

Case Study

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CHIEF COMPLAINT

A 63-year-old man with a history of hypertension and type 2 diabetes complains of a 12-hour history of upper lip swelling.

History of Current Illness

The patient was diagnosed with metabolic syndrome 7 years ago based on a waist circumference of 42 inches, a fasting plasma glucose (FPG) level of 108 mg/dL, and a blood pressure (BP) level of 134/86 mm Hg. He was initially treated with diet and exercise but was unable to sustain any significant weight loss. Four years ago, his BP was 144/92 mm Hg, and he was placed on the Dietary Approaches to Stop Hypertension (DASH) diet. However, his BP control continued to be inadequate, and 3½ years ago, he was started on lisinopril 5 mg/d. His lisinopril dose was titrated upward, and after it reached 20 mg/d, a low dose of hydrochlorothiazide, 12.5 mg/d, was added. For the past 1½ years, his BP has been consistently <130/80 mm Hg on the combination of lisinopril 40 mg/d and hydrochlorothiazide 12.5 mg/d.

He complains today of the onset of upper lip swelling that began last night. He states that his tongue feels normal, and he denies dysphagia, dyspnea, abdominal pain, or diarrhea. He reports that he has taken the same medications for the past year and denies taking aspirin or any other over-the-counter medication or herbal agent. He denies recent insect bites. He denies new food or drink. He denies changes of environment or recent travel.

Medical History

The patient has a 40-year history of psoriasis, a 5-year history of hypercholesterolemia and impaired fasting glucose, and a 4-year history of hypertension. He had an inguinal hernia repaired when he was 15 years of age. His current medications are lisinopril 40 mg/d, hydrochlorothiazide 12.5 mg/d, and atorvastatin 20 mg/d. He has no allergies. Review of systems is notable only for a history of erectile dysfunction and chronic insomnia.

Social History

The patient smoked 1 pack of cigarettes per day for 8 years but stopped >30 years ago. He reports regularly having a glass of wine with dinner.

Physical Examination

The patient is alert and oriented and is in no acute distress. BP is 124/77 mm Hg, pulse is 88 bpm and regular, respiration is 16 breaths/min, temperature is 36.4°C, and pulse oximetry is 97%. His weight is 210 lb, and his body mass index is 32 kg/m². Skin examination reveals the absence of urticaria. Head and neck examination is notable for a symmetrical swelling of the upper lip. His thyroid is normal without nodules. Lung, cardiac, and abdominal examinations are unremarkable. Examination of his feet reveals palpable pedal pulses and a mild hallux valgus deformity bilaterally. Neurologic examination is intact.

Laboratory Results

The patient's FPG is 115 mg/dL. His low-density lipoprotein cholesterol concentration is 90 mg/dL, high-density lipoprotein cholesterol concentration is 36 mg/dL, and serum triglyceride level is 210 mg/dL. His complete blood count with differential is normal. His thyroid-stimulating hormone level is normal. Subsequent laboratory tests revealed that serum tryptase and serum complement levels (C1q, C3, and C4) are normal.

DISCUSSION

Angiotensin-converting enzyme inhibitors (ACEIs) are one of the most commonly prescribed medications in the United States.¹ They are of proven value in patients with hypertension, diabetes, and congestive heart failure, as well as in patients with coronary heart disease with left ventricular dysfunction, and their first-line use has been recommended.²⁻⁵ It is thus no surprise that ACEIs were one of the top 5 classes of dispensed prescriptions in the United States in 2007, ranking only behind antidepressants, lipid regulators, and codeine and combination pain medications.⁶

Although cough is a more common adverse event,⁷⁻⁸ ACEI-associated angioedema, as seen in the case study, is a potentially life-threatening disorder that should not be overlooked. The incidence of this complication is estimated at 0.1% to 0.7%.⁹ Racial differences have been noted, with the risk of angioedema being 3- to 4-fold higher in African Americans and Asians than in the general population.²

The angioedema associated with ACEIs has been linked to a rise in bradykinin levels associated with inhibition of kininase II.^{9,10} Although more likely to occur early after initiation of therapy, this adverse reaction to ACEI use can start years after beginning treatment.^{7,10-12} Most commonly involving the lips and face,¹⁰ it can result in severe airway obstruction if it involves the tongue, neck, or posterior pharynx.

If angioneurotic edema develops, management includes discontinuation of the ACEI and maintenance of an adequate airway. If the airway is threatened, subcutaneous epinephrine is often prescribed. Antihistamine therapy represents the cornerstone of therapy, with systemic corticosteroids and possibly leukotriene antagonists playing an adjunctive role.¹³ A therapeutic agent that does not affect bradykinin should be substituted for the ACEI. Although theoretically angiotensin receptor blockers (ARBs) should not impact bradykinin, angioedema has been associated with the use of different ARBs. In light of this, caution has been advised when using ARBs in a patient with a history of ACEI-related angioedema.¹⁴

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