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Severe and Refractory Hypertension in a Young Woman

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Abstract

Background—Refractory hypertension in a young person is an uncommon clinical problem, but one that may be referred to hypertension specialists. Factitious hypertension is fortunately quite rare, but should be considered when evaluating patients who are refractory to numerous classes of antihypertensive therapies and have failed to achieve control despite input from multiple providers.

Report of a Case—A 19 year old woman was referred to us after failing to achieve blood pressure control by a primary physician and 2 subspecialists in nephrology and hypertension; she also had numerous emergency department visits for symptomatic and severe hypertension. Exhaustive diagnostic testing for secondary causes and witnessed medication dosing in an outpatient setting was unrevealing. Subsequent inpatient admission demonstrated normalization of BPs with small doses of intravenous antihypertensive agents. During the hospitalization, she was observed “pocketing” her oral medications in the buccal folds, and then discarding them in a trash container. Confrontation by psychiatrists and the hypertension specialists led to the admission that she had learned to start and stop beta-blockers and clonidine to induce severe, rebound hypertension.

Discussion—Factitious and induced hypertension is a rare cause of resistant or refractory hypertension. Nevertheless, hypertension specialists should suspect the diagnosis when there is a history of visits to multiple institutions and physicians, negative secondary workup, absence of overt target organ damage, history of psychiatric illness, and employment in the medical field.

Keywords

refractory hypertension; pseudo-resistance; factitious hypertension

Introduction

Refractory hypertension is defined as blood pressure (BP) that remains uncontrolled despite maximal medical therapy.¹ While refractory hypertension is uncommon in clinical practice,

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referrals for this diagnosis are not unusual to hypertension specialists.² When faced with a patient with severe and refractory hypertension, a thoughtful evaluation must be undertaken to identify secondary causes. Prompt interventions must be made to gain control of the BP if it is severely elevated. In addition to the commonly sought causes of secondary hypertension, factitious hypertension, while unusual, must be considered as well. These patients may be highly manipulative and create substantial health care burden and excessive use of physician resources. We present such a patient herein.

Report of a Case

A 19 year old Korean-American woman was referred by a cardiology colleague for evaluation of severe and refractory hypertension. At age 14, she was diagnosed with IgA nephropathy with preserved renal function and was entirely normotensive at that time. At age 18, patient was found to have hypertension and initiated on antihypertensive therapy. During the next year, the severity of hypertension accelerated and she underwent extensive workups by 3 different clinicians for secondary forms of hypertension, none of which were revealing. Included in this evaluation was digital subtraction angiography that showed normal kidney size and no evidence for renovascular disease. Additionally, there was no evidence of hypertensive target organ injury or involvement.

At initial presentation to our practice, the patient had a seated clinic BP of 162/116 mmHg with a heart rate of 86 beats per minute on the following antihypertensive therapies: amlodipine 10 mg, valsartan 320 mg, and hydrochlorothiazide 25 mg all in the morning, carvedilol 25 mg twice daily, and transdermal therapeutic systemic clonidine (0.2 mg daily delivery) changed on Mondays. The patient had also received oral clonidine tablets at a number of visits to her local hospital's emergency department. On these 5 drugs, an ambulatory BP study yielded a 24-hour mean value of 156/106 mmHg with a nocturnal decline in BP to 140/98 mmHg. The following laboratory studies were normal or negative: blood urea nitrogen, serum creatinine and potassium, serum aldosterone, plasma renin activity, serum free cortisol, serum deoxycorticosterone, and plasma metanephrines and normetanephrines. Pregnancy testing and toxicology assessment for amphetamines, benzodiazepines, barbiturates, cocaine and opioids were negative. Computed tomography of the abdomen showed no evidence of adrenal masses or renal abnormalities. Subsequent magnetic resonance angiography of the brain was normal.

Because of the lack of response to her complex medication regimen and negative workup for target organ involvement or secondary causes of hypertension, we became concerned that the patient was non-adherent to her antihypertensive therapies. The patient was admitted to our ambulatory research clinic for directly observed administration of her oral antihypertensive drugs with pre- and post-dosing BP measurements. Over this 4-hour period of observation, there were minimal changes (< 6 mmHg) in pre-dosing BP (180/112 mmHg) following the oral administration of clonidine (0.1 mg), carvedilol 25 mg, chlorthalidone (25 mg), azilsartan medoxomil (40 mg) and amlodipine (10 mg).

Two weeks later, the patient agreed to hospital admission for further evaluation of her severe hypertension and was accompanied by her parents. At the time of admission, the semi-

supine BP was 192/134 mmHg with a heart rate of 92–108 beats/minute. One to two hours after administration of intravenous doses of labetalol (20 mg) and enalaprilat (2.5 mg), the BP was 132/ 80 mmHg with a heart rate of 84 beats/minute. Based on this response to the parenteral medication, the patient was initiated on 2 oral agents (amlodipine and lisinopril) the following morning. Shortly after administration of her morning medications, an echocardiography technician found whole pills in a tissue, which had been used by the patient due to ‘congestion’ and discarded in the garbage in the echocardiography laboratory. The pills were identified as the 2 prescribed oral antihypertensive drugs as well as 2 other medications she was taking for depression. When confronted with this issue, the patient stated, “she only spit out her tablets because they were getting stuck in her throat” and blamed the formulation and taste.

An inpatient psychiatric consultation was requested and they learned that the patient had been previously diagnosed with a borderline personality disorder and had had a suicide attempt with moderate doses of acetaminophen. Following the psychiatric intervention, the patient was committed short-term to the hospital and medication administration was followed by oral examinations to make certain she was ingesting her medications. With just 2 oral agents, the BP remained entirely normotensive. One of us (WBW) interviewed the patient and learned that she had been intermittently taking the BP drugs (which included clonidine and beta-blocker therapies) to induce rebound hypertension. The patient’s parents succeeded in reversing the psychiatric commitment and she was discharged on lisinopril 10 mg and amlodipine 5 mg daily. We informed the 3 other physicians who had been involved in her care of our findings and to make certain that none of them prescribed centrally acting alpha agonists or beta-blockers considering their potential to induce rebound hypertension and/or tachycardia.

One week after hospital discharge, the patient was seen in our faculty practice with a seated BP of 170/118 mmHg and heart rate of 98 beats/minute. We attempted to obtain a urine collection to verify presence of the prescribed drugs in her system, and to ascertain if she was still inappropriately ingesting clonidine or beta-blockers. She refused to submit a urine sample, however. After cancelling 2 appointments, the patient returned approximately 4 months post-hospital discharge, stated she was taking her medications and had an office BP of 144/88 mmHg. She told us she was working on finding a new mental health therapist.

Commentary by and for the Hypertension Specialist

When evaluating patients with severe and refractory hypertension, it is necessary to exclude known secondary causes of hypertension and determine if there is ongoing hypertensive target organ involvement. A diagnosis of non-adherence to medication or feigned illness should be considered only after this work up is completed. There were a number of indicators that the patient described above might have had a factitious form of hypertension: 1) she had an extensive negative workup for all known secondary causes of hypertension, 2) there was no evidence of any target organ involvement, 3) there was evidence that the patient was obtaining secondary gain from her parents (who accompanied her to all visits) due to the severity of her disease (e.g., one reason why she could no longer attend school). The total absence of a BP response to oral administration of antihypertensive pills in the

ambulatory setting was surprising and led to the subsequent admission for evaluation after intravenous BP lowering therapy. The dramatic reduction in BP following parenteral therapy verified the diagnosis of non-adherence to oral antihypertensive therapy. It was fortuitous that an astute echocardiographer found the pills that she had expertly pocketed in her buccal folds until the timing was right to discard. This young patient also became quite savvy at reviewing clinical effects of antihypertensive drugs on the internet and had gained knowledge of the effects of abruptly discontinuing clonidine or beta-blocker therapy, and used that to her advantage to produce markedly elevated BPs when evaluated in the medical care environment, including the emergency department. In fact, we are not certain that this patient even has hypertension since she was prematurely discharged from the hospital before a complete medical and psychiatric evaluation could be completed.

Review of Factitious Disorder and Malingering

Factitious disorder imposed on self, as described by *The Diagnostic and Statistical Manual of Mental Disorders 5th ed. (DSM-5)*, represents a condition wherein a patient falsifies medical or psychological symptoms, so as to assume the 'sick role'. It is currently classified in the *DSM-5* under Somatic Symptom and Related Disorders.³ Its diagnostic criteria include the following: 1. Falsification of signs or symptoms, or induction of injury or disease, and is associated with deception. 2. The individual presents himself as ill, impaired, or injured. 3. Deceptive behavior is evident in absence of external rewards. 4. Behavior is not better explained by another mental disorder.³ Severe forms of factitious disorder were previously referred to as Munchausen's syndrome.

Malingering is a separate clinical entity, where the falsification of symptoms or illness is for obvious external gain (e.g. avoidance of legal proceedings, acquisition of shelter, food, or drugs, or time off work).

Factitious hypertension is rare, but has been documented on occasion in the medical literature. There have been case reports of patients presenting with a pheochromocytoma-like syndrome (Table). Presentations have included ingestion of sympathomimetics in various forms, Valsalva maneuvers during BP measurements, and severe elevations of BP for which the cause was never discovered. Pessina et al⁴ described a case of a 20 year old man, who after extensive workup for secondary hypertension was unrevealing, underwent renal denervation, with no effect on the BP. Years later, he presented to an endocrinology clinic with continued severe hypertension. An adrenal mass was discovered, and despite negative blood and urine catecholamines, the patient ultimately underwent laparoscopic adrenalectomy for presumed pheochromocytoma. Pathology revealed no evidence of pheochromocytoma. There was no blood pressure improvement post-operatively, and it was subsequently discovered that the patient was surreptitiously ingesting amphetamines to feign severe hypertension.⁴

In a separate case of simulated pheochromocytoma, a middle-aged female who worked in the health care setting as a nurse was evaluated for severely elevated BP over many years, and extensive search for a pheochromocytoma was negative. She underwent right adrenalectomy, with no improvement, and just prior to a last resort procedure to remove her

left adrenal gland, it was discovered that she was administering adrenaline and noradrenaline. She had even injected the catecholamines intra-vaginally during an angiographic procedure.⁵

One report described a case of a patient using the Valsalva maneuver to increase blood pressure during BP measurements. In contrast to the other cases, the patient had a concrete secondary gain. He was a prison inmate whose motive was to avoid prison duties. Thus his diagnosis was consistent with malingering.⁶

In yet another variation of falsifying clinical syndromes, a report from 1981 described a patient who had repeated episodes of a pheochromocytoma-like syndrome. When all testing was negative, it was discovered that his mineral water that he drank from bottles contained large amounts of metaraminol, a sympathomimetic amine. It was determined that his wife, a nurse, had been intentionally adding the drug to his bottles of mineral water. When he stopped drinking the water, his symptoms abated, and his wife was charged with attempted murder. This case is consistent with factitious disorder imposed on another, or Munchausen by proxy.⁷

As evidenced by these cases, and by that of our patient, some individuals go to extreme lengths to continue their factitious syndromes. Invasive diagnostic procedures and unnecessary surgeries, with their risks, are performed and in fact may be desirable for these afflicted patients. This again underscores why prompt recognition of the condition, although challenging, is important.

Conclusion

As hypertension specialists we are compelled to fully evaluate patients with refractory hypertension before coming to a conclusion that the patient is non-adherent to medications. In our experience, when faced with the dilemma of diagnosing a patient that is believed to be feigning severe and uncontrolled hypertension, admission to either an ambulatory care unit or inpatient setting for witnessed medication administration and sequential BP measurement is typically helpful. If this is not productive, the next step is hospital admission for administration of parenteral therapy. As in our case, if that is effective, confrontation must be carried out and/or oral cavity checks post-administration of pills may also be required. While this may not change the long-term behavior of such patients, it will elucidate the reason for the refractory nature of the hypertension and avoid unnecessary healthcare utilization as well as avoiding risk from testing and potentially invasive treatments. It is also important to communicate your findings with other treating physicians at other institutions, as these patients may continue the subterfuge elsewhere once the factitious nature of their symptoms is discovered.

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Table 1

Review of factitious hypertension syndromes reported in the literature

Author & Year	Age / Gender	Presenting Syndrome	Subtype	Method of feigning
Present case	19 / Female	Refractory hypertension on > 5 antihypertensive drugs; repeated visits to emergency rooms	Factitious disorder	Manipulation of antihypertensive medications and pill pocketing
Pessina et al 2013 ⁴	20 / Male	Pheochromocytoma-like syndrome	Factitious disorder	Ingestion of amphetamines
Spitzer et al 1998 ⁵	46 / Female	Pheochromocytoma-like syndrome	Factitious disorder	Injection of exogenous catecholamines
Rude et al 1992 ⁶	23 / Male	Accelerated hypertension	Malingering	Valsalva maneuver during BP measurements
Portiolo et al 1981 ⁷	37 / Male	Pheochromocytoma-like syndrome	Factitious disorder imposed on another [*]	3 rd party administration of sympathomimetic drugs

^{*} Diagnosis given to the third party administering the drug to the unknowing victim