Physemata, dural, and peritonitis with kidney composed of the adventitia of the giant cell granulocyte was identified and peritonitis with kidney. Tissue stained with PAS stained tissues revealed marked ischemic necrosis, micro-abscess formation, foreign body giant cell reaction, and the infiltration of large and small vessels by numerous fungi with associated thrombosis. Sections of the paranasal sinuses revealed marked ischemic necrosis and histologic changes similar to those found in the kidney. There was local extension of fungi into the right temporal lobe with necrosis, thrombosis, and invasion of the superficial meningeal vessels. Autopsy also revealed micronodular cirrhosis, panlobular severe diffuse bilateral emphysema, perforated duodenal ulcer walled off by the gallbladder, and peritonitis with ascites (1500 ml).

**DISCUSSION**

We describe a case of disseminated zygomycosis diagnosed antemortem by fine needle aspiration, with rapid confirmation by enzyme immunoassay. A high titer 1:400 of antibody to Zygomycetes was detected. Based on the analysis of preliminary data by one of us (L. K.), the titer noted (1:400) is considered a presumptive diagnosis of zygomycosis. The portal of entry was most likely the upper respiratory tract with hematogenous dissemination to the kidneys with infarction of the right kidney. Direct extension from the lesions in the paranasal sinuses resulted in intracranial lesions. There was extensive hemosiderin laden macrophages and free hemosiderin in the lungs bilaterally, the result of the propensity of this organism to invade blood vessels with subsequent hemorrhage and infection. Enzyme immunoassay provided a rapid noninvasive method for the diagnosis of zygomycosis.

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**Anisocoria and Aerosolized Anticholinergics**

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The use of aerosolized anticholinergics has not previously been emphasized as a cause of pharmacologic pupillary dilation. The diagnosis can be confirmed by instillation of 1 percent pilocarpine hydrochloride in the affected eye, thereby preventing needless neurologic studies and evaluation. We report one patient who had transient asymmetric pupillary dilation secondary to aerosolized anticholinergic treatment. Also, we looked at the incidence of the above complication in 40 outpatients who were treated for acute asthmatic exacerbation.

**DISCUSSION**

Discovery of a dilated and fixed pupil in the absence of clinical evidence of third nerve dysfunction can be alarming. The physician’s concern about possible intracranial neoplasm, aneurysm, or subdural hematoma often precipitates actions that lead to extensive neuroradiologic investigation. Pharmacologic dilation is often the cause of a fixed dilated pupil in a patient who has not sustained ocular trauma and who has no other complaint. We herein present a case report of chemical dilation of the pupil resulting from anticholinergic aerosol use. The increasing use of inhaled anticholinergics for the treatment of airflow obstruction prompted us to look at its incidence in our asthmatic patients.

**CASE REPORT**

A 35-year-old man with asthma presented to Grady Memorial Hospital (GMH) with increased shortness of breath. On arrival at the emergency room (ER), he was treated with ethylopropanol 0.3 ml s.q. ×3, metaproterenol aerosol 0.3 mg, atropine aerosol 3 mg×2, racemic epinephrine aerosol ×1, aminophylline 200 mg IV, and methylprednisolone 80 mg IV. Due to lack of improvement in response to the above medications, he was admitted for continuing intensive treatment. On arrival at the ward, his neurologic examination results were normal except for a right 7 mm pupil, unresponsive to direct or consensual light and convergence, and a left 3 mm pupil, normally reactive. There was no history of previous eye trauma.

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headache, or visual changes. His medication before admission consisted of oral sustained-release theophylline and terbutaline, and a metaproterenol metered-dose inhaler.

Computerized tomographic examination of the head with contrast medium appeared normal. Pilocarpine 0.125 percent (1/8 percent) was instilled in both eyes, with no response within 30 min. On discharge 48 hours later, the patient had bilaterally equal and reactive pupils.

In order to evaluate the frequency of temporary pupillary abnormalities induced by anticholinergic aerosol treatment, patients presenting to the ER asthma treatment room at GMH were examined. Over five consecutive days, 40 patients (21 females and 19 males, age range 16 to 72 years) were checked for pupillary size and reactivity to light before and after initiating treatment. Pupillary size was measured by holding a transparent ruler in front of each eye, barely touching the eyelashes. Patients with history of eye trauma or surgery or stroke were excluded. Also excluded were those using antihistamines and belladonna is commonplace. The atropine-like effect of anticholinergic aerosols is very common in the hospital setting. Over five consecutive days, seven patients had either pretreatment pupillary diameter, or pupils constricted by dilation without underlying neurologic disorder. Accidental rupture by trauma and adhesions may also produce reactive pupils.

Anisocoria, *en& was measured by holding a transparent ruler in front of each eye, barely touching the eyelashes. Patients with history of eye trauma or surgery or stroke were excluded. Also excluded were those using topical ophthalmic medications and those who had pupillary asymmetry before treatment. All patients received nebulized anticholinergics (atropine 3 mg or glycopyrrolate 1 mg) in combination with metaproterenol and/or ethylnorepinephrine aerosols. Twenty-four patients received only one anticholinergic aerosol treatment; ten received two treatments, and six received three treatments. All patients were examined within one hour after each treatment.

Seven patients had pupillary diameter and reactivity changes after treatment with anticholinergic aerosols. Three patients received atropine aerosols, three others received glycopyrrolate (Rubinol) aerosols, and one patient received both. Four patients had anisocoria, with either pupil being larger by >2 mm. Three patients had enlargement of both pupils, compared to pretreatment pupillary diameter. Also, pupillary constriction in response to bright light was either absent or sluggish in the affected pupils. Of the seven patients, five received three anticholinergic aerosol treatments, two received two treatments, and six were admitted to the hospital after failure to respond to conventional outpatient treatment. On discharge, they all had either pretreatment pupillary diameter, or pupils constricted by >2 mm, with a brisker reaction to light.

**DISCUSSION**

Direct contamination of the eye with anticholinergic agents is most often the cause for asymmetric pupillary dilation without underlying neurologic disorder. Accidental instillation of atropine is very common in the hospital population among nurses who are required to instill eye drops and inadvertently rub their eyes with their contaminated fingers. Anisocoria due to spray perfumes containing belladonna is commonplace. The atropine-like effect of antihistamines was reported by Delaney.

A well-described recent observation is the fixed dilated pupil resulting from contact with the motion sickness medication Transderm V, a scopolamine patch applied behind the ear.

Anticholinergic blockade may be easily demonstrated by failure of the pupil to constrict in response to application of 1.0 percent topical pilocarpine solution. Iris sphincter rupture by trauma and synechial adhesions may also produce failure to constrict. Trauma sufficient to generate post-traumatic mydriasis and failure to constrict in response to pilocarpine should not be overlooked by a careful observer. Lack of response of a dilated pupil because of iris ischemia with the sudden onset of high intraocular pressure is not uncommon. Once pressure has been reduced by medica-
tions, the pupil will constrict upon instillation of pilocarpine.

Anticholinergic aerosols are being used frequently for treatment of acute bronchospasm. Fixed dilated pupils as a complication of aerosol treatment has been infrequently reported before. There is a single report of nebulized ipratropium use causing acute glaucoma in a patient with pre-existing shallow anterior chamber. It is likely that acute glaucoma in that patient was caused by the topical effect of nebulizer solution escaping from the face mask, causing fixed dilated pupils.

The same authors had noticed fixed dilated pupils in one or both eyes in three other patients using ipratropium bromide via a nebulizer.

Neurologic deficit resulting from third nerve palsy will show pupillary constriction in response to application of 1.0 percent pilocarpine solution. Cholinergic supersensitivity, as usually seen in Adie's pupil, may first be ruled out by failure to constrict in response to administration of 2.5 percent topical methacholine or 0.1 percent pilocarpine solution. In “simple central” anisocoria, there is no sign of third nerve lesion, and both pupils constrict to light.

While atropine enters the circulation when applied to the mucosal surfaces of the body, ipratropium, a quaternary derivative of atropine and Rubinol, has minimal mucosal absorption. Thus, the presumed mechanism of pupillary dilation is direct contamination rather than systemic effect. This would also explain the unilateral involvement in most cases.

All of the patients who had pupillary changes received more than one treatment. This may be a cumulative dose effect or increased risk of inadvertent droplet contamination with repeated treatment. It is important to be aware that pupillary dilation may last up to three weeks.

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