Refractory hypertension in young—beware of substance abusers!

MJAFI 2012;68:94–95

Dear Editor,

A 34-year-old man became first symptomatic with features of anxiety neurosis about 10 years back (2001). Six months later he was noted to have elevated blood pressure (BP) 160–220/90–130 mmHg. At the same time he also noted episodic headaches, palpitations, and giddiness. He was started on antihypertensives but required four drugs to control his BP. Complete evaluation for secondary hypertension failed to reveal any cause. Since April 2009, his BP was uncontrolled with four drugs and multiple alterations were made in his treatment. At one point of time he was receiving seven antihypertensives in maximal doses (prazosin, propranolol, enalapril, losartan, aliskiren, clonidine, and methyldopa) with persistent wide excursions of BP (140–280/100–180 mmHg). In May 2009, he developed redness of eye. Evaluation by an ophthalmologist was suggestive of keratoconjunctivitis. This was resistant to all forms of treatment offered (antibacterial, antifungal, antiviral, and immunomodulators). He was referred to this centre for further evaluation.

He complained of headache, palpitations, and giddiness which had increased in frequency and duration. He had persistent tremulousness. Detailed history did not point to any specific cause but probability of pheochromocytoma was kept high. His eye symptoms persisted on medications. There was no family history of hypertension.

On examination his pulse was 110/min, regular, bounding, and all peripheral pulses being felt. There was no radio-femoral delay. His BP in supine position was 280/150 mmHg and 270/148 mmHg on standing. He had fine tremors in hands and cold, moist palms. His systemic examination was normal. Examination of eyes revealed keratoconjunctivitis in both eyes. His optic fundii examination was normal. Continuous ambulatory BP monitoring revealed wide fluctuations of BP between normal and abnormal readings. For BP control he was on prazosin and propranolol (keeping possibility of pheochromocytoma) and all other drugs were tapered and stopped.

Investigations revealed haemoglobin of 14.8 g/dL, normal urine examination, fasting and postprandial blood glucose of 86 mg/dL and 110 mg/dL, respectively, serum bilirubin of 1.0 mg/dL, blood urea nitrogen 10 mg/dL, serum creatinine 1.0 mg/dL, serum calcium 10.4 mg/dL, serum phosphorous 3.6 mg/dL, sodium 136 mEq/L, potassium of 3.6 mEq/L, thyroid-stimulating hormone 1.37 μ IU/mL, PTH 10.32 pg/mL, normal electrocardiogram, chest radiograph, and normal ultrasound scan of abdomen.

Two-dimensional echocardiogram did not show left ventricular hypertrophy or any other cardiac abnormality. Products of catecholamine metabolism in 24-hour urine collection were elevated—metanephrine 470.58 μ g/24 hours (52–341); normetanephrine 243.19 μ g/24 hours (27–155); epinephrine 180.67 μ g/24 hours (1.70–22.4); norepinephrine 397.43 μ g/24 hours (12.1–85.5); and dopamine 1,334.71 μ g/24 hours (52–480). Magnetic resonance imaging (MRI) of abdomen and thorax was normal. Meta-iodobenzylguanidine (MIBG) and positron emission tomography (PET) scan did not show any avid uptake. Doppler study of renal vessels, captopril scintigraphy, and angiography of renal arteries were normal. Vasculitic work-up was normal. Electroencephalography (EEG) and MRI brain was also normal. The patient did not have any evidence of target organ damage in spite of long history of hypertension. In view of normal extensive investigation, absence of target organ involvement, presence of hyperadrenergic symptoms, sympathomimetic drug abuse was thought off.

Patient was shifted to the intensive care unit without warn and intra-arterial BP was monitored for 72 hours. The maximum recorded BP was 130/80 mmHg and all readings were within normal limits for his age. The BP measured by cuff method was also in comparable range. Simultaneously 24-hours urine collection was performed and sent for analysis for opiate, cannabinoid, amphetamine, benzodiazepine, and cocaine. It tested positive for cocaine (318.65 ng/mL).

Cocaine abuse can have a wide range of presentations. It can present with hypertension, acute coronary events, cerebrovascular accidents, seizures, red stuffy eyes. The mechanism behind the toxic effects of cocaine is that it blocks the re-uptake of catecholamines—norepinephrine and dopamine at presynaptic level in both central and peripheral nervous system and simultaneously increases their release from central and peripheral store. This causes an increase in the plasma catecholamines which can spill over into urine and be detected. Cocaine has effects on endothelin-1, the sodium channel and nitric oxide which further enhances its untoward cardiovascular effects.¹ Diagnosis of cocaine usage can be made by urinary assays which can be elevated up to 3–5 days after last dose of cocaine was abused. Cocaine abuse can explain all the features in this patient. First, his 'refractory' hypertension without any end organ damage: this can be explained by a nonsustained hypertension caused by cocaine. Secondly, his hyperadrenergic symptoms and raised catecholamine metabolites urine also go well with cocaine abuse. Thirdly his eye symptoms which have been resistant to all forms of treatment, has been reported in

doi: 10.1016/S0377-1237(11)60136-6

literature due to cocaine sniffing.² Finally when he was being monitored under supervision in intensive care unit (ICU) where he had no access to any drugs, he had normal BP tracing. A similar case of 39-year-old patient with refractory hypertension with urinary free catecholamines suspected to be pheochromocytoma, diagnosed as cocaine-induced hypertension on work-up has been reported in the literature.³

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