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Anticholinergic drug-induced benign unilateral anisocoria: common, but frequently overlooked side effect

Gaurav Gheewala, Salim Surani, Rizwan Ishtiaq, Sneha Reddy, Iqbal Ratnani

Abstract

Sudden anisocoria have always been ominous signs among critically ill patients, which requires prompt attention. There are various causes of anisocoria, which call for comprehensive evaluation to rule out neurologic causes such as Adie's pupil, uncal herniation, compression of third cranial nerve, meningeal irritation, and seizures as opposed to the pharmacological causes such as anticholinergic drugs, anesthesia, and recreational drugs versus causes such as migraine and trauma to the eye. We hereby report a case of a patient with unilateral anisocoria from dilated left pupil due to the nebulized ipratropium bromide, a cholinergic antagonist that resolved with discontinuation of the medication. The purpose of this case report is to emphasize the importance of thorough physical assessment, an early review of the medications, and the use of inexpensive diagnostic test to save time and avoid the expensive diagnostic study.

Key words: Anisocoria, dilated pupil, anticholinergic drug, bronchodilators, ipratropium bromide.

Introduction

The new onset of unilateral dilation of the pupil in any patient population is concerning and is alarming when a patient is in critical care with multiple health issues and requires foremost attention. It is very important to differentiate the neurological causes as opposed to the others by performing a detailed neurological examination, imaging study and reviewing medication list to rule out the drug-induced anisocoria. (1) Ipratropium bromide is a cholinergic antagonist medication, which is frequently prescribed in the critical care setting for patients with respiratory insufficiency, asthma, or chronic obstructive pulmonary disease (COPD). This medication is known to cause benign unilateral pupil dilation by antagonizing cholinergic receptors in the eye, (2-4) but it is frequently overlooked.

Case report

A 68-year-old male patient with a past medical history of gastro-esophageal reflux disease, esophageal stricture (that was dilated a few years ago), and hypertension was admitted in the hospital with the sudden onset of shortness of breath, chest and epigastric pain after an episode of retching and forceful vomiting post dinner. Patient examination upon admission showed diminished breath sound in bilateral lower lobs, the abdomen was distended and tender to palpation at bilateral upper quadrants. The patient looked distressed and in pain; on neurological examination, pupils were symmetrical, equal, round, and reactive to light and accommodation, and the patient had no sensory or motor deficit. Patient's laboratory exam was unremarkable, and chest and abdominal X-ray was unremarkable for any pathology. The patient underwent computed tomography (CT) scan of chest, abdomen, and pelvis, which showed extensive pneumomediastinum, extending into upper abdomen centered about the gastroesophageal junction with

From Department of Anesthesiology and Critical Care, DeBakey Heart and Vascular Center, Houston Methodist Hospital, Houston, TX, USA (Gaurav Gheewala, Iqbal Ratnani), Texas A & M University, Corpus Christi, TX, USA (Salim Surani), Department of Internal Medicine, Mercy St Vincent Medical Center, Toledo, OH, USA (Rizwan Ishtiaq), and Pulmonary Associates of Corpus Christi, TX, USA (Sneha Reddy).

Address for correspondence:
Dr. Salim Surani
7613 Lake Bolsena, Corpus Christi, TX 78413, USA
Tel: 361-885-7722
Fax: 361-850-7563
Email: srsurani@hotmail.com

a small amount of free intraperitoneal air and fluid with surrounding inflammatory changes (**Figure 1**). The patient was diagnosed with esophageal perforation at the gastroesophageal junction with mediastinitis and free air in peritoneum in the setting of forceful vomiting. He underwent esophageal stent placement with mediastinal washout and percutaneous gastric jejunum tube placement.

A few days later, chest and abdomen CT scan with oral contrast was performed to evaluate post procedure changes. CT scan results indicated no leak at the distal gastroesophageal junction but a moderate amount of gas and fluid around the distal esophageal stent, which were not amenable to percutaneous drainage (**Figure 2**). Therefore, the patient required re-exploration with mediastinal washout, and decortication for left pleural effusion. He was extubated postoperatively but remained in respiratory insufficiency, hence, was transferred to the intensive care unit (ICU). In ICU, he was started on nebulizer ipratropium bromide but avoided albuterol as, during this hospital stay, he had an episode of atrial fibrillation with rapid ventricular rhythm, which was treated with amiodarone. Next day, the patient's respiratory insufficiency was resolved and was placed on 2 L nasal cannula with oxygen saturation of 96%. The decision was made to transfer the patient to the floor. Immediately before the transfer, the nurse noted mydriasis in his left eye. The left pupil was 5 mm in diameter compared to 2 mm in the right though both pupils were round and reactive to light. Neither any focal neurological deficit was noted, nor did the patient complained of any new blurry vision, diplopia, or vision loss. To rule out any neurological cause, a CT scan of the head without contrast was performed, which did not show any acute intracranial abnormality.

Further workup included magnetic resonance imaging (MRI) of the brain and magnetic resonance angiogram (MRA) of the head/neck without contrast. The results of MRA of the head revealed posterior cerebral artery P1 segment stenosis, which raised concerns for third nerve palsy related to ischemia of the oculomotor nerve (**Figure 3**). As the patient did not show any other neurological deficit and all imaging studies were normal to trivial, the neurological cause was ruled out. Furthermore, to rule out the pharmacological causes, patient's medication administration record (MAR) was reviewed. It was noticed that he received ipratropium bromide right before developing anisocoria. Ipratropium bromide is well known to cause dilation of pupils and therefore, was discontinued. Within 10 hours of last ipratropium bromide treatment or 19 hours of treatment, which he received right before developing anisocoria, mydriasis in the left eye was resolved.

Discussion

Ipratropium bromide, the cholinergic antagonist, is widely used in the critical care setting for COPD and asthma patients as it is a bronchodilator and decreases mucus production by blocking acetylcholine effects on cholinergic nerves. When inhaled, there is minimal systemic absorption, but can cause mydriasis when administered topically or if accidentally spilled in the eyes from broken nebulizer circuit or poorly fitted mask. (2,3) Although ipratropium bromide-induced anisocoria is benign, it may take up to 24 hours to resolve, and therefore, it is essential to rule out any other serious causes. (4)

Pilocarpine is a cholinergic agonist, which acts on the muscarinic receptor of the iris sphincter and ciliary muscles to cause pupil constriction. In the sudden onset of the new unilateral dilated pupil, the different strength of pilocarpine eye drops can be used to differentiate between the neurological and pharmacological cause once the exhaustive neurological examination is normal. (4) When it is administered in the eye with a dilated pupil, it can cause constriction if mydriasis is secondary to the neurological issue, while in the pharmacological cause, it remains unresponsive. (4) In our case, we were not able to use pilocarpine as the patient developed anisocoria late in the evening and by the time we got all the test results in, it was past midnight. Since imaging studies were normal-trivial with no other neurological deficit, it was decided to discontinue ipratropium bromide as the patient developed anisocoria right after the treatment with ipratropium bromide. In addition to this, it has a property to cause dilation of the pupil when it comes in direct contact with the eye from losing or improper placement of the face mask while getting nebulizer treatment. The plan was to re-evaluate for resolution of anisocoria by morning as ipratropium bromide related mydriasis usually gets resolved within 24 hours. Failing plan was to consult a neuro-ophthalmologist for pilocarpine test. Patient's pupil assessment following morning showed left pupil diameter decreased to 3.5 mm from 5 mm, and became equal within 19 hours of treatment, which he received right before developing anisocoria.

Conclusions

The new onset of unilateral dilation of the pupil in any patient population is an ominous sign and requires immediate attention to differentiate the causes. Thorough neurological examination and early use of pilocarpine test may help to avoid the expensive imaging studies as in our case; we could have avoided MRI/MRA scan. Also, it is essential for the provider to review MAR and discontinue any pharmacological drugs immediately, which can cause false dilation of pupils to rule out the neurological cause.

Data availability

Data would be available from the authors upon request.

Figure 1. Pneumomediastinum and pneumoperitonium

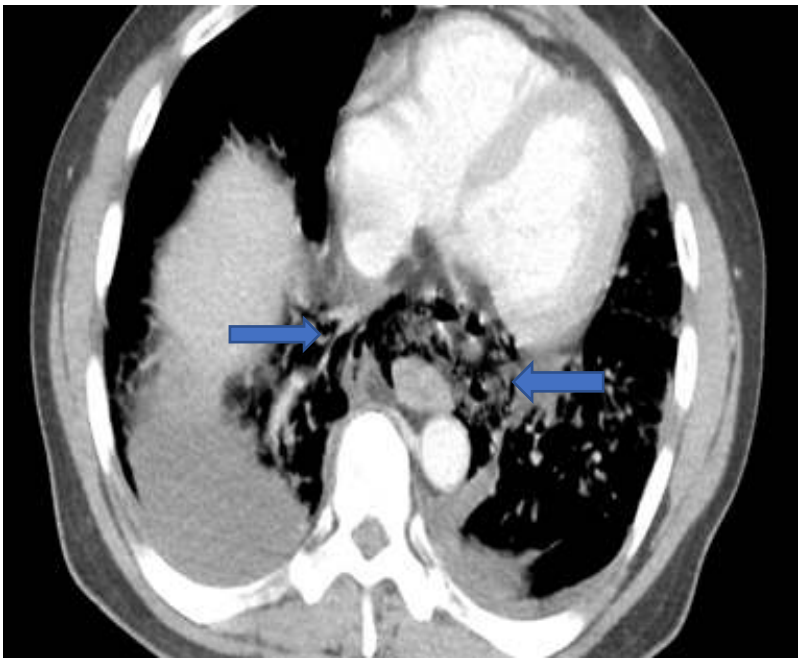


Figure 2. Gas and fluid around the distal esophageal stent

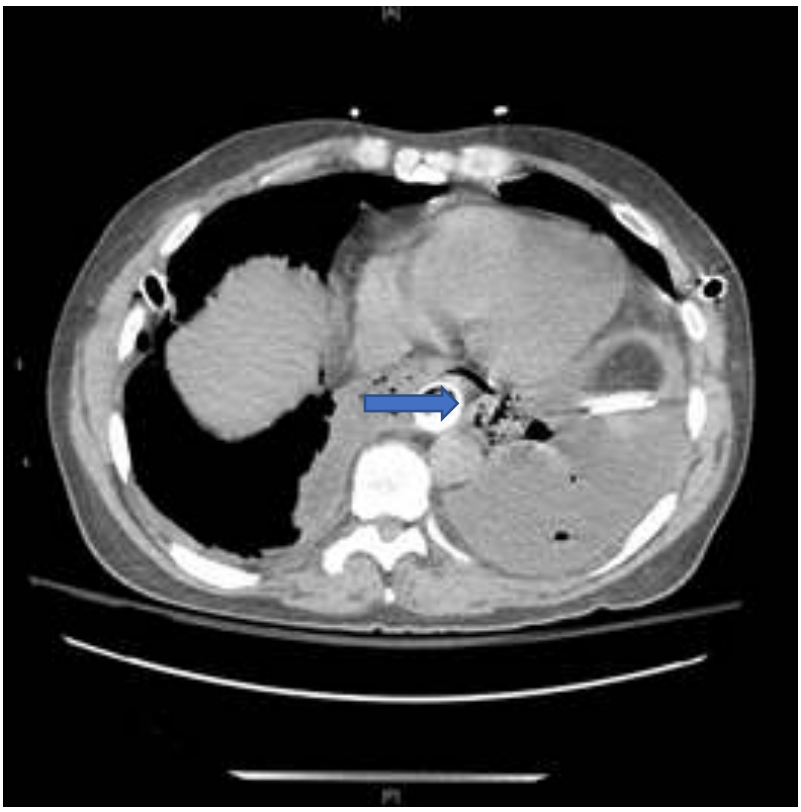
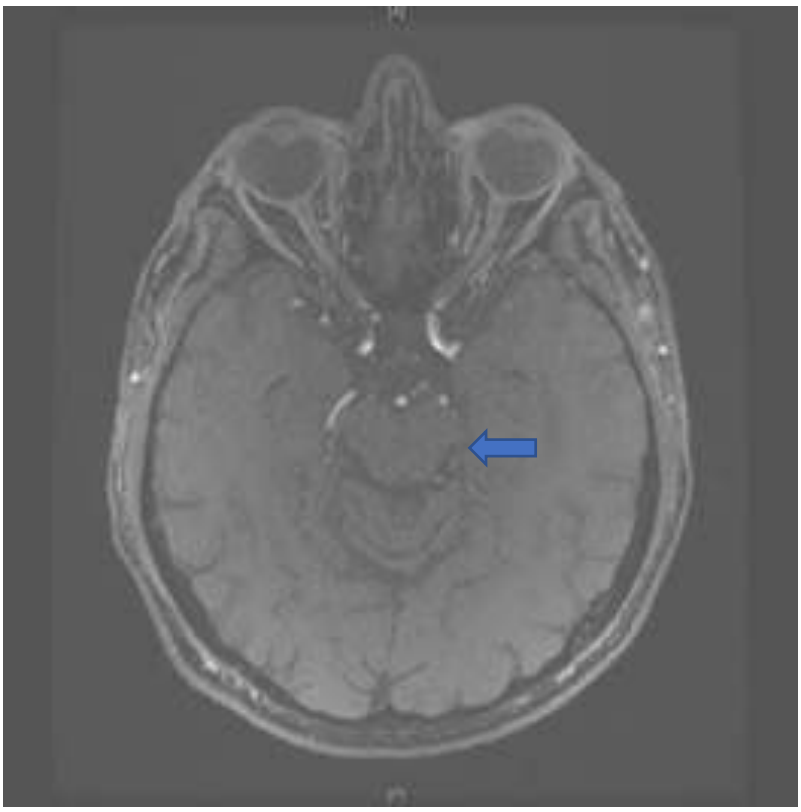


Figure 3. Posterior cerebral artery P1 segment stenosis



References

1. Santana-Cabrera L, Fernandez-Tagarro EJ, Del Amo-Nolasco B, Jaen-Sanchez N, Caceres-Agra JJ. Unilateral mydriasis secondary to ipratropium bromide in a critically ill patient. J Emerg Trauma Shock 2012;5:199-200.
2. Chaudhry P, Friedman DI, Yu W. Unilateral pupillary mydriasis from nebulized ipratropium bromide: A false sign of brain herniation in the intensive care unit. Indian J Crit Care Med 2014;18:176-7.
3. Krovvidi HP, Thillaivasan A. A benign cause for a unilateral dilated pupil in a critical care patient. Eur J Anaesthesiol 2008;25:692-3.
4. Eustace N, Gardiner C, Eustace P, Marsh B. Nebulised ipratropium causing a unilateral fixed dilated pupil in the critically ill patient: A report of two cases. Crit Care Resusc 2004; 6:268-70.
5. Camkurt MA, Ay D, Akkucuk H, Ozcan H, Kunt MM. Pharmacologic unilateral mydriasis due to nebulized ipratropium bromide. Am J Emerg Med 2011;29:576.e5-6.