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Acute angle closure glaucoma precipitated by homeopathic eyedrops containing *Atropa belladonna*

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ABSTRACT

Acute angle closure glaucoma is a sight-threatening condition that may lead to blindness. This is a case report of a woman who presented to the emergency department (ED) with acute angle closure glaucoma following use of an over-the-counter (OTC) homeopathic eye drop containing *atropa belladonna* (deadly nightshade).

A 55-year-old woman presented to the ED with a 5-day history of left eye redness, swelling, tearing, and foreign-body sensation that had acutely worsened in the last two days. Her exam revealed mild left conjunctival injection with watery tearing and a hazy appearance of her left cornea. Fluorescein staining was negative, while tonometry revealed elevated intraocular pressure on the left, suggestive of acute angle closure glaucoma. She was urgently referred to ophthalmology. The etiology of the acute angle closure glaucoma was initially unclear however, with additional prompting, she revealed that two days prior she had started using homeopathic OTC eye drops. Inspection of the eyedrop's ingredients revealed that *atropa belladonna* was the primary ingredient and likely precipitated her isolated episode of acute angle closure glaucoma.

A high level of clinical suspicion and focused ophthalmic exam including tonometry is essential to identify acute angle closure glaucoma in the ED. We present a case report of acute angle closure glaucoma associated with the use of homeopathic belladonna-containing eyedrops. Our report reinforces the necessity to perform thorough medication and supplement history given the prevalence of physiologically active substances available in OTC medications.

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1. Background

Acute angle closure glaucoma is a sight-threatening condition that may lead to blindness. A high level of clinical suspicion with confirmational testing should be followed by an urgent referral to ophthalmology to minimize patient morbidity related to persistently increased intraocular pressures. We present a case report of a woman who presented to the emergency department (ED) with acute angle closure glaucoma following use of an over-the-counter (OTC) homeopathic eye drop.

2. Case description

A 55-year-old woman with history significant for well-controlled diabetes mellitus and primary hypertension presented to the ED with a 5-day history of left eye redness, swelling, tearing, and foreign-body

sensation that acutely worsened over the last two days. She was evaluated by her ophthalmologist when her symptoms first began –it is unknown whether this exam included tonometry with documented normal intra-ocular pressure—but by patient report the examination was noted to have no abnormal findings. She was told she should return if symptoms persisted. She denied a history of trauma, recent upper respiratory infection, previous eye injury, or conjunctivitis exposure. She denied fever, chills, headache, dizziness, loss of vision, painful eye movements, photophobia, or blurred vision. She wore glasses but not contacts. Her past relevant surgical history included LASIK eye surgery 15 years prior.

On presentation, she appeared nontoxic and, aside from an elevated blood pressure of 146/104, her vital signs were within normal limits for her age. Her physical exam was significant for mild left conjunctival injection with clear, watery tearing and a hazy appearance of her left cornea. Her extraocular movements were nonpainful, fully intact, and equal bilaterally. At baseline, her pupils were not miotic or mydriatic and were equal, round, and reactive to light. Ciliary flush was not present. On digital palpation of the globe, her left felt firmer than the right.

Her visual acuity was 20/20 bilaterally, 20/20 on the right, and 20/40 on the left. Fluorescein staining did not reveal evidence of any corneal

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Fig. 1. Image of Similasan “Pink Eye Relief” eyedrops packaging. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

abrasion or ulceration. On tonometry, her intraocular pressure was elevated in her left eye (51 mmHg) compared to her right (11 mmHg). At this time, acute angle glaucoma (AACG) being the definitive diagnosis, an ophthalmologist was urgently consulted.

Given the seemingly unprovoked development of her AACG, a secondary review of medications and supplements was performed. While our patient initially denied using any new medications or supplements, upon further prompting and with use of a mobile identification app, she eventually endorsed starting cetirizine 5 days prior, left-over erythromycin ointment 4 days prior, and a homeopathic remedy by Similasan for “Pink Eye Relief” 2 days prior (Fig. 1). Upon review of the eyedrop’s ingredients, *Belladonna* 6×, *Euphrasia officinalis* (Eyebright) 6×, and Hepar Sulphuris 12× were identified as key active ingredients (Fig. 2). She was advised to inform her ophthalmologist about the belladonna-containing eye drops and was discharged from the ED for an immediate outpatient ophthalmologic evaluation.

3. Discussion

A. belladonna, also known as deadly nightshade, is a plant containing multiple alkaloids including atropine, hyocyamine, and scopolamine [1]. Atropine and these other alkaloids have potent antimuscarinic effects, including cycloplegia and mydriasis. In fact, *A. belladonna* translates to “beautiful woman” and historically was applied topically for its eye-dilating properties which were viewed as aesthetically pleasing [2]. Today, atropine has many FDA approved uses, most notably for certain bradyarrhythmias, organophosphate poisoning, and varying ophthalmologic uses.

AACG is a sight-threatening condition that requires a high degree of clinical suspicion and rapid action to prevent vision loss in the affected eyes. Medications known to cause acute angle closure crisis include a myriad of drug classes, including adrenergic agonists, anticholinergics, cholinergics, histamine antagonists, among many others [3]. Previous reports of over the counter (OTC) substances precipitating AACG have been described including ma-huang (ephedra) and pseudoephedrine [4,5]. Similasin eye drops have been described in a case of anisocoria; however, to our knowledge, this is the first description of AACG secondary to an OTC eyedrop containing belladonna [6]. Systemic belladonna use causing bilateral AACG from an OTC cold and flu remedy has also been reported. Similar to the Similasin eyedrops, there was no product warning describing the possibility of AACG [7].

Assessing potential drug-related adverse events can be a complex issue and while validated scales may not always be helpful, some individual elements may be useful in determining the association of drug and reaction. While there has been evidence that belladonna can cause this reaction and the adverse event appeared after the suspected drug (OTC homeopathy eye drops) was administered, our lack of follow-up for the patient would still yield a possible/probable reaction on the Naranjo probability scale [7,8]. This is particularly true considering that cetirizine is generally considered to have minimal anticholinergic activity, albeit the literature does not reveal reported cases of AACG related to cetirizine. Additionally it is unknown whether the patient used the drops equally in both eyes, but it is notable that the tonometry was asymmetrical.

Our study is unique in that our patient did not initially disclose her use of OTC homeopathic eyedrops because she did not perceive them as pharmacological therapy. Only after detailed retroactive history-taking was it discovered that she had been using eyedrops containing belladonna. While the exact amount of belladonna should have been very small, OTC supplements and medications do not require FDA regulation and without standardized manufacturing processes could have been greater than the concentration on the label implies. Our study highlights the danger of allowing products with physiologically active components to be freely sold.

4. Conclusion

Homeopathic treatments are non-regulated for safety and effectiveness and widely accessible OTC. Most patients and clinicians assume they are benign and do not appreciate their potential for causing significant harm. This case highlights AACG, a serious adverse effect, associated with the use of belladonna-containing eye drops. The etiology was identified by performing a more thorough history of the patient’s medications. It is imperative to always review home medications with patients including OTC as it may provide useful clinical information.

<p>Drug Facts</p> <p>Active ingredients ... Purpose Belladonna 6X[†]dryness, redness, burning, sensation of grittiness Euphrasia officinalis (Eyebright) 6X watery discharge Hepar sulphuris 12X redness, stinging</p>	<p>Warnings (cont.)</p> <ul style="list-style-type: none"> To avoid contamination use within 30 days of opening. Expiration date only refers to unopened bottle. Replace cap tightly after every use. Our drops will not harm contact lenses, however we recommend not wearing contacts while experiencing eye irritation. 	<p>Directions</p> <p>For adults and children ages 2 and over:</p> <ul style="list-style-type: none"> remove tamper-evident seal from neck of bottle twist cap off bottle DON'T squeeze bottle, squeeze plastic tip to release 1 to 2 drops into eye apply as needed replace cap after use 
<p>Uses*</p> <p>According to homeopathic principles, the active ingredients in this product temporarily relieve minor eye symptoms:</p> <ul style="list-style-type: none"> excessive watery (clear) discharge sensation of grittiness redness and burning 	<p>If pregnant, trying to get pregnant or breast feeding, ask a health professional before use.</p> <p>Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.</p>	<p>Other information</p> <p>Active ingredients are manufactured according to homeopathic principles.</p>
<p>Warnings</p> <ul style="list-style-type: none"> For external use only. Children under 2 years of age should be seen by a physician. According to homeopathic principles, symptoms may temporarily worsen before improving (Initial exacerbation of symptoms). To avoid contamination, do not touch the tip of the bottle to any surface. 	<p>Do not use:</p> <ul style="list-style-type: none"> if the solution changes color or becomes cloudy <p>Stop use and ask a doctor if:</p> <ul style="list-style-type: none"> you experience eye pain or changes in vision symptoms worsen or persist for more than 72 hours you might have a serious underlying medical cause for an infection 	<p>Inactive ingredients</p> <p>Borate buffer, Purified water, Silver sulfate (as preservative), Sodium nitrate</p> <p>Questions?</p> <p>Reach our representatives at 1-800-240-9780 or getinfo@similasanusa.com. www.SimilasanUSA.com</p>

[†]containing 0.000002% alkaloids calculated as hyoscyamine

*These statements are based upon traditional homeopathic principles. They have not been reviewed by the Food and Drug Administration.

Fig. 2. Drug Facts of Similasan “Pink Eye Relief” eyedrop. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Author contributions

All authors provided substantial contributions to manuscript content. All authors gave final approval of the version of the article to be published.

Declaration of Competing Interest

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