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CASE REPORT



A Case Report of Acute Bilateral Mydriasis Induced by Herbal Medication

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ABSTRACT

Ma Huang (*Ephedra*), a traditional herbal remedy, which contains pseudoephedrine and ephedrine, has sympathomimetic characteristics. Despite being banned by the Federal Drug Administration in 2004, it is still used for weight loss and energy boosting in some countries. A previous healthy 42-year-old woman experienced sudden blurred vision in both eyes. Her pupils were dilated to 6 mm each, showing diminished light reflex responses, and were not responsive to both 0.1% and 1% pilocarpine. The day before the onset of her symptoms she had taken a herbal supplement. The woman's herbal medicine was believed to contain ephedrine, a component found in Ma Huang. The sympathomimetic effects of this substance could potentially induce mydriasis. After discontinuing the medication, her symptoms improved over 4 days, leading to a suspicion of drug-induced bilateral mydriasis. Herbal products prescribed for weight loss, which may contain potential elements such as Ma Huang, could lead to unforeseen side effects like bilateral mydriasis, and should be appropriately highlighted.

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Introduction

The pupil regulates the amount of light exposure to the retina to facilitate clear vision across varying distances.^{1,2} To achieve this, the diameter of the pupil adjusts flexibly between 2 and 10 mm, via the light and accommodation reflexes, through precise autonomic innervation.^{1,3} The parasympathetic pathway, responsible for pupillary constriction, originates in the dorsal midbrain, activates both Edinger-Westphal nuclei, and its fibers journey via the oculomotor nerve to synapse in the ciliary ganglion before ultimately reaching the pupillary sphincter through the short ciliary nerves.¹⁻³ Conversely, the sympathetic pathway, leading to pupillary dilation, involves a three-neuron system. The first neuron is located in the paraventricular and arcuate nuclei of the ipsilateral hypothalamus, the second forms the ciliospinal nucleus of Budge, while the third is connected to the superior cervical (stellate) ganglion near the carotid bulb.¹⁻³ Bilateral mydriasis typically arises when sympathetic innervation exceeds parasympathetic innervation. This is frequently associated with systemic

disorders such as Fisher syndrome or botulism, specific pharmaceutical agents, midbrain lesions (specifically in the pretectal area and third nerve nuclei), bilateral tonic pupils, iris ischaemia due to vasculitis or atherosclerosis, or a condition known as autoimmune autonomic ganglionopathy.³

Ma Huang (*Ephedra*), a traditional herbal remedy which contains pseudoephedrine and ephedrine – substances structurally similar to amphetamine – has sympathomimetic characteristics. Despite being banned by the Federal Drug Administration (FDA) in 2004, it is still used for weight loss and energy boosting in some countries.⁴ Apart from causing minor and temporary weight loss, this herbal medicine has been linked to a range of serious health hazards such as hypertension, cardiac arrhythmias, seizures, stroke, sudden death, angle-closure glaucoma, and bilateral acute myopia.^{4,5}

We present a case of sudden onset bilateral mydriasis after consumption of a herbal supplement, suspected to contain Ma Huang. This case emphasizes the importance of careful

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consideration when using herbal supplements, as they can potentially lead to unpredictable side effects, such as bilateral mydriasis.

Case report

A 42-year-old woman presented to the emergency department after experiencing a sudden onset of painless blurred vision in both eyes that had commenced the day before her visit. She had no known chronic illnesses, nor were there any accompanying symptoms such as headaches, ptosis, double vision, ocular pain, or visual field defects. She had no prior history of eye surgeries or recent trauma. Interestingly, the day before her symptoms began, she had taken a herbal supplement that had been prescribed 4 years ago, although she had not used the medicine until then. There was no history of rubbing the eyes with the hand that touched the medication or using a scopolamine patch.

On initial assessment, her visual acuity was normal in both eyes. However, in dim and dark conditions, both pupils were dilated to 6 mm, with diminished light reflex responses observed. There were no signs of conjunctival congestion or eyelid swelling, and her eye movements were normal. Other cranial nerve and sensory motor

examinations were also within normal limits and deep tendon reflexes were normal in all four limbs.

After applying 0.1% pilocarpine, both eyes showed no pupillary constriction, and this lack of response also persisted after 1% pilocarpine was administered to both eyes (Figure 1). The cerebrospinal fluid analysis demonstrated normal cell count and protein and glucose levels. Other tests, including rheumatoid factor, antinuclear antibody, anti-double stranded deoxyribonucleic acid antibody, anti-SS antibody, anticardiolipin IgG/IgM, thyroid stimulating hormone, free T4, anti-aquaporin 4 antibody, anti-myelin oligodendrocyte glycoprotein antibody, anti-GQ1b antibody, oligoclonal bands, and IgG4, all returned normal results. Brain magnetic resonance (MR) imaging and MR angiography conducted on the same day did not reveal any abnormalities.

She was diagnosed with bilateral mydriasis, suspected to be caused by her consumption of the herbal supplement, which likely contained sympathomimetic substances such as *Ephedra*. After starting intravenous hydration therapy, her condition showed improvement a day after the treatment began. Four days following the onset of her symptoms, her condition had notably improved, and her pupils returned to their normal size of 3.5 mm in each eye.

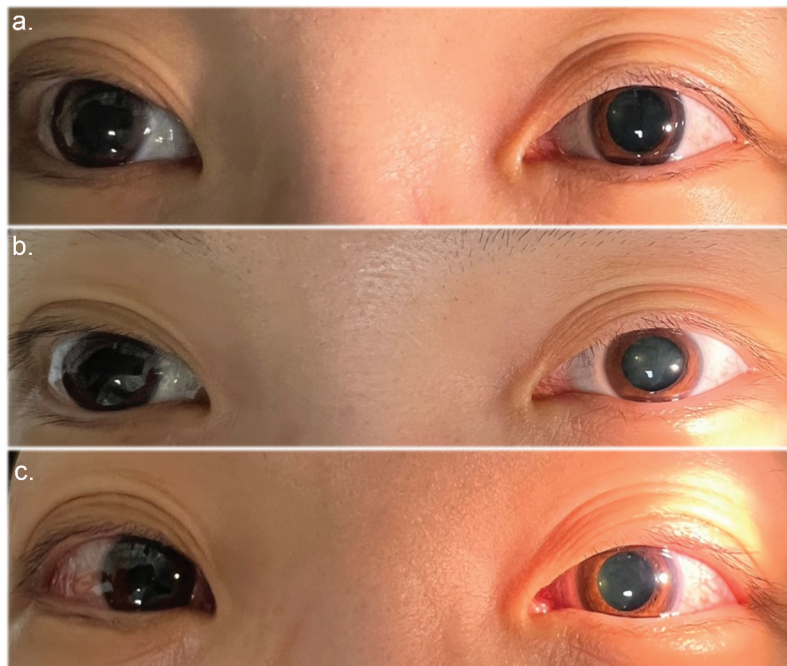


Figure 1. Our patient exhibited bilateral pupil dilation without any response to light stimulation (a). After applying 0.1% pilocarpine, both eyes showed no pupillary constriction (b), and this lack of response also persisted after 1% pilocarpine was administered to both eyes (c).

This study was conducted in accordance with the principles of the Declaration of Helsinki, and the patient provided written informed consent.

Discussion

Our patient's main symptom was an abrupt onset of bilateral, painless blurred vision. The absence of any other neurological symptoms, except dilated pupils, combined with normal brain MR imaging results, effectively ruled out brainstem lesions caused by vascular, inflammatory, or tumor-related conditions. The lack of a recent history of infection, and the absence of additional neurological symptoms such as ataxia, external ophthalmoplegia, areflexia, along with a negative anti-GQ1b antibodies test, further excluded the possibility of systemic diseases such as Fisher syndrome.⁶ Botulism, a severe disease caused by toxins inhibiting acetylcholine release at voluntary motor and autonomic cholinergic neuromuscular junctions, was dismissed due to absence of consuming causative contaminated food, a normal autonomic nervous system otherwise and lack of ophthalmoplegia and weakness.⁷ Autoimmune autonomic ganglionopathy was also considered less likely due to the lack of symptoms such as significant orthostatic hypotension, fainting, constipation, urinary retention, and dry mouth and eyes.⁸ Instead, the isolated dilated pupils with lack of response to both diluted (0.1%) and undiluted (1%) pilocarpine suggested pharmacologically mediated mydriasis.² The sudden onset of symptoms within a day of consuming the herbal medicine further substantiated the hypothesis of a pharmacological cause. Given the supposed weight loss benefits of the medication and the commonality of region-specific traditional herbal medicine formulas in various Eastern countries, Ma Huang (*Ephedra*) was suspected to be the pharmacological agent in question.⁴

Ephedra sinica, an herb with over 5000 years of usage history in traditional Chinese medicine, has been commonly used to alleviate symptoms of conditions such as asthma, bronchitis, and hay fever. Due to its purported weight loss effects and the somewhat relaxed regulations around health supplements, *Ephedra* is still extensively used in herbal medicines. This trend is also observed in Korea, where *Ephedra* is commonly prescribed as

a traditional herbal medicine for weight loss and exercise enhancement. In the United States of America *Ephedra* has been marketed as a dietary supplement for weight loss and has been linked to several serious cardiovascular and central nervous systems adverse effects.^{9–13} These side effects range from mild symptoms such as irritability, anxiety, insomnia, headache, nausea, vomiting, and urinary problems to severe complications such as high blood pressure, rapid or irregular heartbeat, stroke, seizures, hepatotoxicity,^{14,15} neurotoxicity,¹⁶ and transient blindness.¹⁷ Due to its unreasonably high risk of causing illness or injury, the FDA banned the use of *Ephedra* in dietary supplements in 2004, except for specific indications such as asthma, chronic cough, and headache.^{4,12,13,18} Earlier pharmacological studies revealed that ephedrine, the primary active component of *Ephedra*, can cause pupil dilation without blocking the pupillary light reflex when applied directly to the conjunctiva or introduced into the bloodstream.^{12,13,19–21} Subsequent studies on various animals and humans discovered that ephedrine not only strengthens the tone of the dilator muscle but also reduces the tone of the sphincter muscle.^{18,20,22} It was further suggested that ephedrine's effects are primarily directed at the nerve endings, rather than the receptive mechanism.^{18,22}

A question arises about whether other mydriatic agents, aside from ephedrine present in the *Ephedra*-containing dietary supplements, could have potentially contributed to the observed pupil dilation in our case. Several findings have indicated the potential for ephedrine to naturally convert into amphetamine analogues via a straightforward single-step process, which could also lead to mydriasis.²⁰ Additionally, various amphetamine analogues have been detected in the *Ephedra* genus.²³ Moreover, it is plausible that in the 1-year-old herbal supplement that induced the symptoms, ephedrine could have chemically transformed into other closely related sympathetic stimulants, thereby emphasizing the importance of caution.

Herbal weight loss products captivate consumers due to their health-promoting claims, presumed safety, easy accessibility, and extensive advertising. However, these products can greatly vary in their composition, having uncertain concentrations of active compounds and possibly harmful effects.

Table 1. Potential diagnosis of bilateral mydriasis and the response to instillation of pilocarpine eye drops.

Potential diagnosis of bilateral mydriasis	
Pupils constrict with pilocarpine eye drops	Miller-Fisher syndrome
	Botulism
	Midbrain lesions (pretectal area, third nerve nuclei)
	Bilateral tonic pupils
No response to pilocarpine eye drops	Autoimmune autonomic ganglionopathy
	Pharmacological agents
	Sympathomimetic agent (amphetamine, cocaine, dopamine, nicotine, LSD)
	Anticholinergic agent (antihistamine, atropine, carbamazepine, glutethimide, TCA)
	Iris ischaemia due to vasculitis or atherosclerosis

LSD = lysergic acid diethylamide; TCA tricyclic antidepressants.

They might include severely toxic herbs such as *Aristolochia* species, powerful herbs not recommended for weight control such as *Ephedra sinica*, and herbal laxatives that can potentially harm the liver and kidneys such as anthraquinones. Notably, these herbs' presence may not always be revealed on the product's labeling.

This case illustrates reversible bilateral mydriasis, potentially resulting from the ingestion of a weight-loss herbal supplement believed to contain Ma Huang, which could potentially be misdiagnosed (Table 1). It is crucial that physicians and other healthcare practitioners be aware of the problem.

They need to advise their patients regarding the diverse nature of these compounds and the potential risks tied to their use. Particularly, herbal products prescribed for weight loss that might contain potential ingredients like Ma Huang must be flagged for possible side effects, such as bilateral mydriasis.

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Disclosure statement


The authors declare the research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

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Author contributions

Y-EK, JC, TTN, and J-JK wrote sections of the manuscript. S-YO supervised and contributed to the study concept and revised the manuscript. All authors read and approved the submitted version.

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