society journal *Neurología* identified seven separate cases of BEUM presenting to a neuro-ophthalmology clinic at a tertiary hospital. Of the seven cases, three identified no history of migraine. All three of those patients presented due to an incidental finding of pupil asymmetry and had no complaint of headache at the time. Given the original surveyed pool of 780 patients, the number of BEUM cases available for analysis is few.

Medication- and toxin-induced causes of mydriasis and anisocoria have also been noted in the literature, including presentations identified postoperatively. Several case reports identify unilateral mydriasis following administration of ipratropium, a commonly used medication that actively blocks muscarinic acetylcholine receptors.<sup>4,16,17</sup> Other antimuscarinic agents such as hyoscine have also been linked to anisocoria.<sup>8</sup> Hyoscine is a medication that has been used to control motion sickness and as an antiemetic (off-label) in chemotherapy-induced nausea and vomiting. The concerns raised by new-onset pupil asymmetry in a cancer patient are significant, in that the potential exists for space-occupying metastasis in the central nervous system. This would almost certainly require investigation to some extent. Other case reports have identified glycopyrrolate (a direct acetylcholine receptor antagonist) as a cause of intermittent and fluctuating anisocoria,<sup>5</sup> as well as botulinum toxin used for the purposes of facial cosmetics.<sup>1</sup> Ingestion of the plant *Brugmansia* (‘Angel’s Trumpet’), either recreationally<sup>10</sup> or accidentally<sup>13</sup> (a worthwhile item to cover in the history of a child presenting with anisocoria), has also been noted as a cause of mydriasis. Postoperative mydriasis has also been noted in the literature and is often difficult to explain given the multitude of unique causes.<sup>9,15</sup>

In evaluating the patient with unequal pupils, having a systematic approach is useful to ensure that relevant warning signs are not missed. The first step should be to determine which of the pupils is abnormal.<sup>6</sup> Regardless of the relative size, if there is poor reactivity to light or unusual shape, then that pupil is likely the abnormal one. Careful observation for signs such as ptosis, proptosis, or ophthalmoplegia need to be conducted, as well as a review of visual acuity, visual fields, and anterior chamber pressures. Ptosis should prompt a

physician to consider Horner's syndrome (due to damage/interference of the sympathetic trunk), where a sluggish pupillary response with associated absence of knee or ankle jerks would be suggestive of Adie Tonic Pupil, a condition related to postganglionic parasympathetic pupillomotor fiber damage. Consider also the possibility of optic neuritis and giant cell arteritis in the patient with headache and visual disturbance.<sup>3</sup> Life-threatening causes of anisocoria are rare but important to consider. In the absence of readily available magnetic resonance imaging, a clinician needs to be confident with conducting a thorough neurological examination and aware of those signs or symptoms that should prompt further investigation. Stroke, intracerebral bleed, closed-angle glaucoma, and infection are examples of diagnoses not to be missed. As well, the possibility of carotid artery dissection in the patient presenting with Horner's Syndrome should always be considered.<sup>7</sup>

A dynamic flight environment offers separate challenges that may be compounded by conditions that result from an imbalance in the autonomic nervous system, particularly in this case where the patient had no obvious symptoms that would alert them to the phenomenon occurring. Hypoxia, for example, is known to have oculometric effects, including pupil size fluctuation.<sup>19</sup> The autonomic nervous system undergoes multiple changes due to the central depressive effects of hypoxia, therefore the added effect to a condition such as BEUM is not known. Signs such as anisocoria noted by other crewmembers would require further questioning and in-flight investigation into the issue to ensure a more sinister cause was not responsible for the change (such as hypoxia and, subsequently, a potential threat to the entire crew). For those unaware of their condition, this may cause unnecessary problems in the flight environment, particularly if the task load is already high, such as when transport of a critically ill patient is underway, as may be the case for a flight nurse. For flight deck crewmembers, there are several further problematic situations that may arise, including the use of night vision devices or when operating in visual flight conditions. A symptomatic individual (if suffering from blurred vision or migraines) would be more adversely affected in this scenario and further input from flight medicine would be required.

Previous studies on the subject conclude that neuro-diagnostic imaging is not required for cases of isolated benign episodic mydriasis.<sup>11</sup> Confidently reaching a diagnosis, however, and excluding potentially more life threatening causes of anisocoria remains a challenge for physicians, particularly those deployed in the more austere military environments with limited capability to investigate the condition fully. Awareness of BEUM as a phenomenon, including the variability in presenting symptoms, is useful knowledge for the deployed flight surgeon.

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