insufficient to prevent the late recurrence of the spasm because of nitroglycerin's short pharmacologic action. Therefore, the use of a combination of intracoronary nitroglycerin and sublingual long-acting nitrates is, in our opinion, advisable if intense and prolonged neutralization of ergonovine action is desired.

Observation of the patient for 15 min after the last dose of ergonovine is recommended by some authors7 who observed rare cases of recurrence of coronary spasm up to 10 min after induced spasm. Our report suggests that, especially in the case of a strongly positive test, observation of the patient in the catheterization laboratory has to be prolonged even when successful neutralization of spasm has been achieved, because it can recur several minutes later.

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Hilar and Mediastinal Lymphadenopathy with Hypersensitivity Pneumonitis Induced by Penicillin*

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A 54-year-old Japanese man demonstrated a sultamicillin-induced hilar and mediastinal lymphadenopathy with hypersensitivity pneumonitis. A positive lymphocyte stimulation test for sultamicillin and a decreased CD4/CD8 ratio of lymphocytes in BAL fluid suggested that an alteration in cell-mediated mechanisms was responsible for the patient's symptoms. (Chest 1992; 102:1907-09)

Sulbactam, a derivative of the basic penicillin nucleus, inhibits β-lactamase. The use of sulbactam in combination with β-lactamase-sensitive antibiotics can potentiate its effect. Based on this concept, sultamicillin tosylate (Unasyn), a prodruk double ester of ampicillin and sulbactam joined via a methylene linkage, has been developed.

Pulmonary hypersensitivity to antibiotics has been reported to manifest interstitial pneumonitis or eosinophilic infiltrates.1 In this report, we describe a rare case of sultamicillin-induced pulmonary disease in which the prominent manifestation was hilar and mediastinal lymphadenopathy.

CASE REPORT

A 54-year-old Japanese male office worker was referred to Tokyo Medical College Hospital on November 7, 1990, for evaluation of hilar enlargement on a chest roentgenogram. In mid-October 1990, sultamicillin, an antitussive, and an antinflammatory drug were prescribed because of fever (about 40°C) and a nonproductive cough. A mild skin rash appeared mainly on the trunk two days after the medication was initiated, and all drugs were discontinued. On October 30, complaining of occasional cough and low-grade fever, he visited another physician. Coincidentally, sultamicillin was again prescribed along with a mucolytic agent (Mucomil). On October 31, a marked pruritic skin rash became prominent over the entire body, and sultamicillin was discontinued. On November 1, he started to complain of exacerbated cough and sense of fever. Although the skin eruptions gradually improved, bilateral hilar enlargement appeared on a chest roentgenogram on November 2 and became distinctive on November 6. The patient did not sense significant respiratory distress during this period, although a temporal visual disturbance occurred twice in the left eye. In addition to the above-mentioned drugs, he had taken cetirizine (Tagamet) for the treatment of gastritis for about two months before this episode.

His medical history revealed the patient suffered from pulmonary tuberculosis at the age of 27 years. He occasionally felt mild paresthesia of the tongue after oral penicillin. An elder brother had previously developed penicillin anaphylaxis and shock.

On physical examination, the skin over the patient's entire body demonstrated a mild urticaria-like rash. On the forehead, the skin over the temporal artery was particularly reddish and edematous bilaterally. The supravacular, axillary and inguinal lymph nodes were swollen but not tender. Auscultation of the lungs revealed a small amount of fine crackles in the bilateral basilar area. Cardiac examination was unremarkable. The edge of the liver was palpated 3 cm below the costal margin. The spleen was not palpable. Urine examination was normal. Complete blood cell counts showed leukocytosis (9,000/cu mm) with significant eosinophilia (34 percent) and atypical lymphocytes (4 percent). Although it was 3,300/cu mm two months earlier, the lymphocyte count ranged from 1,800 to 2,400/cu mm during admission. (It recovered to 3,500/cu mm after

EB = Epstein-Barr (virus); LST = lymphocyte stimulation test; PPD = purified protein derivative; SI = stimulatory index; TBLB = transbronchial lung biopsy

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Comprised percent (recovery) was noted. Newball, 2 ing NSE the gram negative. results, 2). A CT scan confirmed hilar and mediastinal lymphadenopathy (No. 3, 6, 10, 11) and interstitial shadow at the lung bases (Fig 2). A 14Ga-scan showed uptake in the hilar regions. Electrocardiogram findings were within normal limits. Pulmonary function test results, including carbon monoxide diffusing capacity, were within the normal range. Purified protein derivative (PPD) test was negative. Sputum examination for bacterial and mycotic infection was negative, and spumum cytology revealed class 2. Antibody for HIV was negative. Titers of Epstein-Barr (EB) virus-related antibodies were not suggestive of a primary EB virus infection (EB viral capsid antigen IgM <1:10, IgG 1:20, EB early antigen IgG<1:10, EB nuclear antigen 1:40). The tumor markers, CEA,NSE and CA19-9, were not increased. Serum angiotesin-converting enzyme activity was normal. Although rheumatoid factor and antinuclear antibody (speckled type) were positive, anti-DNA, anti-RNP, and anti-Sm antibodies were negative.

Bronchoscopy was performed with a flexible fiberoptic instrument (Olympus BF-1T10) on November 15. Bronchoalveolar lavage was performed according to the modified technique of Reynolds and Newhall, 2 using a total of 150 ml of sterile saline solution (70 percent recovery). The BAL fluid cell count was 5 x 10 6 cells/ml, with 35 percent macrophages, 60 percent lymphocytes, 3 percent neutrophils, and 2 percent eosinophils. The CD4 and CD8 positive cells comprised 14.5 and 35.7 percent of lymphocytes, respectively, and the CD4/CD8 ratio was 0.41. A transbronchial lung biopsy (TBLB) revealed minimal inflammatory cell infiltration with mild alveolar cell proliferation.

A lymphocyte stimulation test (LST) for sulfamicillin, sulbaetam, ampicillin, and cimetidine, expressed as stimulatory index (SI), 3 yielded values of 7.47, 5.94, and 2.04, and 1.14, respectively.

After the discontinuation of all drugs, the patients symptoms including hilar and superficial lymphadenopathy, peripheral eosinophilia, the presence of atypical lymphocytes, and an increase in discharge.) C-reactive protein value was 2.9 mg/dl, and erythrocyte sedimentation rate was 99 mm/1 h. Complement level was normal. Blood chemistry revealed a slight increase in SGOT and biliary duct enzymes. A moderate increase in values for IgG (2,700 mg/dl) and IgE (731 IU/ml) was noted. A chest roentgenogram and tomogram on admission showed marked hilar and tracheobronchial lymphadenopathy with mild granular opacities in the lower lung fields (Fig 1). (A chest roentgenogram two months earlier was normal.) A CT scan confirmed hilar and mediastinal lymphadenopathy (No. 3, 6, 10, 11) and interstitial shadow at the lung bases (Fig 2).

Figure 1. Chest roentgenogram on admission. Hilar lymphadenopathy was remarkable. Right tracheobronchial lymphnode was pal- pated. Fine granular opacities were seen to a mild degree in the bilateral lower lung fields.

IgG were steadily improved, and the patient returned almost to normal at discharge on November 21, 1980. A chest roentgenogram on December 6 showed no hilar enlargement. At an examination ten months later, the patient was well and had no complaints. His PPD test became positive (20 x 32 mm). The IgE value was normal and antinuclear antibody became negative. However, some EB virus-related IgG antibodies showed significantly increased titers (EB viral capsid antigen IgG 1:320, EB early antigen IgG<1:10, EB nuclear antigen 1:160), which may be suggestive of a reactivation of the EB virus.

**DISCUSSION**

Based on his clinical course, a positive LST for sulfamicillin, and other laboratory data, our patient was diagnosed as having a sulfamicillin-induced pulmonary reaction. Drug-induced pulmonary diseases are classified into the following two categories: those due to cytotoxic drugs and those due to noncytotoxic drugs. 1 In pulmonary disease caused by noncytotoxic drugs, interstitial pneumonitis associated with eosinophilic infiltrates is a common feature. 1 Except for cases involving anticonvulsants such as hydantoin and carbamazepine, 1 we know of no other patient who presented with significant hilar and mediastinal lymphadenopathy due to antibiotics. In the current patient, lymphadenopathy on a chest roentgenogram and CT scan was the most noticeable manifestation. In contrast, hypersensitivity pneumonitis,
evidenced by BAL fluid cell analysis, was less prominent, because fine nodular opacities in the bilateral lower lung on chest roentgenogram and CT scan were modest, and a transbronchial lung biopsy demonstrated subtle inflammatory cell infiltration with mild alveolar septal thickening.

The differential diagnosis for this patient includes sarcoidosis, malignant lymphomas, and viral infection such as EB virus. Sarcoidosis was unlikely because of normal angiotensin-converting enzyme activity, lack of uveitis, no evidence of granuloma in the TBLB specimen, and a rapid recovery of lymphadenopathy without steroid therapy. It has been reported that infectious mononucleosis rarely causes hilar lymphadenopathy. However, no evidence of a primary EB virus infection could be found. Although lymph node biopsy was not performed, spontaneous symptomatic improvement after the discontinuation of all drugs did not suggest malignant lymphomas.

The LST is a useful and reliable measure for the diagnosis of drug allergy and drug-induced hepatitis. The test for sulbactam and sulbactaminulin demonstrated a markedly increased SI (sulbactam 5.94, sulbactaminocillin 7.47), whereas the SI for ampicillin was 2.04. Therefore, the sulbactam in sulbactaminocillin was probably the responsible substance for the hypersensitivity reaction. Ampicillin may also be implicated in this episode, since its SI of 2.04 could be considered positive, and the patient claimed past sensitivity to penicillin.

Despite lymphocyte blastogenesis as suggested by a positive LST for sulbactaminocillin and the presence of atypical lymphocytes, the relative lymphopenia occurred in the peripheral blood. The lymphocytosis in the BAL fluid was remarkable. This finding suggests that the lymphocyte sequestration occurs in the lungs, similar to the situation in active sarcoidosis. However, the decrease in the CD4/CD8 ratio in the BAL fluid lymphocytes observed in our patient is not common in sarcoidosis and is compatible with typical pulmonary hypersensitivity due to amiodarone, gold, or antibiotics, in which hilar or mediastinal lymphadenopathy has not been described. Therefore, the detailed pathogenesis of sulbactaminocillin-induced hilar lymphadenopathy remains largely unclear. However, it is worthwhile to note the possible reactivation of EB virus, the transient appearance of antinuclear antibody, and the positive PPD test results that occurred after the recovery. These observations support the notion that an alteration in cell-mediated immune mechanisms is related to the clinical manifestations of this patient.

NOTE: Sulbactaminocillin tosylate (Unasyn in the oral form) is available in 17 countries including Japan. In some countries, Unasyn is delivered as a mixture of ampicillin sodium and sulbactam sodium.

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Giant Thoracoabdominal Lymphangioma with Features of Lymphangiomyoma*

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A 15-year-old girl who presented with cough and dyspnea was found to have a mediastinal tumor that clinically resembled a lymphangioma. The tumor was unusual for its large size and its histologic features, which showed smooth muscle proliferation, generally considered a feature of lymphangiomyoma. (Chest 1992; 102:1909-11)

The two hamartomas of lymphatic origin that may present as tumors of the mediastinum and retroperitoneum are lymphangioma and lymphangiomyoma. We report an unusual tumor that had features of an intermediate abnormality between lymphangioma and lymphangiomyoma.

CASE REPORT
The patient, a 15-year-old girl, was admitted to the hospital in December 1990 for evaluation of recurrent cough and expectoration since the age of 4 years. A chest roentgenogram in June 1986 showed mediastinal widening with right paracardiac and left parahilar opacities. Results of investigations were normal except for a 50 percent reduction in vital capacity. She underwent an open lung biopsy in July 1986 with a presumptive clinical diagnosis of sarcoidosis. A right thoracotomy was performed and a wedge biopsy specimen was taken from the inferior margin of the right middle lobe. At surgery, reddish cystic swellings were seen at the right hilum that yielded hemorrhagic fluid on aspiration. No biopsy of the hilar tumor was attempted. The lung biopsy specimen showed areas of atelectasis devoid of granulomas, smooth muscle proliferation, or cystic change.

At the time of present hospital admission, she complained of an increase in cough for five months, persistent hemoptysis, two episodes of hematemesis, and class 2 dyspnea on exertion. She was...

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