Stroke Following Cannabis Overuse

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PATIENT DESCRIPTION

A 57-year-old man with a history of moderate aortic insufficiency and no diabetes or hypertension was brought to the emergency department of Laniado Hospital, Netanya, by his girlfriend following a sudden frontal headache on waking, confusional state, and disorientation with regard to place, people, and time. His girlfriend reported that the patient was a regular recreational consumer of cannabis and that the preceding evening he had consumed more of the drug than usual. She denied that he had consumed any other illicit drugs. A physical exam indicated that the patient was conscious; disoriented with regard to place, people, and time; in no distress; and cooperative. His blood pressure at admission was 139/75 mmHg; his pulse was 52 beats per minute (b/m) and regular; and his body temperature was 36.7°C. He had a mild diastolic murmur over the left sternal border and his lungs were clear, with no peripheral motor or sensory focal deficit. There was no evidence of head trauma and his blood chemistry and complete blood count were normal. A urine test was positive for cannabis only and negative for other illicit drugs. An electrocardiogram revealed a sinus rhythm 56 b/m but was otherwise normal. His chest X-ray was unremarkable and within normal limits. An ophthalmologic consult documented findings suggestive of mild hypertensive retinopathy (Grade 1). A computed tomography (CT) scan of the brain with and without contrast material revealed a hypodense temporoparietal cortical area on the left side, suggestive of sub-acute stroke. The patient underwent a lumbar puncture. Analysis of the cerebrospinal fluid revealed that the patient had 3 erythrocytes/ml, 0 leukocytes, 61 mg/ml glucose, and 78 mg/ml protein. A molecular test for enterovirus was negative. An echocardiogram showed moderate aortic insufficiency and no evidence of the stroke being caused by an embolic source. An ultrasound study of the cervical arteries showed mild atheroma of the left external carotid artery.

The patient was treated with 100 mg/d of acetylsalicylic acid and simple analgesics for his headache. He underwent a second CT angiography 2 days after admission that produced approximately the same findings. The density had decreased further, the infarct area was the same size, and no bleeding was found. There was an impression of occlusion of the posterior cerebral artery. During his hospital stay, the patient had gradual but remarkable cognitive improvement and mild improvement in his headache. Four days after admission the patient was discharged with the recommendation that the low-dose acetylsalicylic acid treatment, low-dose angiotensin-converting enzyme (ACE) inhibitor, and tramadol for his headache all be continued.

COMMENT

Although cannabis has favorable effects on different neurological disorders, including neuropathic pain, Parkinson's disease, Tourette's syndrome, muscle spasms, and resistant convulsions [1,2], it also has potentially adverse neurological effects, especially with overuse. One of these adverse effects is acute stroke. A recent study from the United States that assessed national trends in hospitalization for major cardiovascular events (including strokes) among young cannabis users found that 52.3 million such patients were hospitalized between 2007 and 2014, excluding cases of concomitant substance [3]. The frequency of admissions for stroke was significantly higher among cannabis users compared to non-users (0.33% vs. 0.26%, $P < 0.001$) and rose 300% among cannabis users during this period compared to non-users.

In a review of 98 cannabinoid-related strokes, 85% were ischemic and 9% were hemorrhagic [4]. Patient mean age was 32.3 ± 11 years (range 15–63 years). The majority was male, and 81% were chronic cannabis users. Of the cannabis users, 18% had recently increased the amount of cannabis they consumed in the days before their stroke. In 46% of cases, the prognosis was favorable, but the mortality rate was 5%. One striking element reported by the majority of patients was the temporal relationship between their use of cannabinoids (whether natural or synthetic) and the occurrence of their stroke.

Cannabis-induced strokes are thought to be a result of reversible cerebral vasoconstriction. The reason for this vasoconstriction is not fully understood, and a minority of regular cannabis consumers experienced this adverse effect. One of the postulated mechanisms of the vasoconstriction is the generation of reactive oxygen species, which leads to oxidative stress, a known contributing factor for

strokes in humans [5]. Another brain insult that has been found to lead to ischemia is the induction of mitochondrial dysfunction.

In addition to its direct effects, cannabis may also cause orthostatic hypotension, increase blood pressure (specifically systolic blood pressure), and induce atrial fibrillation. All of these effects can eventually lead to central neurological symptoms and signs. More studies are needed on the causes of cannabis-related strokes.

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Trust is the first step to love.

Dhanpat Rai Shrivastava (1880–1936), better known by his pen name Munshi Premchand, Indian writer famous for his modern Hindustani literature

Capsule

Bicycles for HIV elimination

Several sub-Saharan countries have been prioritized by the Joint United Nations Programme on HIV/AIDS (UNAIDS) for HIV elimination. This will require 90% treatment coverage by the end of 2030, but poor transport infrastructure means incomplete access to medication in some countries. **Palk** et al. developed a geospatial model for understanding the difficulties of reaching health care facilities in Malawi, a country severely affected by HIV. They mapped healthcare facilities with the density of HIV prevalence and quantified the difficulty of travel across Malawi's landscape by a friction surface raster map. If bicycles are used, then the catchment size for a health care facility is substantially larger than if people walk, and the required 90% treatment coverage for elimination becomes achievable. Bicycles are already used as ambulances in rural areas, but Malawi's bicycle fleet is small and in poor repair. One straightforward route for beating HIV (and many other health conditions) here and in similar countries could lie simply in boosting the supply of bicycles, an established and well-tested technology.

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Capsule

Antibodies against Alzheimer

A key pathological event in Alzheimer's disease (AD) is the aggregation and deposition of amyloid-β (Aβ). However, the formation of Aβ deposits is a relatively late readout of the Aβ aggregation process. Treatments that affect such deposits may fail to interrupt the critical early seeding stage of Aβ deposition. It remains unclear when pathogenic Aβ seeds begin to form, propagate, and spread through the brain. Furthermore, the precise nature of the initial Aβ seeds remains unknown. Working in mouse models of AD, **Uhlmann** and co-authors tested a variety of known antibodies for their ability to neutralize Aβ seeds before amyloid deposition was detectable. Early administration of one such antibody, aducanumab, significantly reduced Aβ deposition and the resulting pathology. This work points to targeting and removal of early Aβ seeds as promising future therapies for patients developing AD.

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