Stump neuromas usually occur within one year of surgery and have no malignant potential. They are most commonly asymptomatic, but symptoms occasionally occur, particularly after interscapulothoracic amputation. The frequency of symptoms following this procedure may be because the divided nerve end is covered by only a thin layer of skin and subcutaneous tissue rather than muscle as at other amputation sites. Because the nerve is relatively unprotected, it is easily irritated, leading to symptoms.

Our case is unusual in that the amputation neuroma was visualized on a chest roentgenogram. While neural tumors are a fairly common cause of pleural or chest wall masses on chest roentgenograms, an extensive review of the AFIP experience with neural tumors of the thorax did not note any cases of amputation neuroma. Visualization of this patient's tumor is explained by the fact that the brachial plexus passes just anterior to the cupola of the lung, and as the amputation neuroma grew, it pushed into the lung. The intact pleura and Sibson's fascia between the mass and the lung account for the stump neuroma's smooth margins and obtuse angles. The CT features of stump neuroma have been described and include focal or generalized change in the caliber, size, or contour of the nerve trunk in the stump limb compared with the normal limb.

The diagnosis of stump neuroma should be considered whenever pain or a mass occurs at the amputation site. Unfortunately, in the case of amputation for cancer, pain and a mass may also indicate recurrent tumor. Some patients may have both; in one series approximately 8 percent of patients had recurrent cancer concomitantly with stump neuroma, and 32 percent developed recurrent tumors following excision of a neuroma.

Although the clinician or radiologist may be able to suggest the diagnosis of stump neuroma, surgery is usually required for diagnosis, because needle biopsy of suspected sarcoma may be misleading, as in this case. Treatment is high ligation and amputation of the involved nerve. In noncancer patients, conservative management such as local heat and massage may be all that is needed.

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Captopril-Induced Hypersensitivity Lung Disease*
An Immune-Complex-mediated Phenomenon
Phyllis L. Schatz, M.D.;† Dean Mesalogites, M.D.;† Jason Hyun, M.D.;‡ G.J. Walker Smith, M.D.¶ and Bimalin Lahiri, M.D., F.C.C.P.*

Captopril has not yet been included in the list of drugs causing hypersensitivity lung disease. We report a patient with hypertension, congestive heart failure, and chronic renal failure who, when rechallenged with captorpl, developed upper lung field infiltrates associated with productive cough and striking peripheral eosinophilia. Gallium scan, transbronchial biopsy histologic findings, and direct immunofluorescent study were consistent with an immune-complex-mediated hypersensitivity reaction. There was no other etiology discovered for the patient's eosinophilia, nor was there evidence for an infectious etiology to explain his presentation.

(Chest 1989; 95:685-87)

The list of agents implicated in drug-induced pulmonary disease is expanding rapidly, and a recent comprehensive review by Cooper et al. describes the many clinical aspects and pathogenic mechanisms involved. One method of injury involves a hypersensitivity reaction with peripheral and/or pulmonary eosinophilia. It has been suggested that the syndrome involves alterations in the normal immune balance of the lung, or a hyperacute reaction to the drug which acts as a precipitating antigen. Hypersensitivity lung disease has been reported secondary to a variety of cytotoxic and noncytotoxic drugs, but captorpl has not yet been included on this list. The following case describes such a complication of captorpl therapy.

CASE REPORT

A 77-year-old man with a history of hypertension, chronic renal failure, and congestive heart failure was admitted six weeks after AAA resection with a productive cough. He was treated in the past with captorpl and had developed a transient rash, but captorpl was continued for over two years until angio graphic precipitated acute tubular necrosis. Captorpl was discontinued; the resection was postponed two months; subsequent course was uneventful. Four days prior to the present admission, captorpl was restarted at his prior dose of 25 mg. t.id. On the following day, he developed a cough productive of light green sputum, and three days later, an evanescent nonpruritic erythematous macular rash. He denied fever, chills, or dyspnea. He was a 60 pack-year smoker with abstinence for the past three years. Medications were captorpl and furosemide, 40 mg daily, which he had been taking on a long-term basis.

On physical examination, he was afebrile, in mild distress, with a respiratory rate of 20 and a blood pressure of 178/100 mm Hg.

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as the infiltrates and eosinophilia preceded ampicillin treatment. The patient continued his ongoing Lasix therapy, but captopril and ampicillin were discontinued. Gallium scan on day 5 demonstrated increased activity throughout both lung fields. The patient's fatigue and productive cough continued and the eosinophil count reached a peak of 65 percent of 32,000. Transbronchial biopsy of the left upper lobe on day 9 (Fig 2) revealed patchy areas of fibrosis and an interstitial eosinophilic infiltrate. Direct immunofluorescent study (Fig 3) was consistent with an immune-complex-mediated lesion. Serum IgE returned at 970 U/ml (normal 22.5 to 103).

Prednisone, 1 mg/kg-day, was started on day 11, and within two days, the patient's appetite improved, cough decreased, and eosinophilia disappeared. Chest x-ray film on day 15 returned to baseline. He was discharged from the hospital on a tapering dose of prednisone. Chest x-ray film has remained at baseline throughout the subsequent year.

A comprehensive search for other etiologies for the patient's eosinophilia was negative including stool for ova and parasites, titers for Toxocara, typhoid H, O, paratyphoid A & B, Aspergillus fumigatus, niger, and flavus (agar gel), and Bentonite flocculation test for trichinosis. Bone marrow biopsy was negative for eosinophilic myeloproliferative disorder. Cultures of blood, urine, and sputum were negative for bacterial pathogens, as were sputum and bronchial washings for AFB smear and culture, DFA for Legionella and Legionella culture. The CMV titers were consistent with past exposure.

**Discussion**

Although a wide differential was initially considered, the most striking clinical aspect of this patient's course was the rapid onset of cough and rash following reinstitution of captopril, most consistent with a hypersensitivity drug reaction. The 67Ga scan revealed more diffuse involvement than could be appreciated on plain chest roentgenogram. Of interest was the predominance of the upper lung field infiltrates despite the centrilobular emphysema and hyper-inflation expected in this 77-year-old with significant smoking history.

This case is distinguished on clinical grounds from the pulmonary infiltrates with eosinophilia as classified by Crofton (Table 1) which include the following: (a) simple pulmonary eosinophilia ("Loeffler's syndrome") character-
Pulmonary infiltrates with Eosinophilia

Simple pulmonary eosinophilia (Loeffler’s syndrome)
Prolonged pulmonary eosinophilia
Pulmonary eosinophilia with asthma
Tropical eosinophilia
Eosinophilia associated with allergic granulomatosis and angitis (Churg and Strauss)
Chronic eosinophilic pneumonia (Carrington)
Hypersensitivity reaction (drugs, fungi, parasites)

...ized by wandering infiltrates with minimal symptoms; (b) prolonged pulmonary eosinophilia which may be accompanied by high fever and productive cough; (c) pulmonary eosinophilia with asthma; (d) tropical eosinophilia; (e) pulmonary eosinophilia associated with allergic granulomatosis and angitis (Churg and Strauss). Our patient had no history of asthma, residence in the tropics, or evidence of systemic vasculitis. Carrington et al described a chronic eosinophilic pneumonia presenting with high fever, night sweats, weight loss, and dyspnea. The chest x-ray film was uniquely described as rapid progression of dense, lateralizing pneumatic infiltrates sparing the hilum and referred to as the “photographic negative” or “reverse” of pulmonary edema. Histologic findings on lung biopsy revealed interstitial infiltrates of histiocytes, lymphocytes, eosinophils and occasional plasma cells with characteristic flooding of the alveoli predominantly by eosinophils, but including macrophages and multinucleated histiocyctic giant cells, many containing Charcot-Leyden crystals.

Predominant histologic features on our patient's transbronchial biopsy were patchy areas of fibrosis, along with spindle cells and immature connective tissue, suggesting an active process of injury with ongoing repair. There was no evidence of granuloma formation or vasculitis. The absence of cellular intra-alveolar exudate, specifically eosinophils or histiocytes, distinguishes this case from the chronic eosinophilic pneumonia of Carrington et al. The differential diagnosis based on our patient's biopsy would include asthma (excluded by history), hypersensitivity reaction to parasites, fungi (excluded by special stains, cultures, and serology), and eosinophilic drug reaction.

Direct immunofluorescent study of the transbronchial biopsy as shown in Figure 2 is consistent with an immune-complex-mediated lesion. The intense reaction with anti-IgE conjugate is strongly suggestive of hypersensitivity, as such a pattern is not seen secondary to bacterial or viral etiologies. Reactions with anti-IgM and -IgG are evidence of the primary and secondary immune response, while the reaction with anti-C1q was considered a significant part of an immune-complex-mediated lesion. Reactivity with anti-C3 and -C4 indicates involvement of the classic pathway of complement activation. The cells were not reactive with antiproteinid.

Adverse reactions to captopril have included neutropenia, pruritic rash sometimes associated with peripheral eosinophilia, proteinuria, angioedema, and one case of laryngeal edema. Sosoko and Kaneka reported a case of nonproductive cough which developed with captopril treatment, subsided with discontinuation and reappeared with challenge. Semple and Herd observed patients who developed cough due to captopril and enalapril, as well as an additional patient in whom enalapril exacerbated symptoms of bronchial asthma. Additional case reports are now appearing in the literature.

This case represents the first report of a captopril-induced hypersensitivity lung disease. The pneumonitis is associated with peripheral eosinophilia characterized by an eosinophilic interstitial infiltrate with evidence by immunofluorescent staining of immune-complex mediated activation of the classic pathway of complement.

We have recently followed a second patient with advanced chronic obstructive lung disease, congestive heart failure, and chronic renal failure who, when restarted on captopril, developed peripheral eosinophilia and new upper lung field infiltrates. Although no biopsy was done, hypersensitivity reaction to captopril was suspected, and the patient responded to discontinuation of captopril and institution of prednisone therapy.

Captopril therapy often results in significant clinical improvement because of its actions as an antihypertensive, afterload-reducing agent, and angiotensin-converting enzyme inhibitor. The incidence of proteinuria and neutropenia agranulocytosis, the most common adverse reactions, seem to be increased in the presence of preexisting renal disease. The possible relationship between captopril-induced hypersensitivity lung disease and chronic renal failure remains to be explored.

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Postobstruction Pulmonary Edema*

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