



Case Report

Pharmacologic anisocoria due to nebulized ipratropium bromide: A diagnostic challenge

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ABSTRACT

Anisocoria may be physiological or seen in fatal conditions, such as intracranial hemorrhage. Newly developing anisocoria may cause confusion and diagnostic difficulty in the emergency department (ED). A 35-year-old female was admitted to the ED with an asthma attack and dyspnea. On examination, the patient was observed to have bilateral rhonchi and was treated with nebulized albuterol (salbutamol) and ipratropium bromide. After the treatment, the dyspnea improved, and mydriasis developed in the left eye (left pupil diameter 9 mm, right 4 mm). An examination revealed that the left pupil was dilated and unreactive to light, but there was no neurological finding. Afterwards, the patient reported that, during the treatment, some aerosol had leaked from the left side of the mask and may have come into contact with her left eye. Given this information, a pilocarpine test was performed, and the patient was diagnosed with pharmacologic anisocoria. The pupil returned to normal within 24 h. Ipratropium bromide is a drug frequently used in patients presenting to the ED with dyspnea. During treatment, nebulized ipratropium may leak from the edge of the facial mask into the ipsilateral eye and may cause mydriasis. A pilocarpine test can be used to differentiate pharmacological anisocoria from other causes, such as third nerve palsy and Adie's pupil. Through the awareness of emergency physicians and the use of the pilocarpine test, a diagnosis can be made without engaging in time-consuming and costly analyses. In addition, this complication can be prevented using masks that better fit the face, as well as protective goggles or eye patches, during treatment.

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1. Introduction

Patients presenting with anisocoria often cause diagnostic difficulties in the emergency department (ED), since this condition is not only physiological but can also be seen in postocular trauma or life-threatening cases that require urgent treatment, such as uncal herniation [1,2]. Emergency physicians (EPs) should be able to distinguish between benign anisocoria and life-threatening disorders, while at the same avoiding unnecessary and costly tests. In reporting this case, we aim to draw the attention of EPs to pharmacological mydriasis, a benign cause of anisocoria. In patients with anisocoria that presents with normal neurological findings and no eye trauma, taking this diagnosis into consideration will eliminate the need for time-consuming and expensive examinations.

2. Case report

A 35-year-old female was admitted to the ED with dyspnea. The patient did not have any disease other than asthma. Her prescribed asthma medication had been finished three months earlier, but the patient had not been using any further medication since she no longer had any complaints. Upon admission, the patient's vital signs were as follows: a BP of 110/70 mmHg, heart rate of 83 beats/min, SpO₂ of 96% (room air), and body temperature of 36.3 °C. On physical examination, all systemic findings were normal, except for wheezing and the presence of bilateral rhonchi on auscultation. Nebulized albuterol (salbutamol) and ipratropium bromide were administered to the patient three times at intervals of 20 min. After 1 h, the patient stated that she felt relief, and her wheezing and rhonchi were reduced. However, at the time of discharge, the patient's husband reported that her pupils appeared abnormal. A repeated examination revealed that the left pupil was round, fixed, and dilated to a diameter of 9 mm, and the right pupil was round and 4 mm in diameter and had a normal light reflex in room light (Fig. 1). The examination was conducted in dim light and bright light, and the anisocoria was more evident under bright light. The

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Fig. 1. Patient's eyes in room light. The left pupil is dilated to 9 mm, and the right pupil is normal.

patient's extraocular eye movements were normal, and a slit lamp examination revealed no pathology on the eyelids, conjunctiva, or cornea. Visual acuity, visual fields, a fundoscopic examination, intraocular pressure, and a neurological examination including cranial nerves provided normal findings. The patient had no headache, loss of vision, or eye pain. She also had no history of trauma. We examined the patient's photographs taken within the last week on her smartphone and social media accounts and noticed that her pupils were isochoric, confirming that the anisocoria had just developed. Head-neck computed tomography (CT) and CT angiography were performed to eliminate central causes (spontaneous carotid artery dissection, intracranial lesion, third nerve palsy, etc.). The CT and CT angiography findings were normal. The patient's history was revisited. The patient stated that when the nebulized medication was administered through a face mask, some of the drug had leaked from the left side of the mask and might have touched her left eye, upon which we decided to conduct a pilocarpine test to confirm the diagnosis of pharmacologic mydriasis. During this test, first, diluted pilocarpine (0.125%) was dropped into the patient's left eye, and upon observing no pupil constriction, the possibility of Adie's (tonic) pupil was eliminated. Then, a nondiluted pilocarpine (2%) test was conducted, which showed no change in the mydriasis, confirming the diagnosis of pharmacologic mydriasis due to ipratropium bromide. The patient was discharged after being informed about her status. At the follow-up session 24 h later, the patient had no complaints, and the mydriasis in the left eye had been resolved.

3. Discussion

Anisocoria, defined as having pupils of different sizes, may have a variety of causes. The etiology of anisocoria is challenging to clarify in the ED. It is also time-consuming and costly due to the requirement of detailed examinations. The most common cause of anisocoria is physiological anisocoria, which occurs in almost 20% of the general population [1,2]. For a diagnosis of physiological anisocoria, the condition should have been present for a long time (old photographs can be examined to find this out), the size difference between the pupils should be ≤ 1 mm, and the amount of anisocoria should not change between light and dark environments [1]. Other causes of anisocoria include Adie's (tonic) pupil, trauma, third nerve palsy (e.g., intracranial tumor or aneurysm compression), Horner syndrome (e.g., due to carotid artery dissection), uncal herniation, and pharmacological agents [1–7]. The agents causing anisocoria due to pharmacological mydriasis are drugs (including scopolamine patches, topical glycopyrrolate, nasal vasoconstrictors, and inhaled ipratropium) and plants such as Jimson weed and Angel's trumpet [1,4–9].

Ipratropium bromide is one of the most commonly used drugs in patients presenting to the ED with dyspnea; it is an atropine-derived anticholinergic agent that blocks the binding of acetylcholine to muscarinic receptors [1–10]. If the conjunctiva are exposed to ipratropium bromide through inhalers or nebulizers, mydriasis or acute glaucoma may develop [6,10]. If the face mask or noninvasive bilevel positive airway pressure (BiPAP) mask does not closely fit the face, the aerosol may leak out of

the mask and come into contact with the eye surface [6,10]. As a result, ipratropium bromide will affect the muscarinic receptors and lead to pupil dilatation. This seemingly rare complication may be more frequent than expected. In a previous study, it was reported that ipratropium bromide-induced anisocoria developed in 3% of patients who had received that treatment in the intensive care unit [11].

It is important to distinguish whether the newly developed pupillary dilatation or anisocoria is caused by a life-threatening factor or has a benign cause, such as pharmacological mydriasis. For this purpose, it is necessary to obtain the patient's medical history in detail. It is also important to be aware of the presence of certain signs and symptoms, such as third nerve palsy, changes in consciousness, or severe headache. Once all these factors have been reviewed, if the patient is suspected to have pharmacological anisocoria, the diagnosis can be confirmed by a pilocarpine test. Although 1–2% pilocarpine causes narrowing not only in a normal pupil but also in a dilated pupil due to third nerve palsy, it does not cause any constriction in pharmacological mydriasis.

4. Conclusion

Patients with anisocoria need careful and systematic evaluation to eliminate potential life-threatening conditions. Anisocoria-related algorithms outline the best approach to evaluating the patients and can guide the physician. In addition, a detailed history and examination provide necessary information about the etiology of this condition. If the patient does not have a new symptom or examination finding other than anisocoria, and if there is a history of ipratropium bromide administration in the near past, then pharmacological anisocoria should be considered in the etiology of anisocoria. Observation of the neurological status and a pilocarpine test can be helpful in a differential diagnosis, thus preventing detailed and costly diagnostic procedures.

Conflict of interest

No conflict of interest was declared by the authors.

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