Uncontrolled Agitation and Flushed Face Due to Tropicamide: A Missed Diagnosis

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Introduction
Tropicamide is a well-known short-acting mydriatic and cycloplegic ophthalmic agent used in eye examinations and therapeutic applications in both adults and children. It is therefore widely used by clinicians. Tropicamide blocks muscarinic receptors in the peripheral and central nervous system and muscles, with actions similar to those of atropine. Adverse effects and toxicity associated with tropicamide occur because of its anticholinergic property. However, the anticholinergic syndrome may develop very rarely. Initially, the recognition of toxidromes by clinicians is essential for the treatment of the anticholinergic syndrome. We report a case of a child initially administered an antihistaminic agent for allergic drug reactions, with anticholinergic toxidrome induced by tropicamide.

Case Report
A 2-year-old boy presented to our pediatric emergency department with flushing of the face and uncontrolled agitation. Medical history revealed that the patient had been receiving eye drops containing 1% tropicamide at 10-min intervals for 1 h, 3 h before ophthalmologic evaluation. The patient’s mother noted that agitation occurred within 30 min of eye drop administration. The patient was currently under the care of our pediatric neurology department for epilepsy and cerebral palsy and was under a treatment regime of 5 mg/kg/day topiramate. It was also determined that the patient had been experiencing rhinorrhea and cough symptoms for 3 days but had no fever. Physical examination revealed that the body temperature was 36.7°C, pulse 120 beats/min, blood pressure 120/80 mmHg, and respiratory rate 30 breaths/min, with uncontrolled agitation, mydriasis in both eyes.

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participated in this case. Written informed consent was obtained from patient's parents who
toms were observed. The patient was discharged 6 days later.
proved. On the second day of observation, no anticholinergic symp-
tachypnea, breathing pattern, tachycardia, and body temperature had
administrated for sedation. Ceftriaxone and oseltamivir were admin-
ments were given due to shock, and midazolam (0.1 mg/kg) was
mydriasis, and phenylephrine and atropine-
side-effects related to topical eye drop administration may not be rec-
table 1. Features of the anticholinergic syndrome
<table>
<thead>
<tr>
<th>Central nervous system symptoms</th>
<th>Peripheral symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altered mental status</td>
<td>Tachycardia</td>
</tr>
<tr>
<td>Changes in mood (anxiety, fear, and euphoria)</td>
<td>Dry and erythematous skin</td>
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<tr>
<td>Hallucinations</td>
<td>Mydriasis</td>
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<tr>
<td>Ataxia</td>
<td>Dry mucosa</td>
</tr>
<tr>
<td>Seizures, coma, and death</td>
<td>Hyperthermia</td>
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<tr>
<td></td>
<td>Decreased bowel sounds</td>
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<td></td>
<td>Urinary retention</td>
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</tbody>
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cataract in the left eye, flushing of the face, dry oral mucosa, spas-
ticity in all extremities, and wheezing on both sides of the chest. Be-
cause drug-related side-effects or an allergic reaction to the eye drops were
the suspected causes of the symptoms, pheniramine maleate (1
mg/kg) and methylprednisolone (1 mg/kg) were administered, and
both eyes were washed with normal saline. After 1 h, the patient's
symptoms deteriorated, with increases in body temperature (38.6°C),
pulse (210 beats/min), respiratory rate (56 breaths/min), and blood
pressure (80/50 mmHg) and a decrease in oxygen saturation (92%)
when breathing ambient air. Symptoms of the anticholinergic syn-
drome were observed, including respiratory distress, dryness of the
skin, decreased levels of saliva and sweat, eyelid depression, reduced
turgor pressure, urinary retention, and excessive agitation. Laboratory
examination revealed the levels of the following parameters: Hb 10.2
g/dL, white blood count 15,100/mm³, platelet count 454,000/mm³,
blood glucose 220 mg/dL, blood gas pH 7.05, pCO₂ 41 mmHg, pO₂
86.7 mmHg, HCO₃ 10.4 mEq/L, BE -17.4 mEq/L, and blood lactate 14
g/dL. Other biochemical parameters were normal. Sinus tachycar-
dia was revealed by electrocardiography. Chest radiography revealed
peribronchial thickening and perihilar lung consolidation.

Normal saline (20 mL/kg) was administered two times as a bolus and
then as an intravenous fluid at 2000 mL/m². Other supportive treat-
ments were given due to shock, and midazolam (0.1 mg/kg) was
administered for sedation. Ceftriaxone and oseltamivir were admin-
istered to combat the lung infection and to treat possible influenza,
and physostigmine was obtained for use if necessary, but was not
required. The patient was admitted to the pediatric intensive care
unit for further observation and treatment. At follow-up, the patient’s
tachypnea, breathing pattern, tachycardia, and body temperature had
recovered, and his anticholinergic symptoms had regressed. Addition-
ally, his metabolic acidosis and hyperlactatemia had dramatically
improved. On the second day of observation, no anticholinergic symp-
toms were observed. The patient was discharged 6 days later.

Written informed consent was obtained from patient’s parents who
participated in this case.

Discussion
Topical eye drops are widely used to facilitate cycloplegia and reti-

tal examination for mydriasis, and phenylephrine and atropine-
like agents are commonly employed agents. These agents can be
toxic when administered in high concentrations or at frequent
intervals and can pass into the systemic circulation through the
skin, nasal mucosa, cornea, conjunctiva, or aqueous humor (1, 2).
Life-threatening side-effects or death are rare, but are mostly seen in
infants or young children when they do occur. Atropine or atropine-
like drugs are competitor antagonists of acetylcholine that interact
with muscarinic receptors. Cases of anticholinergic poisoning follow-
ing the administration of topical eye drops containing atropine or
atropine-like substances have been previously reported (1, 3-5). When
a patient has nonreactive dilated pupils, tachycardia, flushed skin,
dry mucosa, hyperthermia, urinary retention, and changes in con-
sciousness, anticholinergic poisoning should be considered (3, 4, 6).
Decreased sweat levels, reduction in bowel sounds, visual and audi-
tory hallucinations, delirium, seizures, coma, and even death may also
represent part of the anticholinergic toxidrome (Table 1) (6). To the
best of our knowledge, no previous reports have described central
or peripheral anticholinergic effects with eye drops containing only
tropicamide in pediatric patients. Although antihistamine was given
because of the initial diagnosis of an allergic drug reaction, the pres-
ence of central and peripheral anticholinergic effects during the initial
reaction stages suggested systemic poisoning with tropicamide. No
drug–drug and drug–allergy interactions or content duplication be-
 tween topiramate, tropicamide, and pheniramine maleate have been
determined, and delirium and anticholinergic symptoms are not ex-
pected conditions in epilepsy and cerebral palsy (5). Considering all
the characteristics of our patient, we think that the case is compat-
ible with anticholinergic poisoning. Indeed, recognizing toxidromes
in the early stages of poisoning cases is essential. However, systemic
side-effects related to topical eye drop administration may not be rec-
ognized or may be ignored by the patient’s family or physicians. It is
therefore essential to know the signs and symptoms of the toxidrome
to begin appropriate treatment.

The use of physostigmine to treat anticholinergic intoxication is
controversial (7). However, if life-threatening conditions and severe
central nervous system dysfunction such as seizures, coma, or car-
diac involvement are observed, physostigmine may be useful. Phys-
sostigmine is a reversible anticholinesterase inhibitor in both the pe-
ripheral and central nervous systems. Physicians should be wary of
administering physostigmine to patients with asthma, ileus, epilepsy,
or dysrhythmia because it may exacerbate these diseases (7). Physo-
sostigmine is administered intravenously over 5 min at a dose of 0.04-2
mg/kg, which may be repeated after 10-40 min if necessary (8).

Conclusion
In this case, the patient was exposed to a higher than recommend-
ed dose of tropicamide in a short period of time. At a time, one or
two drops of tropicamide should be administered to each eyeball
while compressing the lacrimal duct to avoid systemic effects, and
this may be repeated after 5 min. The undesirable effects of tropi-
camide may be stronger because it is found in the same drugs as
cycloplegic agents. Therefore, mydriatic eye drops should be used
for ophthalmological examination or any other procedure at the
appropriate dose and under the supervision of an ophthalmologist.
Informed Consent: Written informed consent was obtained from patient’s parents who participated in this case.

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References