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Case Report

Hypertensive Crisis Following Co-ingested Tobacco, Marijuana, and Red Wine: A Case Report

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INTRODUCTION

Monoamine oxidase (MAO), an enzyme found in the stomach, intestines, and liver, metabolizes tyramine as well as other monoamines, including dopamine and norepinephrine (NE). For most individuals, consuming tyramine-rich foods, such as red wine, dark chocolate, hard cheeses, and fermented foods, does not pose a problem. However, hypertensive crises following excessive tyramine ingestion are well-documented, particularly in patients taking monoamine oxidase inhibitors (MAOIs) for depression.[1]

When MAO is inhibited, tyramine enters systemic circulation and is taken up by nerve terminals via the NE uptake pump, displacing NE from intracellular stores. The resulting surge of NE in the bloodstream leads to increased blood pressure.[1] Since MAO also metabolizes NE, its inhibition allows unchecked NE accumulation, potentially triggering hypertensive emergencies.

We report a case of debilitating dizziness episodes culminating in a hypertensive emergency in an older woman. No definitive cause of her hypertensive crisis was identified; however, the temporal and repeated association of symptoms with red wine ingestion suggested possible MAO inhibition. In the absence of relevant case reports, we explore whether chronic cannabis and tobacco use may have contributed to insidious inhibition of monoamine oxidase-A (MAO-A), the primary isoform in the gut and liver.

CASE REPORT

A 72-year-old Caucasian woman with a history of well-controlled mild hypertension, hypercholesterolemia, depression, and prediabetes presented for an office visit due to worsening episodes of dizziness and nausea. She had high health literacy, was medication-compliant, and had a BMI of 17.8. Her medications included sertraline 50 mg, atorvastatin 40 mg, and amlodipine 2.5 mg. She engaged in moderate physical activity weekly, followed a low-sodium Dietary Approaches to Stop Hypertension (DASH)-compliant diet, and consumed approximately 12 ounces of wine once per week. She had a 40-pack-year smoking history, reporting "10 smokes/day," later revealed to be hand-rolled cigarettes containing both tobacco and marijuana.

The patient had been on amlodipine 2.5 mg daily for years. Two years prior, she discontinued amlodipine and simultaneously stopped smoking, but when she resumed smoking, she required the reintroduction of amlodipine. Her dizziness began approximately nine months before admission, initially positional and associated with recumbency and physical therapy for left hip osteoarthritis. During a telehealth visit, she was diagnosed with benign paroxysmal positional vertigo (BPPV) and advised on maneuvers to alleviate symptoms. Her dizziness resolved within a month without intervention, and her blood pressure (BP) increased from low levels. Three months later, she underwent a left hip replacement, completed post-operative therapy, and was able to walk up to three miles. Despite ongoing intermittent dizziness, nausea, and epigastric discomfort, a trial of proton-pump inhibitors was declined in favor of dietary adjustments and probiotics, which did not alleviate symptoms.

Her dizziness worsened significantly following a weekly social event where she consumed 350 mL (11 ounces) of red wine. She awoke with dizziness, nausea, and dry heaves, remaining bedridden for two days. The dizziness was described as profound disequilibrium and instability rather than vertigo. A second episode followed after reducing wine intake to 125 mL (4.2 ounces). In response, she maintained a food diary, reduced dairy intake, and tried over-the-counter remedies for her symptoms. Concerned about hypotension, she discontinued amlodipine without checking her BP at home. Upon evaluation the next day, her BP was normal, but it subsequently increased to ~150/80 mmHg, the highest she recalled. Amlodipine was restarted.

Four days later, she reported nearly five weeks of persistent dizziness, primarily occurring after wine consumption. Examination revealed intact cranial nerves and a normal ENT and cardiovascular exam. Lateral nystagmus was provoked but did not reproduce symptoms, making BPPV unlikely. Her BP was 162/90 mmHg, decreasing to 122/72 mmHg on retake, and no medication adjustments were made. One week later, she returned with profound ataxia and disequilibrium, describing a need to hold onto walls while ambulating but denying vertigo or orthostatic symptoms. She was alert, oriented, and had no neurological deficits. Her BP readings were 164/86 mmHg sitting, 162/100 mmHg standing, and 182/106 mmHg supine.

Due to concerns for hypertensive emergency and possible cerebrovascular accident (CVA), she was sent to the emergency department (ED). While hospitalized, she disclosed for the first time that she regularly smoked "spliffs" (hand-rolled cigarettes with equal parts tobacco and cannabis), about 10 per day. Imaging (computed tomography angiography and magnetic resonance imaging) was negative for CVA. Her BP improved to ~150/70 mmHg with an increase in amlodipine to 5 mg. She abstained from smoking during hospitalization, and urine drug testing was positive only for tetrahydrocannabinol (THC).

At discharge, she was advised to continue amlodipine 5 mg and to reduce or cease smoking. She fully discontinued smoking within 10 days post-discharge, with a negative cannabinoid screen after four weeks. Her nausea and abdominal discomfort resolved following smoking cessation, with no further adverse events. Table 1 shows the timeline of events.

Table 1. Timeline of events.

Time	Dizziness	Amlodipine (mg)	Blood Pressure (mm Hg)	
			Office	Home
Month -28 to -10	absent	2.5a	130/80	129/80
Month -9	moderate	2.5	n/a	115/78
Month -8 to -1	absent	2.5	121/77	124/80
Week -3	severe	2.5	n/a	n/a
Week -2	severe	2.5	n/a	n/a
Week -1	mild	0b	122/72	137/83
Admission	moderate	2.5	182/106	151/92
Week +1	absent	5	138/78	128/80
Week +2	absent	5	n/a	129/81
Week +3	absent	5	n/a	124/80
Month +1	absent	5	122/66	127/78

Note: Office blood pressure (BP) represents single or averaged double measurements; home BP is an average of 7 to 244 measurements. n/a = not available
(a) Amlodipine was discontinued by patient during 10-week smoking cessation; reinstated after resuming smoking and BP increased from 124/78 mmHg to 136/82 mmHg
(b) Amlodipine was discontinued by patient for 10d following severe dizziness; reinstated after home BP showed increase

DISCUSSION

Given the lack of a clear etiology, pheochromocytoma was considered but deemed unlikely due to the patient's response to amlodipine and symptom association with red wine. MAO inhibition was not initially suspected, as her medication list lacked known inhibitors. However, after learning that she rolled her own cigarettes with tobacco and cannabis, we explored the possibility that MAO-A inhibition resulted from these substances.

Cigarette smokers have long been known to have 20-30% lower MAO-A activity than non-smokers.[2] The irreversible MAO-A inhibitor, 1,4-benzoquinone, was recently identified as a component of tobacco smoke that appears in physiological relevant concentrations.[3] Irreversible inhibition persists until new MAO-A is synthesized, on the order of weeks. Loose tobacco (used in self-rolled cigarettes) inhibits MAO-A more than factory-made cigarettes due to higher tar concentrations.[4] Simultaneous alcohol and cannabis use increases systemic THC levels, potentially exacerbating these effects.[5] Finally, chronic drug administration causes a change in the dose-response curve that describes inhibition of MAO,[6] allowing lower doses of inhibitors to cause the same degree of inhibition. The combined influence of loose tobacco, heavy cannabis use, and alcohol likely impaired MAO-A activity, increasing susceptibility to tyramine's sympathomimetic effects. Normally metabolized by MAO-A in the gut and liver, tyramine can accumulate when MAO is inhibited, leading to norepinephrine release and dangerous hypertensive episodes.[1] Elevated plasma tyramine levels have been linked to essential hypertension, and individual responses vary widely, with some experiencing extreme blood pressure spikes after dietary tyramine exposure.[7]

The patient had a long history of drug use without recent changes in frequency or source, raising the question of why hypertensive emergencies occurred now. Age-related factors, such as the natural increase in systolic blood pressure and reduced hepatic/renal function, may have contributed to prolonged drug effects. Moreover, MAO inhibition can be progressive, with time-dependent accumulation leading to increased sensitivity.[6]

Prodromal symptoms, including unexplained gastrointestinal discomfort, may have been early signs of tyramine accumulation. Although dizziness was initially attributed to BPPV, home monitoring showed hypotensive episodes, suggesting a complex interplay between tyramine and blood pressure regulation.

Clinical Implications:

- MAO inhibition should be considered in atypical hypertensive cases, especially in patients using tobacco, cannabis, and alcohol.
- Primary care physicians should be aware of increasing cannabis use among older adults. Daily or near-daily use is now more common than alcohol use in the U.S., and cannabis-related emergency visits among the elderly have risen sharply.
- A non-judgmental approach to substance use history can help uncover hidden risk factors. The patient underestimated the cardiovascular risks of smoking and cannabis, only recognizing them after a health crisis.

While this case strongly suggests MAO inhibition as the underlying mechanism, the absence of direct MAO activity measurements remains a limitation. The patient provided written informed consent for this report.

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