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CASE REPORT

Toxicology

The green man enigma: Unique presentation of toxicology in the emergency department

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Abstract

We describe a case report of hypertensive crisis induced by a combination of amphetamine and Marwitt's Kidney Pills. Diagnosis was delayed because of nonspecific physical findings including chest pain, abdominal pain, coughing, and diarrhea. This was confounded by puzzling physical examination findings, including green-colored urine and fingernails. Diagnosis was aided with point-of-care ultrasound, which presented a picture of acute cardiac insufficiency, pulmonary congestion, and bilateral effusions. Laboratory values on admission indicated acute multiorgan injury. Detailed patient history revealed chronic consumption of "Kidney," an over-the-counter drug available in Thailand with the primary ingredient methylene blue and used for a myriad of renal and genitourinary conditions. The patient also had a history of amphetamine use, which ultimately initiated his acute presentation.

KEYWORDS

amphetamine, green fingernails, green urine, hypertensive crisis, "Kidney"–Marwitt's Kidney Pills, methylene blue, point-of-care ultrasound

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1 | CLINICAL RECORD

A 41-year-old citizen from Thailand with an unclear history of a kidney illness presented to our emergency department (ED) in Israel with nonspecific chest pain, abdominal pain, coughing, and diarrhea. The preliminary clinical picture at a private outpatient clinic showed generally apathy and weakness. The language barrier made ascertaining a precise history of patient illness difficult; a medical history was later obtained over the phone through a translator from the Embassy of Thailand in Israel. The patient had a history of genitourinary complaints and was taking Marwitt's Kidney Pills, an over-the-counter supplement available at the time in Thailand. It was determined that the patient had been well until 3 days before his admission, at which point he suddenly developed chest pain with coughing and intermittent nonspecific abdominal pain. The development of symptoms coincided with his acute use of "Ice," an illegal substance predominantly composed of amphetamine.

On presentation to our ED, the patient appeared ill and rapidly deteriorated. An electrocardiogram (ECG) demonstrated normal axis, sinus tachycardia of 116 beats, ST-elevation in lead V3, and biphasic T-wave in leads V1 and V2. Vital signs on arrival were a pulse of 116 beats per minute, blood pressure of 210/112, and oxygen saturation of 99% in room air. Physical examination findings were notable for bilateral clubbing in the fingers and bilateral edema of the lower extremities. The patient's fingernails were noted to have a distinct green hue (see Figure 1). The color could not be scratched off or removed.

After the detection of these odd physical findings, ED staff were equipped in full personal protective equipment as the etiology of his condition may have been an infectious organism or attributed to an environmental exposure. The patient was attached to a monitor, 2 large-bore intravenous cannulas were placed, blood cultures were taken, and 0.9% NaCl 1000 mL (normal saline) was administered.

A second ECG performed in the ED showed P-wave inversions in leads V2 and V3, a prolonged QTc interval of 472 milliseconds, poor R-wave progression through V1 to V5, and T-wave inversionsin leads V2 and V4, and augmented Vector Left (aVL). Point-of-care ultrasound (POCUS) in the ED showed poor cardiac contractility, no focal akinesia, and a mitral valve without flick to the left ventricle wall. Chest ultrasound demonstrated the presence of bilateral B-lines, a classic finding indicative of pulmonary congestion. Furthermore, no peritoneal fluid was identified on the right upper quadrant and left upper quadrant views, but a positive spine sign indicated pleural

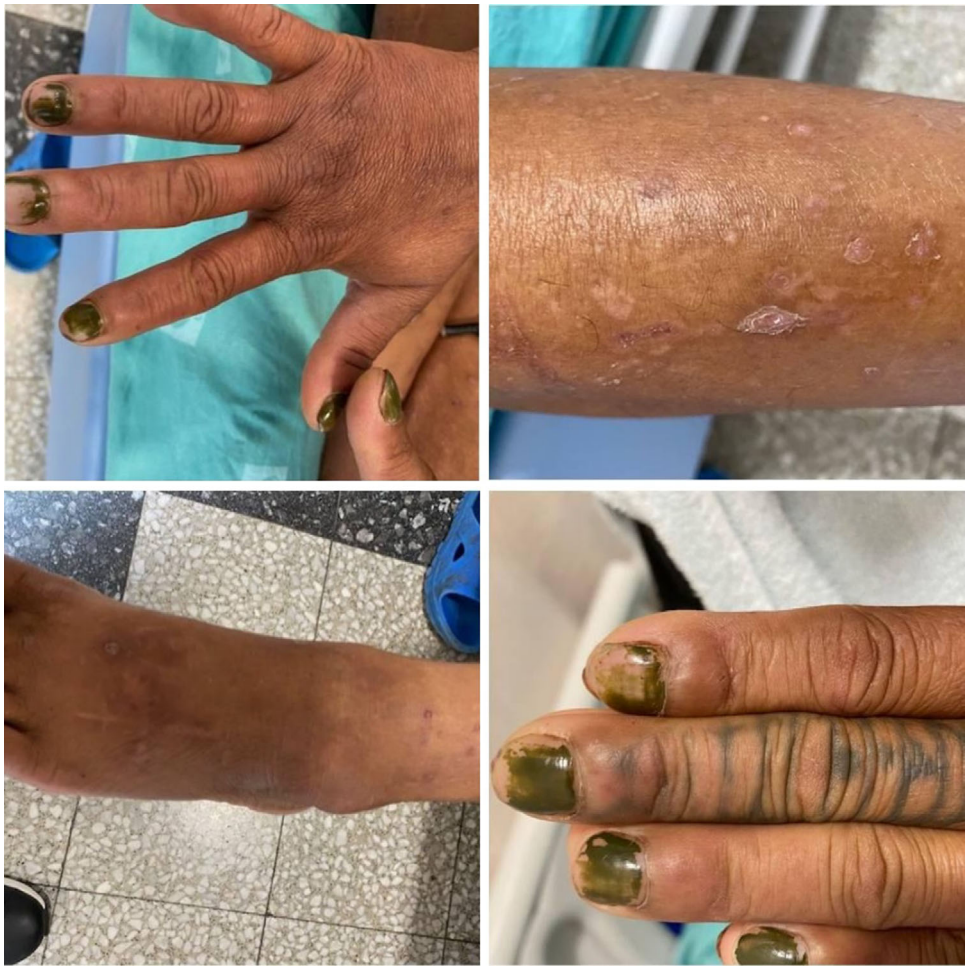

FIGURE 1 Patient's physical examination notable findings

FIGURE 2 Green-colored urine

TABLE 1 Selected laboratory values from time of admission

	Patient laboratory value	Normal value
Troponin	0.1 ng/mL	<0.013 ng/mL
Creatinine	2.45 mg/dL	0.70–1.20 mg/dL
Urea	78 mg/dL	20–45 mg/dL
Potassium	6.2 mmol/L	3.5–5 mmol/L
C-reactive protein	15 mg/L	<10 mg/L
Amylase	142 U/L	23–85 U/L
Lipase	63 U/L	0–160 U/L

effusions. A chest X-ray confirmed a pleural effusion in the right lobe with bilateral perihilar consolidations and pulmonary congestion. At this stage, a presumptive diagnosis of cardiogenic pulmonary edema was made.

A Foley catheter was inserted, and odd, green-colored urine was noted (Figure 2). Urinalysis showed the presence of nitrites, proteins, erythrocytes, and leukocytes. A urine toxicology screen, which tested for amphetamine, Δ-9-tetrahydrocannabinol, cocaine, opioids, and phencyclidine, was negative, although in retrospect, we could not determine why. Cell microscopy was not performed. Blood work is shown in Table 1. A follow-up POCUS in the ED demonstrated hydronephrosis with no visible evidence of obstructive stones as well as an ejection fraction between 20% and 25%, with a significant decrease in left ventricle function, intermediate mitral insufficiency, and minimal pericardial effusion.

In the ED, treatment was initiated with bisoprolol, hydralazine, amlodipine, Isoket (isosorbide mononitrate), and furosemide. Within a few hours, the patient had significantly improved urine output, and his blood pressure had dropped to between 140 and 100 systolic.

A few hours after admission, a more detailed patient history was ascertained through a translator. The patient admitted to regularly taking an over-the-counter drug called Marwitt's Kidney Pills, which he purchased in Thailand for an unspecified "chronic kidney problem" (see

FIGURE 3 Herbal supplement called "Marwitt's Kidney Pills"

Figure 3). It is probable that the patient had an underlying renal disease as evidenced by elevated creatinine, which may have explained his use of "Kidney," then a readily available and widely used drug for kidney problems. In the ED, the patient had proteinuria, and we suspected rapidly progressive glomerulonephritis or hemolytic uremic syndrome, most likely attributed to drug use. It appears that this drug is no longer available for sale, either over the counter or through a prescription in Thailand.

The patient arrived at the ICU with hyperkalemia of 6.2 mmol/L and was treated with kayexalate. Repeat blood tests showed a maximum troponin of 1 ng/mL and repeat troponin levels between 1 and 0.9 ng/mL, with no rise or fall of troponin as is expected in acute coronary syndrome.

On day 4, the patient underwent a myocardial perfusion scan that showed no evidence of significant myocardial ischemia. A decrease in left ventricular contraction after dipyridamole injection may indicate a non-ischemic cardiomyopathy. A repeat echocardiogram demonstrated a significant improvement in global cardiac function with an increased ejection fraction of 40%.

On day 14, the patient was hemodynamically stable with a blood pressure of 121/69. Although the patient's creatinine level remained as high as 2.1 mg/dL, his urine output and color improved steadily. At discharge, the patient was instructed to abstain from consuming "Ice" in the future, in any form. It was also recommended that he stop taking Marwitt's Kidney Pills, the over the counter drug. Follow-ups with cardiac, pulmonary, and renal specialists were recommended.

2 | DISCUSSION

In our case report, accurate diagnosis was complicated by an incomplete patient history and rare clinical features. The patient's hypertension along with unique dermatologic findings initially prompted us to suspect a connective tissue disorder or other systemic diseases. We looked for further evidence of vasculitis, systemic sclerosis, or an infectious agent. Rheumatological factors were tested including anti-nuclear antibody (ANA), antineutrophil cytoplasmic antibodies (ANCA), Rh antibodies, Complement system antibodies, antitopoisomerase I antibodies (anti-SCL-70), anti-centromere and anti-dsDNA antibodies. All of these test results were negative. An extensive infectious and immunological serological test was taken, including hepatitis, rickettsia, brucella, Q-fever, chlamydia, gonorrhea, syphilis, Epstein-Barr virus (EBV), cytomegalovirus (CMV), and tuberculosis (TB). These test results also all came back negative.

Indeed, during the patient's time in the ICU, his creatinine level was between 2.4 and 3.25 mg/dL. His baseline creatinine was not known. An underlying renal condition can most probably explain his chronic hypertension. Furthermore, the patient's use of Marwitt's Kidney Pills can explain many of his atypical findings, including discoloring of the nails and urine as well as thickened skin, particularly of the upper extremities.[1]

A consultation with a team of doctors and pharmacists from Thailand confirmed the drug's biochemical and clinical profile and commonly seen adverse effects. Marwitt's Kidney Pills are a common over-the-counter medicine in Thailand and often taken for a myriad of urinary problems. It contains methylene blue, a metabolite of which can cause methemoglobinemia, although we found no evidence of this in our patient. A common adverse effect of this drug is color change in urine, and in our patient specifically, nail beds as well, although we have not found other similar reported cases of a color change in nail beds.[2] This adverse effect, although typically surprising to the patient and medical care team, is usually reversible when medication usage is stopped.

The patient's presentation in hypertensive crisis demanded further investigation. The patient's chronic renal disease could not explain his acute deterioration with significant heart failure. Use of POCUS aided in surveillance of cardiac function and ejection fraction. An ophthalmologist evaluation did not reveal acute fundus changes, and in conjunction with the absence of left ventricular hypertrophy, reduced the probability of hypertensive heart disease, acute coronary syndrome, or acute myocarditis.

The patient admitted that in the week before his admission, he had consumed large quantities of alcohol and used a drug called "Ice," which he consumed both intravenously and through inhalation. The primary active ingredient of "Ice" is methamphetamine, although there are often various other compounds added unbeknownst to the users. Although a urine toxicology screen in our ED came back negative for amphetamines, a study in 2019 suggested that emergency clinicians should not rely on the results of urine drug screens to diagnose patients with methamphetamine or amphetamine toxicity as the results of these tests are preliminary and are subject to many external variables that can affect the results. We, therefore, concluded that his acute presentation in hypertensive crisis was caused by his recent use of amphetamine.

Patient care was focused on managing his hypertension and acute presentation of heart and renal failure. The patient's hypertensive crisis resolved shortly after arriving in the ED with appropriate treatment as mentioned previously, including β-blockers, calcium-channel blockers, and nitrates. His heart and renal failure stabilized within a few days with supportive treatment. Many other findings associated with his drug use would improve naturally with time after the cessation of use.[3]

3 | CONCLUSION

To summarize, we identified 2 distinct processes that contributed to our patient's clinical presentation. First, his acute use and abuse of "Ice," the amphetamine stimulant that triggered a hypertensive crisis and may have caused a reversible cardiomyopathy, although we did not find a direct link. His underlying renal condition may have predisposed him to a rapid decline into a hypertensive crisis. POCUS in the ED provided immediate cardiac and hemodynamic indications in this dynamic patient with an unclear history and aided our clinical work-up. Despite the odd clinical picture, POCUS allowed us to rapidly "rule out" life-threatening pathologies associated with hypertensive crisis and aortic dissection, such as focal myocardial akinesia. This permitted early pharmacologic and fluid interventions and helped further focus the diagnosis workup in a patient with unique and seemingly unrelated clinical findings.

Second, we determined that the patient's unique clinical findings, including discoloration of urine and nails, were caused by his use of Marwitt's Kidney Pills and its active ingredient of methylene blue. We were unfamiliar with this drug and its effects until this presentation.

Together, these 2 parallel clinical developments created a unique patient presentation that required us to methodically and sequentially move through a differential diagnosis and use many resources at our disposal in the ED, such as POCUS, to exclude life-threatening causes.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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