Case Report

Topical Atropine Induced Acute Psychosis - A case report

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ABSTRACT

Introduction: Atropine, an anticholinergic agent is widely used topical agent in ophthalmology practice. We present a case report on central anticholinergic syndrome in a patient receiving topical atropine.

Case and observation: An eighty-two years old female who had received a penetrating keratoplasty five years ago in the left eye for non-healing corneal ulcer which had failed within 6 months presented with long standing pain in the eye. She was on topical carboxymethylcellulose 1% and moxifloxacin since the last two weeks and was against the advice for evisceration. We used 1% atropine sulphate eyedrops thrice daily for persistent pain of the left eye. Three days after using topical atropine, she developed acute psychomotor agitation, disorientation, confusion and lack of insight with visual hallucination and lowered level of consciousness. These symptoms resolved after cessation of topical atropine and reappeared on its use. A single dose rechallenge under the supervision of a psychiatrist confirmed that the acute psychosis was induced by topical atropine. The reaction was definite according to Naranjo's algorithm.

Conclusion: The present case shows that a patient on topical atropine can experience central nervous system side effects seen with systemic absorption. The possibilities of such side effects warrants discussion in patients receiving the medication in routine ophthalmology practice.

Keywords: Acute psychosis, Central anticholinergic syndrome, Topical atropine

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INTRODUCTION

Topical atropine is used in uveitis, early amblyopia, myopia, neovascular glaucoma & malignant glaucoma and post cataract surgery. Atropine mainly causes side effects that are linked to its receptors in both the central and peripheral nervous systems. Central Anticholinergic Syndrome (CAS) occurs due to an absolute or relative inhibition of cholinergic neurotransmission and can show various signs and symptoms of CNS excitation or depression depending on the types of receptors involved at receptor site. Longo first described it in 1966. , Anticholinergic syndrome may manifest at the recommended therapeutic doses which may be due to the idiosyncrasy.

Generally, clinicians usually associate central anticholinergic syndrome (CAS) with parenteral route. However we report an uncommon case of an elderly woman who developed acute psychotic symptoms after using a topical atropine preparation.

CASE REPORT

An eighty two year old female presented to us with a long-standing pain in her left eye. The eye had received penetrating keratoplasty five years ago for non-healing corneal ulcer. The graft failed within 6 months. She was on topical Carboxymethylcellulose 1% and Moxifloxacin 0.5% since the last two weeks (prescribed in other institute) and was against the advice for evisceration.

On examination, her BCVA in the right eye was 6/9 and she had no perception of light in the left eye, lid and other adnexal structures of both the eyes were normal, corneal examination showed arcus senilis in the right eye while the cornea in the left was total white opaque with superficial & deep vascularization along with the central thinning of the graft (impending perforation). There was PCIOL in the right eye, pupil was round, regular & reactive, fundus evaluation didn't reveal any significant findings while on the left eye posterior segment evaluation

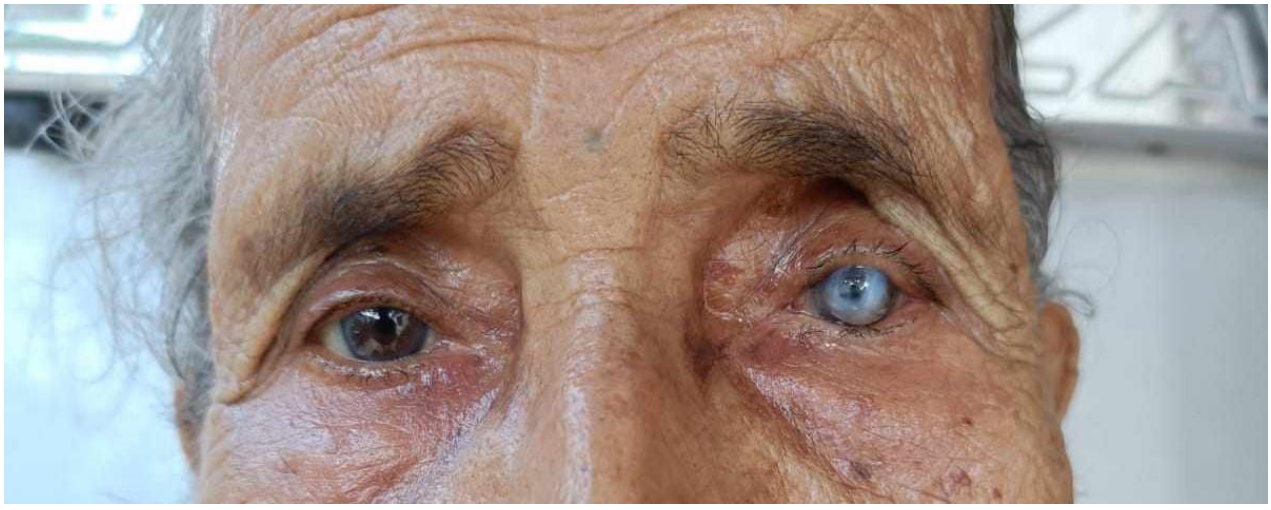

Fig: shows the patient's left non seeing eye in which she had no perception of light, cornea was totally white opaque along with superficial and deep corneal vascularization and impending perforation.

couldn't be done. On USG B-scan of the left eye, no significant pathology was seen. After thorough examination, she was advised atropine sulfate 1% eye drops thrice daily for persistent pain.

She was brought to the clinic three days later by her family after they noticed episodes of agitation, abnormal flow of speech and behavior with lowered level of consciousness. She was not well oriented to her surroundings. According to her guardian, who happened to be a medical doctor himself, these symptoms were noticed only after application of atropine eye drop, persisted throughout the night and fluctuated in intensity when eye drop was reapplied. She had no history of associated medical illness and substance abuse. There was no personal or family history of any psychiatric illness. All routine investigations including complete blood count, liver function test, renal function test, serum electrolyte, blood sugar, thyroid profile, urine routine examination, ECG, CT scan of brain, ultrasonography of abdomen and chest X-ray were normal.

Patient was thus referred for further psychiatric evaluation which revealed acute psychomotor agitation, disorientation, confusion and lack of insight with visual hallucination. Similar episodes were noted on previous two prescriptions with atropine as well. General and neurologic examinations did not reveal any other additional abnormalities, except for the neuropsychiatric abnormalities described above.

After a brief literature review and consultation with the psychiatrist, the possibility of atropine-induced acute psychosis from topical application was taken into consideration and it was discontinued immediately. The symptoms then improved dramatically over the next 10-12 hours. A single dose rechallenge was also attempted after the consent with the guardian. It was observed that the patient's symptoms worsened within a day and improved over the next day after stoppage. Atropine sulphate 1% eye drops of two different pharmaceutical company was used for confirmation of rechallenge.

The Naranjo Algorithm, or Adverse Drug Reaction Probability Scale Score was found to be 9 which corresponds to definite adverse reaction (acute psychosis) following use of topical atropine sulphate 1% eyedrops.

DISCUSSION

The role of atropine as a causative agent in acute confusional states and psychosis was first mentioned in in 1935 by Melivier. Listwan and Whealy (1953) described the characteristic mental symptoms of atropine intoxication as a confusional state with vivid visual hallucinations, restlessness, muscular incoordination, and later-increased emotionalism with a short period of retrograde amnesia.

It is well known that atropine may produce delirium in addition to its characteristic autonomic effects, and that in certain sensitive subjects these effects will arise with normal pharmacological doses. On the other hand, it is less well known that atropine can produce delirious states with minor or absent peripheral signs of intoxication and that severe mental reactions can follow routine instillation of atropine eye-drops.

In our case, delirium associated with hyperactive state is suggestive of central muscarinic receptors involvement. We see temporal correlation between the use of topical atropine eye-drops and the onset of delirium which was further validated by a rechallenge. The symptoms improved after discontinuing the eye-drops; suggesting an association of delirium with topical atropine eye-drops usage in our case.

Mechanism of delirium due to atropine is still not clear. Evidence suggests that acetylcholine acts as a neurotransmitter in pathways associated with arousal and awareness. Those drugs which contain tertiary amine, like atropine, can easily cross the blood-brain barrier. Atropine induced inhibition of acetylcholine mediated impulses might be a reason for delirium. Atropine toxicity depends on the route of administration, duration, exposure, drug interaction and dosage. Delirium caused by atropine is mainly related to its toxic plasma concentration level (10 - 20 mg)

Previous literature indicates that 30%–80% dose may enter the general circulation after conjunctival instillation. Eye drops can be absorbed by capillaries and reach the brain through the angular veins of the deep cerebral veins and cavernous sinuses. When applied topically, they are well absorbed, entering both the eye and systemically. This is because both the conjunctiva and nasal mucous membranes are excellent surfaces for drug absorption, and eye drops easily pass through the nasolacrimal duct into the nose. , Topically instilled atropine is rapidly absorbed in both adults and children. The peripheral signs and symptoms of atropine poisoning might vary and can go unnoticed.

To minimize systemic absorption and toxicity, consider using the lowest concentration of the medication available. Do not exceed the recommended number of drops. For example, instill one drop of 0.5% or 1% in the eye, followed by another drop of 0.5% or 1% after 5 minutes if necessary. Additionally, occlude the lacrimal passage (punctum) after topical administration, and blot away any excess drops after administration. It's important to gently and quietly close your eyelids for 3 min after drug instillation. You can also decrease the size of eye dropper tip, employ drug suspensions instead of drug solutions along with the use of a preceding local anesthetic such as proparacaine to enhance the effect of drugs by increasing trans corneal absorption.

The present case emphasizes the significant central nervous system side effect of a topically administered atropine. It's important to understand all the negative impacts of the medication so that early detection and the best possible treatment can be provided. The drug should be used judiciously in the prescribed amount and techniques to minimize systemic absoprtion decrease absorption into the body and prevent further harm to the patient.

Therefore, care must be taken and clinician should remain vigilant while prescribing topical atropine to elderly and as well as small children. Also, it would be wise to counsel about such unwanted side effects to the patient and their guardian.

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