capacity 83% predicted. During the preceding 5 years, the patient had required 2–3 monthly courses of intravenous anti-pseudomonal chemotherapy administered at home by an indwelling subcutaneous vascular access port. During a routine clinic review, the patient mentioned that her great-nephew had recently been diagnosed with cystic fibrosis (mutations Q43X and D1152H). Subsequent genetic testing of our patient revealed her to be a compound heterozygote for two recognized cystic fibrosis alleles: delta F508 and D1152H.

Delta F508 is the most common mutation worldwide and occurs in up to 80% of cystic fibrosis patients in the UK. D1152H is far less common, having first been identified in Ashkenazi Jews and Northern Europeans, with most data on this mutation arising from studies on infertile males.1 The many different phenotypes observed in cystic fibrosis are believed to relate to the effect of the specific mutation on the production of the cystic fibrosis transmembrane conductance regulator protein. Low values of the protein (class I mutations) are associated with severe disease, and intermediate values (class V) with mild disease.2–5 D1152H is a class IV mutation, and is generally associated with late presentation, mild pulmonary disease, pancreatic sufficiency, normal sweat chloride values and advanced survival.4,5

It is not common for cystic fibrosis to be diagnosed after adolescence, let alone beyond 60 years of age. Although the clinical implication in our patient was limited, her family has received appropriate genetic counselling. Moreover, despite the absence of extra-pulmonary symptoms, advanced age and other plausible causes of bronchiecasis being present (previous ‘chest infections’, tuberculosis and allergic bronchopulmonary aspergillosis), the diagnosis of cystic fibrosis was still made in this particular patient.

K. Carter
G.P. Currie
G. Devereux
Department of Respiratory Medicine
Aberdeen Royal Infirmary
Foresterhill
Aberdeen
email: graeme.currie@nhs.net

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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...

...
involve 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.

A. Karagiannis
A. Pyrpasopoulou
K. Tziomalos
M. Florentin
V. Athyros

Second Propedeutic Department of Internal Medicine
Aristotle University of Thessaloniki
Hippokration Hospital
Thessaloniki
Greece
email: astkar@med.auth.gr

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