Angioedema may not be a class side-effect of the angiotensin-converting-enzyme inhibitors

Sir,

Angioedema is a well-documented and potentially life-threatening side-effect of treatment with angiotensin-converting-enzyme (ACE) inhibitors, occurring in 0.1–0.2% of patients treated with these drugs.1 Given the growing number of patients with hypertension or heart failure treated with these drugs, and the long duration of treatment, the frequency of this complication is probably set to rise. Although most cases of angioedema occur within the first week of treatment, recent reports indicate that late-onset angioedema may be more prevalent than initially thought. This side-effect of ACE inhibitors is not an allergic reaction and can occur after many years of uneventful drug use.2 Black patients appear to be at increased risk.

We report the case of a 57-year-old Caucasian man, who was admitted to hospital because of severe dyspnoea. Clinical examination revealed intense swelling of the lips and the tongue that did not allow intubation, and emergency tracheotomy was performed to relieve airway obstruction. He had been treated for hypertension with an ACE inhibitor (ramipril 2.5 mg/day), with no side-effects over the last three years. His blood pressure was not well-controlled, however, and a family physician decided to change from ramipril to another ACE inhibitor (trandolapril 2.0 mg/day). Two days later, the patient presented with symptoms of angioedema.

Angioedema is a swelling involving the deeper layers of the skin or submucosal tissue, and usually presents as episodic attacks of swelling of the face, lips, tongue and airways, although it may also

References


Angioedema involves visceral tissues. If angioedema occurs in the upper airways it can become life-threatening; in the gastrointestinal tract it can become very painful. Two patients with recurrent severe abdominal pain, nausea and vomiting underwent three unnecessary laparotomies before the correct diagnosis was made. Angioedema associated with ACE inhibitors appears to be linked to the decreased degradation of bradykinin, because ACE not only converts angiotensin I to angiotensin II, but also inactivates bradykinin. Angioedema due to C1-inhibitor deficiency and ACE-inhibitor-related angioedema are the two forms of angioedema that result from a bradykinin-mediated increase in vasopermeability. Plasma bradykinin increases during acute angioedema in patients with hereditary C1-inhibitor deficiency, but is normal or marginally increased during remission. In three patients with a history of angioedema related to the use of ACE inhibitors, bradykinin levels were high during ACE inhibitor treatment. In another patient, the increased levels of bradykinin during an acute attack were decreased by 93% after withdrawal of the ACE inhibitor.

The appearance of angioedema with trandolapril in a patient previously uneventfully treated with ramipril shows that angioedema may not be a class side-effect of ACE inhibitors, and that safe treatment with an ACE inhibitor does not rule out the occurrence of angioedema with another drug of the same family. Patients should be advised to report mild and self-limited episodes, and physicians must stop the ACE inhibitor immediately. If the diagnosis is missed, recurrent and more severe episodes may occur, with potentially serious consequences.

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