MAYO CLINIC

58-Year-Old Man With Hypertension and Diffuse Swelling

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A 58-year-old previously healthy man presented to the clinic with an 8-week history of swelling involving his face and both knees, ankles, and hands. He reported a 4.5-kg weight gain over the same time period. He also noted persistent flushing of his face and a sensation of pressure behind his eyes with no headache or visual changes. He did not have palpitations, shortness of breath, chest pain, paroxysmal nocturnal dyspnea, or orthopnea. Frothy urine and hematuria were not reported. He had no joint pain, rash, abdominal fullness, easy bruising, or striae. The patient took no prescription, over-the-counter, or illicit drugs. His medical history was unremarkable. He was a lifelong nonsmoker, rarely consumed alcohol, and lived an active lifestyle. The patient presented for annual health care visits and was up-to-date on all preventive services.

On examination, the patient was alert and had obvious facial plethora. Vital signs were as follows: blood pressure (BP), 194/108 mm Hg (average of 3 readings, roughly equal in both arms); pulse rate, 92 beats/min and regular; respiratory rate, 18 breaths/min; and body mass index, 25.2 kg/m^2. Of note, the patient was normotensive at a clinic visit 10 months previously. Cardiac examination revealed normal rate and rhythm, normal heart sounds, and no murmurs or gallops. His lungs were clear on auscultation, and his neck veins did not appear distended. Pulses were symmetric with no radioradial or radiofemoral delay. Examination of the abdomen revealed no organomegaly, masses, audible bruits, or clinical ascites. Moderate pitting edema of the lower extremities was present to the midshin. Both hands were diffusely swollen with no evidence of synovitis. Funduscopic examination demonstrated a normal optic disc.

Initial laboratory evaluation yielded the following results (reference ranges provided parenthetically): hemoglobin, 16.2 g/dL (13.5-17.5 g/dL); leukocytes, 11.6 $\times$ 10^9/L (3.5-10.5 $\times$ 10^9/L); platelet count, 133 $\times$ 10^9/L (150-450 $\times$ 10^9/L); sodium, 139 mmol/L (135-145 mmol/L); potassium, 3.9 mmol/L (3.6-5.2 mmol/L); calcium, 8.9 mg/dL (8.5-10.2 mg/dL); fasting glucose, 99 mg/dL (70-100 mg/dL); creatinine, 1.0 mg/dL (0.8-1.3 mg/dL); N-terminal pro-B-type natriuretic peptide, 178 pg/mL (<300 pg/mL); and thyrotropin, 2.1 mIU/L (0.27-4.2 mIU/L). Urinalysis was negative for protein and hemoglobin. Electrocardiography revealed normal sinus rhythm with no ST-, T-, or Q-wave changes. Chest radiography demonstrated a normal cardiac shadow and clear lungs.

1. Which *one* of the following terms *best* classifies the patient's presentation?

a. Normal BP
b. Prehypertension
c. Stage 1 hypertension
d. Stage 2 hypertension
e. Hypertensive emergency

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)[1] classified hypertension as follows: normal BP, systolic less than 120 mm Hg and diastolic less than 80 mm Hg; prehypertension, systolic BP of 120 to 139 mm Hg or diastolic BP of 80 to 89 mm Hg; stage 1 hypertension, systolic BP of 140 to 159 mm Hg or diastolic BP of 90 to 99 mm Hg; and stage 2 hypertension, systolic BP of 160 mm Hg or higher or diastolic BP of 100 mm Hg or higher. The JNC 7 also required that the BP be consistently elevated at each of 2 or more office visits at least 1 week apart. The JNC 8 report did not address the classification of hypertension and focused primarily on treatment. Of note, our patient had been advised to purchase an automated home BP cuff and

See end of article for correct answers to questions.

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reported systolic BPs above 180 mm Hg over several weeks, confirming the diagnosis of stage 2 hypertension in the absence of evidence for end-organ damage. Hypertensive emergency is defined as a systolic pressure of 180 mm Hg or higher and/or a diastolic pressure of 120 mm Hg or higher *with* evidence of end-organ dysfunction (such as encephalopathy, papilledema, or myocardial ischemia) requiring immediate BP reduction with parenteral agents.

Patients with stage 2 hypertension rarely respond to a single antihypertensive agent, and the JNC 7 recommends starting combination therapy in this population.[1] This approach is controversial among clinicians who may argue that starting 2 drugs simultaneously could lead to an unpredictable BP response with possible confounding in the event of intolerance or allergy. For our patient, chlorthalidone, a potent yet well-tolerated thiazide diuretic with a long half-life, and lisinopril, an angiotensin-converting enzyme inhibitor with nephroprotective benefits, were chosen as a 2-agent combination for stage 2 hypertension. Calcium channel blockers were initially avoided because of the potential for worsening peripheral edema. The patient remained very active, and β-blockers were also not chosen because of concern regarding poor tolerability. After 2 weeks, the patient's edema improved in the setting of diuretic use, but his BP remained elevated at 166/92 mm Hg with a heart rate of 72 beats/min. Initiation of amlodipine, a calcium channel blocker, resulted in improved BP control at 139/82 mm Hg.

2. In addition to the evaluation obtained thus far, further investigation should be performed *next* for which *one* of the following conditions?

a. Essential or primary hypertension
b. Renovascular and endocrine disease
c. Primary intrinsic renal disease
d. Coarctation of the aorta
e. "White coat" hypertension

Any patient with severe hypertension or an acute increase in BP who has had previously normal values should undergo investigation for secondary causes of hypertension. Therefore, stopping the work-up at the diagnosis of essential hypertension would not be appropriate. Renovascular disease and endocrinopathies including hypercortisolemia, pheochromocytoma, and primary hyperaldosteronism are all causes of secondary hypertension and need to be further evaluated. The history, physical examination findings, and laboratory results thus far are not sufficient to exclude these conditions. Primary renal disease is unlikely given the patient's normal creatinine concentration and unremarkable urinalysis results. The patient's age at presentation and symmetric BP readings with no pulse delays make coarctation of the aorta an improbable scenario. White coat hypertension is a diagnosis that applies to patients who exhibit modestly elevated BPs in health care settings but normal home and ambulatory BP recordings. Our patient had markedly elevated in-office as well as home BP readings.

Additional evaluation yielded an undetectable aldosterone concentration, undetectable plasma renin activity, normal plasma fractionated metanephrine level, and a 24-hour urinary free cortisol level of 841 μg/24 h (3.5-45 μg/24 h). Renal artery Doppler ultrasonography revealed normal renal arteries and normal renal parenchyma but incidentally demonstrated a 7-cm irregular right-sided adrenal mass. Subsequent testing yielded a suppressed corticotropin level of 5.6 pg/mL (10-60 pg/mL), an elevated dehydroepiandrosterone sulfate concentration of 291 μg/dL (35-179 μg/dL), and an elevated 17-hydroxyprogesterone level of 244 ng/dL (<220 ng/dL). Androstenedione and estradiol levels were unremarkable.

3. On the basis of the results of these investigations, which *one* of the following is the *most likely* cause of this patient's hypertension?

a. Pheochromocytoma
b. Corticotropin-dependent Cushing syndrome
c. Corticotropin-independent Cushing syndrome
d. Primary hyperaldosteronism
e. Exogenous glucocorticoid intake

Plasma fractionated metanephrine levels are highly sensitive for the diagnosis of pheochromocytoma, and our patient's normal value

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