CASE REPORT

Hypertensive urgency: an important aetiology of rebound hypertension

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SUMMARY

A 46-year-old African-American man with a history of hypertension, end-stage kidney disease (on haemodialysis) and previous cocaine misuse presented to the emergency room with a sudden onset of severe headache and diaphoresis without other neurological or cardiovascular signs/symptoms. He checked his blood pressure at home and found it to be 230/130. It did not improve despite taking two serial doses of oral clonidine 0.3 mg. Evaluation with head CT and lumbar puncture demonstrated no acute intracranial process, such as subarachnoid haemorrhage. These symptoms started after he took Libido-Max, an over-the-counter supplement for erectile dysfunction. This supplement includes yohimbine, an α -2 antagonist, which counteracts the effects of oral clonidine, one of his routine antihypertensive medications. This led to rebound hypertension and made his hypertensive urgency resistant to oral clonidine. He was successfully treated with intravenous labetalol and his symptoms quickly resolved after lowering of his blood pressure.

BACKGROUND

Hypertensive urgency and rebound hypertension are very common and can be challenging to evaluate and treat since there are a large number of potential contributors to these problems. Yohimbine previously was available as a prescription medication and its side effects and medication interactions were more closely monitored. However, since it is no longer commonly used as a prescription medication in the USA (only available at compounding pharmacies), many physicians do not realise it is present in unregulated supplements. Thus, its effects may be frequently unrecognised.

CASE PRESENTATION

A 46-year-old African-American man with a history of hypertension, end-stage kidney disease (ESKD on haemodialysis), and previous cocaine misuse presented to the emergency room with a sudden onset of headache, described as 'the worst headache of my life'. He experienced an episode of diaphoresis followed by an escalating sharp and 'electric-like' headache at the vertex and frontal regions, without associated photophobia, phonophobia or nausea. There was no dysarthria, weakness, or numbness. He had taken his blood pressure earlier at home and found it to be 230/130. He took two serial doses of clonidine 0.3 mg with persistent elevation and called emergency medical services. When EMS checked his blood pressure it was 234/100.

On initial presentation to the emergency department (ED), his blood pressure was 235/119 and he remained symptomatic. CT head (without contrast) was performed, which did not detect acute haemorrhage or other abnormalities. Lumbar puncture was performed and revealed white cell count 40, red blood cell (RBC) 7520, protein 40 and glucose 64. There was no xanthochromia, so the elevated RBC count in the cerebrospinal fluid was felt to be secondary to traumatic lumbar puncture. The patient's last cocaine use was 1 month prior, and he had a negative urine drug screen in the ED. Neurology and neurosurgery consultations in the ED revealed a normal neurological examination with normal cranial nerve, motor and sensory examinations, 2+ reflexes throughout and normal gait.

After receiving labetalol 20 mg intravenously, his blood pressure improved to 190/110 and with repeated doses it further improved to 162/88 with concomitant resolution of his headache and diaphoresis.

A diagnosis of hypertensive urgency was made. On further questioning, the patient reported having used the supplement 'Libido-Max' in hopes of overcoming erectile dysfunction, in the setting of chronic hypertension, hyperlipidaemia, type II diabetes mellitus, cocaine misuse and ESKD. He developed the aforementioned symptoms 5–10 min after taking this. It was the second time he had used Libido-Max and he had experienced similar symptoms the first time he used it, but his symptoms were not as severe and he did not seek medical attention at that time.

DIFFERENTIAL DIAGNOSIS

This patient had a history of cocaine misuse and illicit drugs can lead to hypertensive urgency. However, he had not used cocaine for at least 1 month by history and urine drug screen was negative, confirming this was not the aetiology. However, in a case of this type, if cocaine misuse is a concern, one would want to avoid using intravenous labetalol as a β -blocker. The patient also had a history of ESKD and was on haemodialysis through an arteriovenous fistula (AVF). He had missed haemodialysis in the past, which can lead to elevated blood pressures due to volume retention. Similarly, some patients develop AVF-related vascular access problems and are unable to have adequate dialysis sessions. However, this patient had undergone a complete, uncomplicated haemodialysis session the morning of presentation to the ED. If he had incomplete dialysis secondary to

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vascular access problems, he would have needed a fistulogram for further evaluation of his AVF and he certainly would need haemodialysis if he missed one or more sessions. Medication non-compliance with oral clonidine can lead to rebound hypertension, but in this case, the patient confirmed he had been adherent with therapy and, in fact, took extra doses. Furthermore, if his hypertensive urgency was secondary to non-compliance, it would have quickly responded to oral clonidine, but it did not. In addition, EMS noted his usage of clonidine in their report (based on obtained initial history on their arrival at his house). Lastly, this was the second time this patient had used Libido-Max and he had similar symptoms both times (soon after using it).

TREATMENT

Intravenous labetalol was effective in treating his hypertensive urgency and rebound hypertension, utilising repeated dosages of 5–20 mg.

OUTCOME AND FOLLOW-UP

The patient stopped using Libido-Max and has not had recurrent hypertensive urgency or similar symptoms in the 6 months since the aforementioned episode.

DISCUSSION

Libido-Max is an over-the-counter supplement that contains yohimbine, an α -2 antagonist, in addition to being a mild monoamine oxidase inhibitor. This medication may cause an acute, paradoxical dose-dependent increase in blood pressure, which appears to be most pronounced in those with underlying hypertension. This is thought to be secondary to increased norepinephrine and vasoconstriction.^{1–3} In fact, a moderate dose has been found to be effective in decreasing orthostatic hypotension, particularly in patients with autonomic neuropathy.^{4 5} Thus, as in this case, over-the-counter enhancement supplements containing yohimbine may be a cause of hypertensive urgency. In addition, in this particular case, it appeared to have a role in acutely antagonising the action of his antihypertensive, oral clonidine, causing rebound hypertension akin to the reaction of a patient suddenly stopping oral clonidine. Furthermore, when our patient attempted to take oral clonidine, it was ineffective, likely because of the α -2 antagonistic effects of the yohimbine counteracting its mechanism of action. Although we do not often think about yohimbine because it is not currently frequently prescribed, it is present in a large number of over-the-counter products for erectile dysfunction. It is unclear if haemodialysis patients or those with impaired renal function may be particularly susceptible to this effect of yohimbine, but currently available data on yohimbine suggests variable

metabolism with most metabolism and clearance not being performed by the kidneys.^{6 7}

Patient's perspective

The patient noted that he had no idea that an over-the-counter supplement could interact with his prescription medications to make one of them ineffective. He also said he would not have brought up the fact that he was using a supplement for erectile dysfunction unless directly asked about over-the-counter medications.

Learning points

- ▶ Yohimbine, available in over-the-counter supplements for erectile dysfunction, can cause rebound hypertension in patients using oral clonidine.
- ▶ Yohimbine can render clonidine ineffective when treating hypertensive urgency.
- ▶ Yohimbine increases blood pressure in hypertensive patients.
- ▶ It is important to carefully ask about use of over-the-counter medications and supplements, with consideration of medication interactions.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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