**DISCUSSION**

Pulmonary capillary hemangiomatosis is an extremely rare lung condition. Only three cases\(^1\)\(^,\)\(^2\)\(^,\)\(^3\) have been described in the literature, of which one is doubtful. It is an extremely rare cause of pulmonary hypertension.\(^4\) The condition was first described by Wagenvoort.\(^5\) It can pose considerable diagnostic problems to the clinician and the histopathologist.

In this condition, abnormal blood vessels infiltrate the lung parenchyma, interlobular septa, bronchial walls and pleura. A secondary pulmonary veno-occlusive disease can be produced by the infiltration of the pulmonary veins and venules.

The physiology of the condition is precapillary hypertension which produces a restrictive ventilatory pattern.\(^6\) Pulmonary hypertension is invariably progressive and can be demonstrated by serial cardiac catheterizations. Normal pulmonary capillary wedge pressures will confirm that the obstruction is proximal to the large pulmonary veins.\(^7\) Open lung biopsy is often diagnostic.

The x-ray film was interesting in that it showed a reticuloonodular pattern that resembled pulmonary fibrosis, and also was mistaken for sarcoidosis. A similar pattern can be seen in mitral stenosis\(^8\) and pulmonary veno-occlusive disease. It has been attributed to longstanding interstitial edema and fibrosis.\(^9\)

In this case, the capillary hemangiomatosis affected the parenchyma of both lungs, bronchi, pleura and in addition, the pericardium, which has not been reported previously.

This unique case highlights some important aspects of pulmonary capillary hemangiomatosis: 1) an infantile heart in an adult may be a clue to congenital anomaly of both heart and lungs; 2) vascular abnormalities of pulmonary blood vessels may masquerade as diffuse interstitial lung disease and should be considered in the differential diagnosis;\(^3\) cardiac catheterization and pulmonary angiography are indicated if hemangiomatosis is considered in the differential diagnosis; 4) open lung biopsy is an important consideration, and may be diagnostic, although it is often confused with pulmonary veno-occlusive disease. If the angiomatous change is missed, the true nature of the lung malformation might also be missed.

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**Captopril-Induced Cough**

James K. Stoller, M.D., F.C.C.P.;*** Ahmed Elghazawi, M.D.;\(^\dagger\)
Atul C. Mehta, M.D., F.C.C.P.;\(^\ddagger\) and
Donald G. Vidt, M.D., F.C.C.P.\(^\ddagger\)

Since the advent of angiotensin-converting enzyme inhibitors (captopril and enalapril), cough has been recognized sporadically as a side effect, but has received little attention in the pulmonary literature. To emphasize that angiotensin-converting enzyme (ACE) inhibitors should be considered among possible etiologies of cough, we report recent experience with two patients and review the available experience with ACE inhibitor-induced cough.

Although cough is a common clinical pulmonary symptom and, in large series, is most frequently due to bronchitis, postnasal drip, or reactive airways disease,\(^1\)\(^4\) less common etiologies must sometimes be considered. Medications are rarely implicated as the cause of cough; however, recent experience with the angiotensin-converting enzyme (ACE) inhibitors (captopril and enalapril) suggests that these drugs may sometimes cause cough.\(^5\) Because the described experience is both sparse and not previously reported in the pulmonary literature, we have reviewed 17 previously described patients with cough due to angiotensin-converting enzyme inhibitors, and describe two patients with captopril-induced cough (Table 1).

**CASE REPORTS**

**Case 1**

A 59-year-old nonsmoking woman was referred to the Pulmonary Department for evaluation of a cough of 10 months' duration. She had been on therapy with both captopril 50 mg PO QD and Dyazide, one tablet PO 12 months before for treatment of hypertension. Two months after initiation of captopril therapy, the patient noted a cough which was productive of a scant amount of yellowish sputum. Previous evaluation had included a chest x-ray examination and spirometric tracing, both of which showed normal findings. On the presumption the patient had asthma, she was treated empirically with both a theophylline preparation and an inhaled beta agonist, without relief of her cough. With persistence of the cough for ten months, the patient was subsequently evaluated with a repeat chest x-ray examination and spirometry, including bronchodilator inhalation, both of which showed normal findings again. On the suspicion she had captopril-induced cough, captopril was discontinued and the patient was begun on therapy with metolol 50 mg PO, BID for hypertension. Within seven days of stopping captopril, the patient's cough completely subsided.

**Case 2**

A 58-year-old black woman was referred for pulmonary evaluation of a persistent, dry cough of one year's duration. Twelve months before evaluation, the patient had been started on therapy with captopril 50 mg PO QD for treatment of hypertension. Pulmonary evaluation included a chest x-ray examination, spirometry with

\(^*\)From the Departments of Pulmonary Disease, and Hypertension and Nephrology, The Cleveland Clinic Foundation, Cleveland.
\(^\dagger\)Staff Physician, Department of Pulmonary Disease.
\(^\ddagger\)Resident, Department of Internal Medicine.

Reprint requests: Dr. Stoller, Pulmonary Diseases, 9500 Euclid Avenue, Cleveland 44122
Table 1—Summary of 19 Patients with Cough Induced by an Angiotensin-Converting Enzyme Inhibitor

<table>
<thead>
<tr>
<th>Case</th>
<th>Author</th>
<th>Date</th>
<th>Patient Age, Gender</th>
<th>Associated Conditions</th>
<th>Angiotensin Converting Enzyme Inhibitor</th>
<th>Dose and Frequency</th>
<th>Duration of Use Before Cough (months)</th>
<th>Cough Workup</th>
<th>Rechallenged?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sesoko and Kaneko</td>
<td>1985</td>
<td>67, F</td>
<td>Nonsmoker</td>
<td>Captopril</td>
<td>12.5 mg TID</td>
<td>3</td>
<td>CXR normal</td>
<td>Yes; 2 rechallenges before cough each time</td>
</tr>
<tr>
<td>2</td>
<td>Semple and Herd</td>
<td>1986</td>
<td>47, F</td>
<td>*</td>
<td>Captopril</td>
<td>50 mg QD</td>
<td>*</td>
<td>*</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>Semple and Herd</td>
<td>1986</td>
<td>62, F</td>
<td>*</td>
<td>Enalapril</td>
<td>10 mg QD, ↑ to 40 mg QD</td>
<td>*</td>
<td>*</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>Semple and Herd</td>
<td>1986</td>
<td>53, F</td>
<td>Atenolol</td>
<td>Enalapril</td>
<td>10 mg QD</td>
<td>*</td>
<td>*</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>Mitchell et al.</td>
<td>1986</td>
<td>65, F</td>
<td>*</td>
<td>Captopril</td>
<td>25 mg to 37.5 mg QD</td>
<td>1</td>
<td>*</td>
<td>Yes; 2 rechallenges with recurrence each time</td>
</tr>
<tr>
<td>6</td>
<td>Mitchell et al.</td>
<td>1986</td>
<td>42, F</td>
<td>*</td>
<td>Captopril</td>
<td>25 mg BID, ↑ to 300 mg QD</td>
<td>2</td>
<td>*</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>Caruthers</td>
<td>1986</td>
<td>61, F</td>
<td>Gold-induced interstitial pneumonitis</td>
<td>Propranolol</td>
<td></td>
<td>12</td>
<td>Spirometry normal Diffusing capacity normal Gallium scan of chest normal UGI without reflux</td>
<td>Yes; 3 challenges with recurrence each time</td>
</tr>
<tr>
<td>8</td>
<td>Alvarez et al.</td>
<td>1986</td>
<td>44, F</td>
<td>Scleroderma</td>
<td>Captopril</td>
<td>12.5 mg TID</td>
<td>1</td>
<td>CXR normal Spirometry normal Diffusing capacity normal</td>
<td>Yes; 1 rechallenge with recurrence</td>
</tr>
<tr>
<td>9</td>
<td>Hallwright</td>
<td>1986</td>
<td>46, F</td>
<td>Nonsmoker</td>
<td>Enalapril</td>
<td>20 mg QD</td>
<td>7 days</td>
<td>*</td>
<td>Yes; 1 rechallenge with recurrence</td>
</tr>
<tr>
<td>10</td>
<td>Hallwright</td>
<td>1986</td>
<td>60, F</td>
<td>*</td>
<td>Enalapril</td>
<td>10 mg QD</td>
<td>3 days</td>
<td>CXR normal Spirometry normal Methacholine normal</td>
<td>No</td>
</tr>
<tr>
<td>11</td>
<td>McNally</td>
<td>1987</td>
<td>59, M</td>
<td>*</td>
<td>Captopril</td>
<td>75 mg to 300 mg QD</td>
<td>2</td>
<td>CXR normal Spirometry normal Methacholine normal</td>
<td>Yes; 1 rechallenge with recurrence within 24 hours of stopping captopril</td>
</tr>
<tr>
<td>12</td>
<td>McNally</td>
<td>1987</td>
<td>25, F</td>
<td>Propranolol</td>
<td>Captopril</td>
<td>75 mg QD</td>
<td>*</td>
<td>*</td>
<td>No</td>
</tr>
<tr>
<td>13</td>
<td>McNally</td>
<td>1987</td>
<td>63, M</td>
<td>Former smoker</td>
<td>Captopril</td>
<td>75 mg to 100 mg QD</td>
<td>*</td>
<td>*</td>
<td>No</td>
</tr>
<tr>
<td>14</td>
<td>McNally</td>
<td>1987</td>
<td>56, F</td>
<td>Cardiomyopathy</td>
<td>Captopril</td>
<td>37.5 mg to 100 mg QD</td>
<td>3</td>
<td>*</td>
<td>No</td>
</tr>
<tr>
<td>15</td>
<td>McNally</td>
<td>1987</td>
<td>70, F</td>
<td>*</td>
<td>Captopril</td>
<td>50 mg QD</td>
<td>Several weeks</td>
<td>*</td>
<td>No</td>
</tr>
<tr>
<td>16</td>
<td>McNally</td>
<td>1987</td>
<td>72, F</td>
<td>Congestive heart failure Mitral valve regurgitation</td>
<td>Captopril</td>
<td>75 mg</td>
<td>*</td>
<td>*</td>
<td>No</td>
</tr>
<tr>
<td>17</td>
<td>McNally</td>
<td>1987</td>
<td>63, F</td>
<td>Questionable asthma</td>
<td>Captopril</td>
<td>75 mg</td>
<td>2</td>
<td>CXR normal Spirometry normal Methacholine broncho-provocation normal Bronchoscopy normal</td>
<td>No; cough remitted within 7 days of stopping captopril</td>
</tr>
<tr>
<td>18</td>
<td>Current series</td>
<td>1987</td>
<td>50, F</td>
<td>Nonsmoker</td>
<td>Captopril</td>
<td>50 mg QD</td>
<td>12</td>
<td>CXR normal Spirometry normal Methacholine broncho-provocation normal Bronchoscopy normal</td>
<td>No; cough remitted within 3 days of stopping captopril</td>
</tr>
<tr>
<td>19</td>
<td>Current series</td>
<td>1987</td>
<td>58, F</td>
<td>Nonsmoker</td>
<td>Captopril</td>
<td>50 mg QD</td>
<td>12</td>
<td>CXR normal Spirometry normal Methacholine broncho-provocation normal Bronchoscopy normal</td>
<td>No; cough remitted within 3 days of stopping captopril</td>
</tr>
</tbody>
</table>

*Not reported
bronchodilator inhalation, methacholine challenge, and bronchoscopy, all of which gave normal findings. Therapy with captopril was discontinued, and within three days, the patient's cough had completely subsided. Follow-up three months later showed that the cough had not returned. Rechallenge with captopril was not performed.

**DISCUSSION**

With the advent of the angiotensin-converting enzyme (ACE) inhibitors, cough has been recognized as a complication of both captopril and the newer agent, enalapril. The investigational ACE-inhibitor, cilazapril, has also been implicated. Prevalence estimates for ACE inhibitor-induced cough vary widely among series. For captopril, the largest available series (N = 4,949) suggests a prevalence of 0.7 percent among captopril recipients, though estimates from smaller series are higher (6 percent and 16.7 percent), perhaps reflecting the effects of patient selection or referral. For enalapril, even fewer prevalence estimates are available; data from pharmaceutical companies suggest a prevalence rate of 1.3 percent among 2,677 enalapril recipients (vs 0.9 percent reported in placebo recipients), and Hallwright et al report that up to 10 percent of their enalapril recipients have experienced cough. The preliminary report of cilazapril-induced cough suggests a prevalence of 23.3 percent (7/30).

Though the literature alludes to a total of 93 patients with captopril and/or enalapril-induced cough, clinical descriptions are available for only 19 (present cases included) and are summarized in Table 1. Other potential causes of cough (including smoking, possible asthma, interstitial pneumonitis, and use of beta-blockers, which can produce cough in patients with airway obstruction or congestive heart failure) were present in nine of the 19 patients, but the only maneuver associated with the long-term cessation of cough in all 19 patients was discontinuation of the ACE inhibitor, captopril (15 patients) or enalapril (four patients). Also, extensive work-up of other causes of cough in at least six of the patients (cases 7, 8, 11, 12, 18, 19) was unrevealing, and rechallenge with the ACE inhibitor was performed in eight of the 19 patients with prompt return of cough in all. Notably, in one patient with captopril-induced cough, rechallenge with enalapril also reproducibly caused cough, demonstrating crossover toxicity. Onset of cough after starting an ACE inhibitor ranged from three days (case 10) to 12 months (cases 7 and 19), and cessation of cough after discontinuation of the drug was as early as one day (case 11) and no longer than four weeks (case 7). Notably, most of the patients described (83 percent, or 20/24 patients whose gender is reported) are women.

While some investigators have speculated that captopril causes cough by either a hypersensitivity mechanism or by accumulation of bradykinin and/or prostaglandin, others speculate that, like beta-blockers, captopril may produce cough by unmasking clinically latent asthma. While experience with these 19 patients does not clarify the pathogenetic mechanism, the absence of airway hyperreactivity in three of the 19 patients (cases 11, 13 and 19) argues against unmasked asthma as the sole cause of captopril-induced cough. The occurrence of captopril-induced cough in a father and daughter pair also raises the possibility of a genetic disposition.

With the availability and widespread use of newer ACE inhibitors, chest physicians may encounter ACE inhibitor-induced cough with increasing frequency.

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**Acute Cardiac Tamponade due to Cardiac Actinomycosis**

**John J. Orloff, M.D.;† Michael J. Fine, M.D.;‡ and John D. Riha, B.S.‡**

Cardiac actinomycosis occurs in less than 2 percent of the patients with infections due to Actinomyces israelii. We describe the findings in a patient with acute cardiac tamponade who survived through pericardial drainage and aggressive medical therapy. Although uncommon, this disorder is important to recognize because it is curable with current medical and surgical therapy.

*From the Department of Medicine, University of Pittsburgh, and the Oakland Veterans Administration Medical Center, Pittsburgh.†Instructor in Medicine.‡Microbiologist, Oakland VA Medical Center.