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Power Failure: Acromegalic Cardiomyopathy

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PRESENTATION

During his college years, the patient, at 6 ft, 8 in and 280 lb, aroused the attention of professional basketball scouts. But exertional fatigue and shortness of breath truncated his athletic aspirations. These symptoms continued in the ensuing years, necessitating approximately 15 hospitalizations at outside institutions for progressive dyspnea. No discernible etiology was established on any of these occasions. Now 35 years old, he presented to the Emergency Department reporting chronic shortness of breath, chest pain, and fatigue, symptoms of heart failure that had plagued him repeatedly in the past.

The patient was African American. He had no history of smoking, alcohol consumption, or illicit drug use. His family history was unremarkable. Because his medical care had been staggered, he was unable to provide definitive details about any of the therapeutic regimens he followed in the past or his compliance with them.

ASSESSMENT

Upon arrival, the patient was in moderate respiratory distress and was speaking in 3-word sentences. He was afebrile, his pulse rate was 85 beats per minute, his blood pressure was 193/111 mm Hg, his respiratory rate was 24 breaths per minute, and his oxygen saturation was 97% on 4 L of oxygen by nasal cannula. Physical examination disclosed frontal bossing, enlarged hands and feet, doughy skin texture, prominent skin tags, acanthosis nigricans around his neckline, and macroglossia (Figure 1). His jugular venous pressure was 12 cm, his lungs had diffuse crackles bilaterally, and the cardiac point of maximum impulse was laterally displaced. His cardiac rhythm was irregularly irregular; no murmurs, rubs, or gallops were evident, and 3+ pitting edema was noted below his knees, bilaterally.

Laboratory data were as follows: leukocytes, 4.3×10^3 cells/mm^3; hemoglobin, 13 g/dL; glucose, 81 mg/dL; troponin I, 0.11 ng/mL (reference, <0.05 ng/mL); brain natriuretic peptide, 606 pg/mL (reference, ≤100 pg/mL). A chest film showed cardiomegaly, an enlarged right heart border, and pulmonary vascular congestion (Figure 2A). Computed tomography of the chest demonstrated enlargement of all 4 cardiac chambers (Figure 2B). Transthoracic echocardiography showed preserved biventricular function, severe concentric left ventricular hypertrophy (septum, 2.7 cm; posterior wall, 2.6 cm), and massive atrial enlargement (left, 12 × 16 cm; right, 12 × 6 cm; Figures 3A and B). Cardiac catheterization identified elevated right and left heart pressures and mild narrowing of large-caliber (>4 mm in diameter) coronary arteries.

The findings pointed toward a diagnosis of acromegaly and associated cardiomyopathy. Further test results included growth hormone, 17.8 ng/mL (reference, 0.05-3 ng/mL), and for 2 separate samples, insulin-like growth factor-1, 700 and 771 ng/mL (reference, 81-225 ng/mL). A complete endocrine evaluation indicated that the patient had low testosterone and normal levels of luteinizing hormone, follicle-stimulating hormone, prolactin, and cortisol. Magnetic resonance imaging of the brain demonstrated a mild prominence at the left side of the pituitary gland, suggesting a 2-3-mm pituitary microadenoma. With additional questioning, the patient reported that his clothing and shoe sizes had increased over the previous decade; his shoe size went from 14 to 19, and he was unable to wear a cap on his head due to his enlarging forehead. This information further supported a diagnosis of acromegalic cardiomyopathy.

DIAGNOSIS

Acromegaly is rare, with a prevalence of 40 cases per million people. Slowly progressive enlargement of the face and extremities is accompanied by cardiac, rheumatologic, respiratory, and metabolic derangements tied to elevations in circulating growth hormone and insulin-like growth

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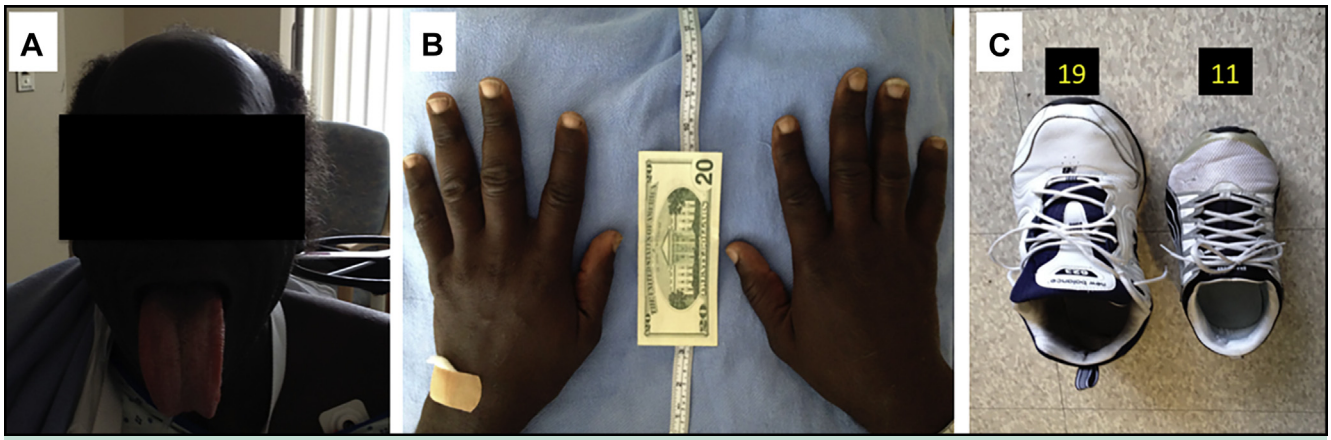

Figure 1 (**A**) The patient had bossing and macroglossia. (**B**) Swelling of the soft tissue, along with growth of the bone, cartilage, and muscle, produced enlargement of the hands. (**C**) The patient's shoe, size 19, is compared with a size 11 shoe.

factor-1.[1] Characteristic structural changes include thickening of the heart muscle and dilation of the ventricles, which contribute to diminished diastolic function. Anatomical changes are compounded by common comorbidities: hypertension, dyslipidemia, and insulin resistance. Hypertension results from the sodium-retaining effects of growth hormone, inhibition of atrial natriuretic peptide by insulin-like growth factor-1, and the increased peripheral vascular resistance triggered by both hormones. Altered hormonal function also changes the sympathoadrenomedullary pathway, promoting endothelial dysfunction, valvular disease, and acromegalic cardiomyopathy.[2] In addition, excess growth hormone increases production of proinflammatory mediators that degrade structural elements of the aortic and mitral valves, precipitating regurgitation. Finally, progressive myocardial fibrosis and involvement of the cardiac conduction system increase the risk for arrhythmias and conduction disorders.

Clinical manifestations of acromegalic cardiomyopathy depend on the degree and duration of cardiovascular dysfunction. Initially, cardiovascular dysfunction, propelled by the effects of growth hormone and insulin-like growth factor-1, is characterized by abnormally increased myocardial contractility and augmented cardiac output.[3] This early aberration likely put our patient in a hyperkinetic state during his stint as a college athlete. But a decade later, in the absence of any treatment, his once-normal myocardium was marked by interstitial fibrosis, collagen deposition, myofibrillar derangements, and monocyte necrosis, alterations that led to diastolic dysfunction and exertional intolerance.

Unfortunately, most patients fail to present until the third and advanced stage of acromegalic cardiomyopathy, when systolic dysfunction is superimposed on the preceding abnormalities, resulting in congestive heart failure.[4] Ambulatory monitoring demonstrates complex ventricular arrhythmias in about 50% of all patients with acromegalic

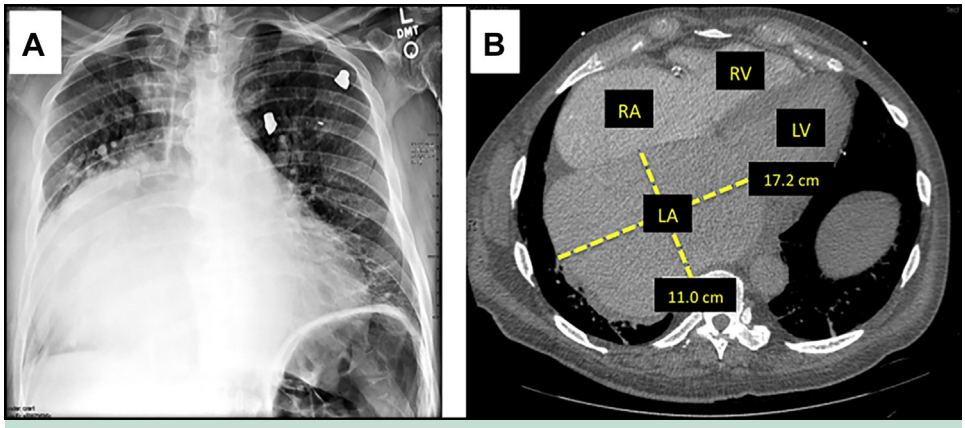

Figure 2 (**A**) This chest film showed severe cardiomegaly and pulmonary vascular congestion. The right border of the heart is prominent and obscures the right lung field. Two bullet fragments were found incidentally in the left lung field. (**B**) Computed tomography of the chest revealed enlargement of all 4 cardiac chambers. Notice the massive enlargement of the left atrium (LA). LV = left ventricle; RA = right atrium; RV = right ventricle.