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Acute progressive midbrain hemorrhage after topical ocular cyclopentolate administration

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Cyclopentolate is a synthetic anti-cholinergic agent widely used in ophthalmology clinics. It can cause cardiovascular side-effects such as hypertension, ventricular arrhythmias and tachycardias. A 55-year-old male lost his consciousness after topical cyclopentolate hydrocloride (1%) administration for routine fundoscopic examination in another center. An urgent cranial magnetic resonance imaging examination revealed a midbrain hemorrhage and he was transferred to our hospital. The Glasgow Coma Scale score was at 4 points at admission. The patient was transferred to the intensive care unit and mechanically ventilated. Despite vigorous medical treatment, spontaneous respiration and brainstem reflexes disappeared 12 h after his administration. A control cranial computerized tomography showed enlargement and opening of the hemorrhage into the ventricular system. The patient died on the 12th day of his administration. Systemic side-effects of topical ocular cyclopentolate administration and prevention methods were discussed with regard to the current literature.

Key words: Cyclopentolate, midbrain hemorrhage, systemic anticholinergic toxicity

Spontaneous brainstem hemorrhages account for approximately 9% of all intracerebral hemorrhages.^[1] Most of the brainstem hemorrhages are located in the pons with a predilection to basis pontis and tegmentum, on the contrary, midbrain is involved infrequently.^[2] Cyclopentolate is a synthetic anti-cholinergic agent widely used in ophthalmology clinics for its powerful mydriatic and cycloplegic activity. Although rarely reported in the literature, cyclopentolate can cause cardiovascular side-effects, subconjuctival hemorrhages, skin flushes and behavioral changes.^[3] We present a patient with massive brainstem hemorrhage after topical use of cyclopentolate.

Case Report

A 55-year-old male patient with a previous history of hypertension and diabetes mellitus was transferred to our

hospital due to acute loss of consciousness secondary to an acute midbrain hemorrhage. Topical cyclopentolate hydrocloride (1%) eye drops were administered to the patient for routine fundoscopic examination in another center. A total of six drops (three drops in each eye) with a drop size of 30μ l were applied in a 30-min time period. A few minutes later, the patient started feeling dizzy and developed a severe headache and vomiting. His blood pressure was measured 240/150 mmHg in this period and he was given 50 mg captopril for anti-hypertensive medication. However, the patient lost consciousness. An urgent cranial magnetic resonance imaging examination revealed a midbrain hemorrhage of 16 × 18 mm and nodular contrast enhancement suggesting a cavernous angioma in the midbrain [Figure 1a, b]. At the time his blood biochemistry was normal except the high blood glucose level (211 mg/dl). He was intubated and transferred to our hospital a few hours after the event. Neurological examination of the patient in our emergency room revealed minimal extensor motor response to central painful stimuli with preservation of superficial spontaneous respiration and brainstem reflexes. His Glasgow Coma Scale score was recorded as 4 points. The patient was transferred to the intensive care unit and had to be ventilated mechanically. Despite vigorous anti-hypertensive and anti-



Figure 1: Acute hematoma in the midbrain with a thin rim of hypointensity in the periphery and surrounding high-intensity edema on axial T2-weighted image (a) and intravenous Gadolinium enhanced axial T1-weighted image showing nodular contrast staining suggesting a cavernous angioma in the midbrain (b)

Tarkan Calisaneller

Baskent Universitesi Hastanesi, Beyin Cerrahisi B-blok zemin kat, Hoca Cihan Mahallesi, Saray caddesi, No. 1 Selcuklu/Konya, 42080 Turkey. E-mail: tarkan_ca@yahoo.com edema treatment, spontaneous respiration and brainstem reflexes disappeared 12 h after his admission and cranial computerized tomography showed enlargement and opening of the hemorrhage into the ventricular system [Figure 2]. The patient did not respond to medical treatment and died on the 12th day of his admission.

Discussion

Non-traumatic primary midbrain hemorrhages are rarely reported in the literature and predominantly seen in males (55%) and in the middle-older ages.^[1,4] Hypertension (26%), vascular malformations (35%) and bleeding disorders (5%) are the best-known etiological factors, though it is not always possible to identify a specific etiology.^[1,4] Prognosis in brainstem hemorrhages is related to age, hematoma size, medical history and consciousness level.^[5] Surgical treatment is indicated only in selected cases and most authors advocate medical treatment.^[1,5]

Cyclopentolate is used in ophthalmology for its strong mydriatic and cycloplegic activity. Although only the topical effect of the drug is desired, the passage through the naso-lacrimal duct to highly vascular nasal mucosa and transconjuctival absorption may cause systemic toxicity. The side-effects of cyclopentolate are due to anti-cholinergic toxicity and they are well documented in the literature. These side-effects include hypertension, tachycardia, ventricular extra-systoles, subconjuctival hemorrhages, skin reactions, psychological changes and anaphylaxis.^[3,6,7] Central nervous system toxicity including hallucinations, cerebellar signs and seizure is due to anticholinergic action causing stimulation of the medulla and/or cerebral centers and usually occurs within 20-30 min of administration.^[3,8-10]

These adverse reactions appear to be dose-related and are more frequent among children with high concentrations of cyclopentolate, but have also been described in adults receiving normal doses.^[3,7] Systemic absorption of topical ocular drugs occurs mainly via te nasal mucosa,



Figure 2: Axial brain CT reveals increased hematoma size in the midbrain with intraventricular extension

as approximately 80% of the drops pass through the nasolacrimal duct. Several methods have been proposed to decrease the systemic absorption such as wiping the excess fluid off the cheek after instillation, occlusion of the nasolacrimal system for 3-4 min and using of microdrops (5 μ l) instead of normal drops (30 μ l).^[11-12]

In our patient, the etiology of the brainstem hemorrhage could be either the spontaneous bleeding from a cavernous angioma or topically administrated cyclopentolate could induce a sudden increase in blood pressure and due to degenerative effects of chronic hypertension and diabetes mellitus; this acute raise in the blood pressure could have triggered the brainstem hemorrhage. Although the presence of the brainstem hemorrhage together with the application of topical ocular cyclopentolate might be a coincidence, the probability score for adverse drug reaction (ADR) based on Naranjo's algorithm (Score of >9 = definite ADR, 5-8 = probable ADR, 1-4 = possible ADR, 0 =doubtful ADR) for our patient was at 2 points suggesting a possible connection.^[13] To our knowledge, this is the only report of brainstem hemorrhage after topical ocular cyclopentolate administration. In conclusion, patients with systemic diseases should be given topical medications cautiously and possible systemic sideeffects of these drugs should be kept in mind.

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