"I can'd tawk pwobbewy..."

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A 57-year-old black man presents with a grossly swollen tongue. The swelling began spontaneously about one hour before his arrival, and is progressing rapidly to the extent that he is now having difficulty speaking. He has no history of anaphylaxis, no known allergies, and is otherwise healthy. He does have mild hypertension, but it is being well-controlled with long-term hydrochlorothiazide, 12.5 mg/day, and enalapril, 5 mg/day. He has no stridor or respiratory distress, and his chest is clear to auscultation. He has no rash, and, apart from a largely swollen, slightly asymmetrical tongue, his examination is normal.

10% to 25% of angioedema can be ascribed to ACE inhibitor therapy.

Questions:

1. What is the most likely cause of his condition?
2. Why is he only getting it now?
3. What is the treatment?
4. What else is important?
5. What about angiotensin receptor blockers (ARBs)?

Answers:

1. What is the most likely cause of his condition?

He is suffering from acute angioedema. Although other causes of angioedema need to be excluded (contrast media, hereditary, *etc.*), this is most likely secondary to the angiotensin-converting enzyme (ACE) inhibitor he is taking.

Angioedema is a well-known side-effect of ACE inhibitors, with a reported incidence of 0.1% to 0.2%.[1] It has been shown that 10% to 25% of angioedema presentations can be ascribed to ACE inhibitor therapy.[1] The black population is at increased risk.

Angioedema generally presents as swelling of the lips, tongue, and airways, but it may also involve visceral tissue (see answer to question 4). Most of the time, the symptoms are mild and regress spontaneously, while the patient is still taking the medication. Because of this, many patients are not aware of this complication and continue taking the drug. Therefore, the reported incidence is likely underestimated. If the diagnosis is missed, recurrent and more severe episodes may occur, with potentially serious consequences.

2. Why is he only getting it now?

Clinical presentation is variable and unpredictable. Most cases were believed to occur in the first week of ACE inhibitor treatment, but reports have shown that late angioedema may be more common than previously thought.

Angioedema associated with ACE inhibitors is not believed to be an allergic reaction and can occur after many years of uneventful drug use. The exact pathogenesis is unclear, but appears to be related, at least in part, to bradykinins.

It is possible that this patient has had previous, unrecognized, minor episodes. What is paramount in this instance is recognizing the likely association with his ACE inhibitor, despite the fact that he has been taking it for many years.

3. What is the treatment?

The most important aspect of treatment is immediate withdrawal of the ACE inhibitor, with eventual institution of alternate therapy. In cases of acute angioedema, observation with symptomatic supportive therapy (if

required) is usually all that is necessary. It is recommended that patients be admitted and observed for 12 to 24 hours. Severe cases, involving significant tongue swelling or respiratory compromise, are treated with epinephrine, diphenhydramine, and steroids, although no controlled studies have demonstrated the efficacy of these treatments.[1] If the patient's blood pressure is low, intravenous fluids should be given. In emergent, life-threatening cases, airway management may be very difficult, and cricothyroidotomy may be indicated.

4. What else is important?

ACE inhibitors can also cause isolated visceral angioedema, a rarely reported complication. Patients present with episodes of recurrent abdominal symptoms. In one study, two women with recurrent severe abdominal pain, nausea, and vomiting actually underwent three unnecessary laparotomies, until cessation of their ACE inhibitors finally relieved their symptoms.

5. What about ARBs?

ARBs were not expected to produce angioedema; however, despite some controversy in the literature, it is now apparent that angioedema is also occasionally associated with ARBs. ARB-related angioedema may be more likely to occur in patients who have previously experienced angioedema while receiving ACE inhibitors. Therefore, starting someone on an ARB after an episode of ACE inhibitor angioedema should be done with extreme caution.

With about 35 to 40 million people worldwide taking ACE inhibitors, and their use increasing, we can probably expect the frequency of ACE inhibitor-related angioedema to rise dramatically. We should be prepared to recognize the various presentations of this troublesome, and potentially lethal complication. Dx

Reference

1. Vleeming W, van Amsterdam JG, Stricker BH, et al: ACE inhibitor-induced angioedema. Incidence, prevention, and management. Drug Saf 1998; 18(3):171-88.

This department covers selected points to avoid pitfalls and improve patient care by family physicians in the ED. Submissions and feedback can be sent to diagnosis@sta.ca.

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