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Case Report Open Access

"Don't Believe Your Eyes" Ipratropium Induced Mydriasis: A Case Report and Review of the Literature

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Abstract

Unilateral fixed mydriasis can be an ominous sign; however in many cases, it is benign and represents pharmacologic mediated action on the iris dilator or sphincter. Differentiation between pharmacologic mediated anisocoria and physiologic anisocoria can be challenging but may save on costly imaging. An 83 year-old woman was admitted with critical limb ischemia and subsequently developed respiratory failure treated with positive pressure ventilation and ipratropium nebulizers. She was noted to have left unilateral mydriasis without other neurologic deficits. Brain magnetic resonance imaging with MR angiography showed no evidence for a mass lesion or posterior communicating artery aneurysm. Her anisocoria self-resolved within 36 hours after nebulizer treatments were stopped. Ipratropium bromide is one of the most common medications used in the hospital setting and should be consider as a possible etiology when examining patients with unilateral mydriasis in the absence of other neurologic findings.

Keywords: Anisocoria; Mydriasis; Iatrogenic; Pharmacology; Ipratropium

Introduction

Unilateral fixed mydriasis, aka a "blown pupil", is often considered to herald an underlying ominous impending process, raising concern for an acutely evolving space-occupying mass lesion progressing toward uncal herniation.

However, in many cases unilateral mydriasis is benign and due to pharmacologic agents mediating direct action on the iris dilator or sphincter. Medications known to cause mydriasis include atropine, scopolamine, amphetamines, and serotonergic medications.

While systemic medications cause bilateral mydriasis, direct ocular inoculation with topical medications can cause unilateral mydriasis. Sympathetic adrenergic stimulation causes constriction of the iris dilator and subsequent pupillary dilatation; whereas, parasympathetic stimulation mediates iris sphincter and pupillary constriction. Aerosolized ipratropium bromide, a medication that blocks muscarinic acetylcholine receptors, is often used to treat obstructive airway disease.

It has been well described in numerous case reports and case series as causing unilateral mydriasis [1-6], mediating pupillary dilatation through its direct parasympatholytic effect; however, unilateral mydriasis associated with ipratropium remains poorly recognized in the [1,5] hospital setting [7].

We report reversible unilateral mydriasis associated with recent inhaled ipratropium in a patient without other neurologic deficits, and review previously published literature of this phenomenon to describe its chief clinical characteristics.

Case Report

An 83 year-old woman was admitted for critical limb ischemia and subsequently developed acute respiratory failure treated in the Intensive Care Unit with bilevel positive pressure ventilation and ipratropium/albuterol nebulizations (0.5-2.5 mg) delivered non-invasively via a full face mask every 4 hours. After transfer back to the ward, physical examination demonstrated left pupillary mydriasis unreactive to light and accommodation, as well as incidental left extotropia without limitation of extraocular movement (Figure 1). No other neurologic abnormalities were noted, and the patient was asymptomatic. Nebulizer treatments were discontinued, but anisocoria persisted one day later. Brain magnetic resonance imaging with MR angiography showed no evidence for a mass lesion or posterior communicating artery aneurysm. Within 36 hours following onset, her mydriasis completely resolved.

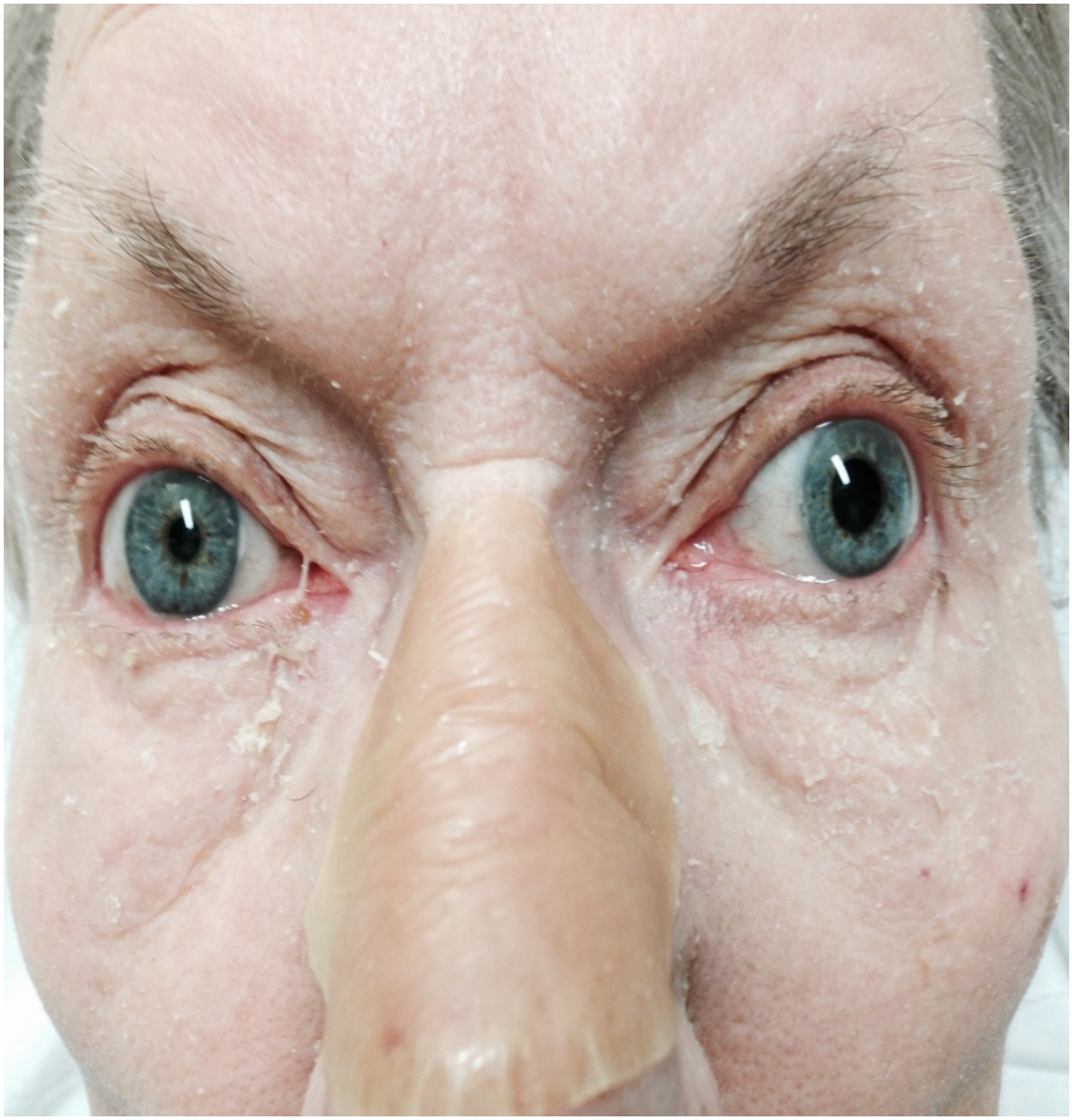

Figure 1: Left mydriasis induced by ipratroium bromide in a 83 year old woman. She had left exotropia due to strabismus, and no weakness of extraocular muscles was observed

Discussion

Ipratropium bromide is one of the most commonly used medications in the hospital setting, and is being used in conjunction with positive pressure ventilation with increasing frequency. Ipratropium bromide has been known to cause unilateral mydriasis from topical administration secondary to a poorly fitting face mask allowing for medication to directly inoculate one eye [1,3-5,8-10] or broken nebulizer circuit [2]. This phenomenon has been more commonly reported in intensive care and pediatric patient populations, since maintaining proper fitting facemasks may be more challenging in these patients.

We reviewed previously published literature in the English language concerning mydriasis and ipratropium bromide on PubMed between the years of 1986 and 2015, using the search terms "mydriasis, ipratropium bromide" and "anisocoria, ipratropium bromide", and identified 14 articles describing 20 case reports of ipratropium-induced mydriasis in the adult population (Table 1).

Age	Sex	Affected Pupil	Duration of affect	Dosage of ipratropium	Co-morbidities	Mechanism of ocular contamination
69	M	Left	Hours	0.5 mg every 4 hours	Lung CA, right frontal craniotomy, left sided facial weakness and hemiparesis	Facial weakness resulting in mask leak
32	F	Right	<24 hours	Unknown dose every 4 hours	Left frontal intracerebral hemorrhage resulting in right sided hemiparesis	Facial weakness resulting in mask leak
45	F	Right	8 hours	Unknown	Scrub Typhus Syndrome, Coma	Faulty Nebulizer Circuit
52	M	Right	<24 hours	Unknown	COPD, depression, biliary leak	BiPap mask with right sided leak
42	F	Right	<24 hours	Unknown	Alcoholic Cirrhosis, Hepatitis B, Hepatitis C, Fungal Pneumonia	BiPap mask with right sided leak
78	F	Right	24 hours	Unknown	Acute myelogenous leukemia, atrial fibrillation, coronary artery disease, posterior reversible encephalopathy syndrome	BiPap mask with right sided leak
64	M	Left, Right	Hours	Unknown dose every 6 hours	Acute lymphoblastic leukemia, pnuemonia, hydrocephalus	Loose fitting facemask
29	F	Right	<24 hours	0.25 mg every 6 hours	Pregnancy	Unknown
36	M	Left	48 hours	Unknown	Asthma	Unknown
76	F	Left	24 hours	Unknown	Coronary artery disease, pneumonia, cerebrovascular accident	Improper facemask use causing left sided leaking
31	F	Left	Unknown	Unknown	Unknown	Mechanical administration from contaminated hands
22	F	Left	24 hours	0.25 mg every 6 hours	Cystic Fibrosis	Improper facemask use causing left sided leaking
22	M	Unknown	36-48 hours	Unknown	Acute myelogenous leukemia, enterrococcal meningitis	Unknown
64	M	Unknown	Unknown	Unknown	Acute myelogenous leukemia, alveolar hemorrhage, atrial fibrillation, renal failure	Unknown
42	M	Unknown	6 hours	Unknown	Acute myelogenous leukemia, alveolar hemorrhage, atrial fibrillation, renal failure	Unknown
40	M	Unknown	36-48 hours	Unknown	Non-Hodgkins lymphoma, aspergillus pulmonary infection	Unknown
62	M	Left	24 hours	Unknown	Mitral valve replacement, pneumonia	Unknown
68	M	Unknown	Unknown	Unknown	Cardiac Arrest, coma	Unknown
38	F	Left	Unknown	Unknown	Asthma	Faulty Nebulizer Circuit
24	F	Bilateral	Unknown	High dose	Asthma	Unknown

Table 1: Summary of previously reported cases of ipratropium bromide induced anisocoria.

In all reported cases, the affected pupil side was equally represented; and mydriasis was the only new neurologic finding. The reported duration of mydriasis following discontinuation of ipratropium bromide ranged from a few hours to 48 hours with most cases resolving within 24 hours [1-6,8,10-12] and 3 cases taking at least 36 hours for the mydriasis to resolve [7,11]. The remainder of the cases did not report duration of the mydriasis. Most cases were attributed to an improperly fitting face mask either from facial weakness [1] or a faulty seal on the mask [3-5,8,10], which we believe was the case in our patient. Faulty nebulizer circuit [2,13], and mechanical contamination of the nebulizer with the eye [9] were also cited as a potential cause. The remainder of the cases did not have a clear etiology. Dosage,

frequency of administration, administration with positive pressure ventilation, and patient specific pharmacokinetics likely play a role in both the induction and duration of mydriasis; unfortunately, this data cannot be gleaned from the current literature.

New onset unilateral mydriasis often raises the concern for an acutely evolving mass lesion such as intracranial hemorrhage, an expanding posterior communicating artery aneurysm (which has particularly close proximity to the third cranial nerve), or tumor leading to uncal herniation; however, mydriasis is rarely the sole neurologic symptom or finding. Moreover confirmatory testing with pilocarpine administration (which demonstrates pupillary constriction in non-pharmacologic etiologies but failure to constrict when the cause is an iatrogenic pharmacologic agent) can also confirm a diagnosis of pharmacologically induced mydriasis and potentially obviate need for imaging [14,15]. However, ophthalmologic consultation is often not promptly available in an inpatient setting when the clinical question arises. Persistent fixed mydriasis beyond the most commonly reported timeframe for pharmacologic causes also suggested necessity for neuroimaging to exclude a compressive mass lesion, as in our case.

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