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CLINICAL VIGNETTE

Cocaine Induced Acute Midbrain Infarction Presenting as Unilateral Ptosis

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A 20-year-old male, with no significant medical history, presented to the emergency department (ED) with obvious drooping of his right eyelid. He recalled being well when he went to bed the previous night and denied changes in visual acuity or diplopia. He did not report other associated symptoms, trauma, new medication, recreational drug use, or occupational exposures. His family and social history were unremarkable. On physical exam, his vital signs were normal, and he appeared to be in no distress. Evaluation of all the major organ systems was unremarkable. Meticulous cranial nerve testing revealed an isolated right eye ptosis and the inability to abduct his right eye beyond the midline. Extraocular movements of the left eye were intact. Direct and consensual light reflexes of both eyes were preserved. A bedside fundoscopic exam was also normal without evidence of retinopathy or optic disc anomalies. On leaving the room, his bedside nurse confided that the patient mentioned that he snorted cocaine with his friends the evening prior. In the ED, he had a non-contrast computed tomography (CT) scan of his head with contrast of his face, orbits, and sinuses, followed by a magnetic resonance image (MRI) with contrast of the neck and orbits which were all unremarkable. Blood work, including Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP) were within normal limits. Based on patient's age and risk factors our differential included intracerebral aneurysm, arterio-venous malformation or vasculitis. The imaging thus far had been negative and ruled out a hemorrhagic stroke, his painless, unilateral third nerve palsy without the involvement of other cranial nerves was unexplained and probably cocaine related. We felt the most likely localization to be intracranial, ipsilateral, distal to the nucleus, but above the subarachnoid space as no aneurysms were seen with normal venous sinuses, and no signs of meningeal infection. The possibility of an ischemic event in this area was not completely ruled out as scans had been limited to the orbit and below. Given our high clinical suspicion, the patient underwent a dedicated contrast enhanced (MRI) of his brain, which demonstrated a small infarct in his midbrain. Further evaluation for stroke included transthoracic echo, and additional inflammatory, autoimmune and hypercoagulable testing, which all returned negative. A final diagnosis of isolated complete oculomotor nerve palsy with pupillary sparing due to cocaine induced acute midbrain infarction was established.

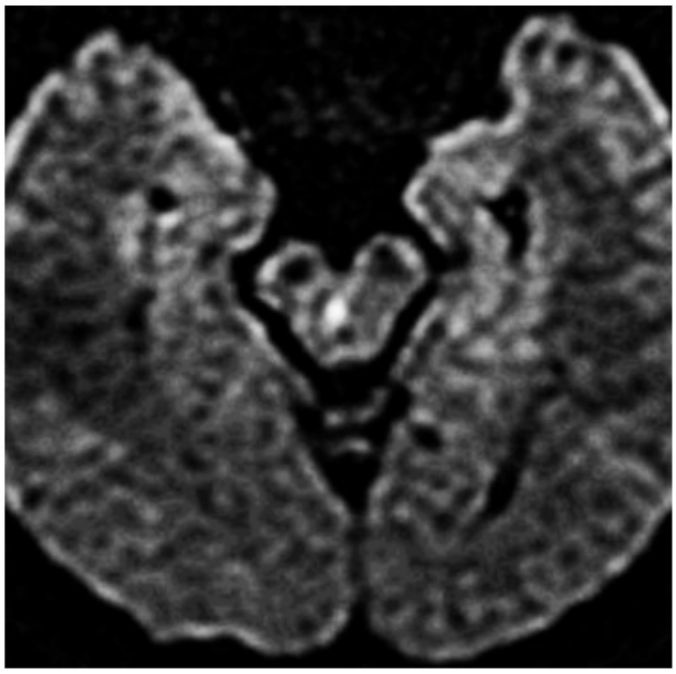
Discussion

The third cranial nerve innervates all extraocular muscles (except the lateral rectus and superior oblique), the levator palpebrae, the ciliary body, and pupillary constrictors.[1] It originates at the oculomotor nucleus, a paired structure located in the ventral border of the periaqueductal gray of the midbrain.[2] Fibers extend ventrally in the midbrain, crossing the medial longitudinal fasciculus, red nucleus, substantia nigra, and medial part of the cerebral peduncle. The nerve then courses between the posterior cerebral artery and the superior cerebellar artery to pass through the basal cisterns before piercing the dura as it enters the cavernous sinus. The nerve is divided into superior and inferior portions, with the superior innervating the superior rectus and levator palpebrae muscle. The inferior innervates the inferior oblique, inferior rectus, and medial rectus muscles and provides parasympathetic input to the pupillary constrictors.[2] Any lesions to this nerve lead to crossed syndromes of hemiplegia and ocular palsy. Complete lesions of the nerve manifest with the drooping of the upper eyelid (ptosis), rotation of the eye up, down, or in, and pupils that are non-reactive to light and accommodation as the parasympathetic fibers are compromised. Depending on the location and etiology of the lesion there are several different presentations. Usually, the nerve is impacted by tumors at the base of the brain, trauma, ischemic infarctions, or aneurysms. The less common presentations are due to Guillain-Barre syndrome, herpes zoster, vasculitis, migraine, carcinomatous or lymphomatous meningitis, infiltrative processes, myasthenia gravis, and Tolsa-Hunt syndrome. Commonly seen in diabetics (but also seen in other compressive processes) is infarction of the central portion of the nerve thus sparing the pupil due to the parasympathetic fibers being unaffected as they lie near the surface. If the pupil is enlarged this is a sign of an extramedullary lesion of the nerve.[3] Mid-brain infarctions as in our patient, are rare in stroke patients. Oculomotor fascicular lesions should be suspected when presented with pupillary and inferior rectus muscle sparing.[3] Our patient was eventually found to have an acute midbrain infarction in the setting of cocaine use. Interestingly, due to the midline and unpaired arrangement of the central caudal nucleus and the crossed and uncrossed composition of the fibers innervating the levator palpebrae, unilateral ptosis from a nuclear lesion is very rare.

Cocaine continues to be one of the most widely abused drugs in the United States. The national annual prevalence of cocaine use was 1.5% but as high as 5.8% for the 18–25-year-old age group depending on geographical location.[4] Statistics from the National Survey on Drug Use and Health showed that in 2015 968,000 people aged 12 or older used cocaine, which was a 26% increase compared to 2014 estimates. Young adults aged 18-25 were of particular concern and accounted for a large percentage

of new cocaine users.[5] Cocaine has long been associated with a wide spectrum of adverse health effects including strokes, cardiac arrhythmias, acute myocardial infarction, sudden cardiac arrest, convulsions, and death. Cocaine users have a four-to-eight-times higher mortality rate when compared to corresponding age groups in the general population. In the last two decades studies have reported a 19% increase in the incidence of strokes due to cocaine use. Cocaine associated stroke was first described in 1977 and since then has been reported in both anterior and posterior circulation territories. The actual mechanism of cocaine-associated stroke remains unclear however as many confounding risk factors such as hypertension, hyperlipidemia, amphetamine use, lifestyle and patient demographics have prevented definitive conclusions. Given that cocaine is commonly contaminated with substances including procainamide, levamisole, quinidine and antihistamines this further complicates the understanding of the pathophysiology underlying cocaine induced strokes.[6] Cocaine is also a potent central nervous system stimulant with multiple effects that predispose users to strokes by disrupting cerebral autoregulation and blood flow. These mechanisms include vasospasm, cerebral vasculitis, enhanced platelet aggregation and cardio-embolism.[6] Enhanced sympathetic activity due to inhibition of catecholamine reuptake at sympathetic nerve terminals is seen at lower doses of cocaine which results in tachycardia, hypertension and vasoconstriction.[7] Blockade of sodium and potassium channels is seen from higher doses of cocaine which results in depressed myocardial contractility and ventricular arrhythmias.[7] Cheng et al found that stroke was more likely in patients who have used cocaine more than once per week in the last year compared to controls as well as acute cocaine use in the previous 24 hours was strongly associated with increased risk of stroke.[7] Cardiogenic stroke or cryptogenic non lacunar stroke is the most common type of ischemic stroke among cocaine users. This study also highlighted those additional factors such as manner of ingestion, dose effect, and potential contaminants which make it difficult to fully understand the role cocaine plays in cerebrovascular events. However, via a variety of mechanisms, cocaine use continues to be a risk factor for stroke and thorough screening for cocaine use should be a part of the work up for stroke in a younger individual. Cocaine also contributes to a prothrombotic state by increasing platelet activation, platelet aggregation, platelet α-granule release, increasing plasminogen activator inhibitor activity and increasing levels of fibrinogen and von Willebrand factor.[8] Cerebral vasculitis results in inflammatory vasculopathy and vessel wall necrosis leading to potential vessel wall rupture and at the very least endothelial injury potentiating thrombosis formation. Cerebral vasculitis has been demonstrated in cocaine induced strokes as well as other drugs including amphetamines which is commonly mixed in cocaine preparations. A combination of cerebral vasoconstriction reducing the cerebral blood flow and oxygenation, its prothrombotic nature along with its arrhythmogenic potential all work together to create risk factors for ischemic stroke in cocaine users.[9]

Figures



MRI head axial diffusion-weighted scan showing the midbrain isolated periaqueductal signal abnormality slightly inclined to the right side where the oculomotor nucleus (ON) is located.

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