Syphilitic Pneumonitis in an HIV-Infected Patient

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Pneumonitis and symptomatic hepatitis are very rare complications of syphilis. Symptomatic hepatitis and subclinical reticulonodular pulmonary infiltrates were observed when an HIV-infected patient presented with secondary syphilis. The Jarisch-Herxheimer reaction included a flare of hepatitis symptoms, resembling cholangitis. In a patient with syphilis, it may be appropriate to delay an aggressive evaluation for suspected pneumonitis or cholangitis pending the outcome of specific antitreponemal therapy.

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\[ ALP = \text{alkaline phosphatase; RPR = rapid plasma reagin} \]

Syphilitic involvement of the lung has received scant attention in the literature. While pulmonary gummas and congenital pulmonary syphilis have been historically recognized, the occurrence of a pneumonitis during secondary syphilis has been either ignored or specifically refuted as not existing. Recent reports suggest that such an entity exists, however; no patients were known to have human immunodeficiency virus (HIV) coinfection. We report the appearance of subclinical bilateral pulmonary infiltrates in a patient with early HIV infection.

Symptomatic syphilitic hepatitis was also seen in our patient. A local exacerbation, resembling cholangitis, occurred during a treatment-related Jarisch-Herxheimer reaction. Although local flares in involved organs are common in Jarisch-Herxheimer reactions, symptomatic exacerbation of hepatic disease has not previously been reported, to our knowledge.

CASE REPORT

A 37-year-old HIV-seropositive man, Walter Reed Stage II A, presented with a 1-day history of abdominal pain and nausea. A pruritic rash had appeared the day before the abdominal pain started. He denied pulmonary symptoms.

His temperature was 37.6°C. A diffuse macular rash, more prominent on the palms and soles, was observed. Several resolving painless ulcers were noted on the penis. Prominent inguinal adenopathy was palpable, as well as minimal diffuse adenopathy that may have been unchanged from baseline. The abdomen was normal, as was the rest of the examination.

A complete blood cell count was normal. Both the rapid plasma reagin (RPR, at 1:512) and the fluorescent treponemal antibody-absorbed (FTA-ABS) were positive. A chest radiograph revealed bilateral reticulonodular infiltrates (Fig 1). The aspartate aminotransferase was 206 U/L (nl < 37), the alkaline phosphate (ALP) was 892 IU/L (nl < 126), the γ-glutamyl transpeptidase was 643 IU/L (nl < 50), and the total bilirubin was 1.6 mg/dl (nl < 1.0). Results of other serum chemistry studies and the urinalysis were normal. Serologic tests for Q fever, brucellosis, hepatitis A and C, and psittacosis showed either negative or nonrising titers; serologic evidence for preexisting cytomegalovirus, Epstein-Barr, and hepatitis B virus (antigen negative) infection was found. A right upper quadrant ultrasound was normal. A lumbar puncture was normal except for six lymphocytes per cubic millimeter. There were 603 CD4 cells per cubic millimeter.

Bronchoscopy was performed to evaluate the reticulonodular densities in the setting of HIV infection. Lavage fluid and transbronchial biopsy material were negative when sent for routine, viral, acid-fast bacilli, and fungal stains and cultures. Histopathologic examination revealed chronic inflammation with foci of epithelioid granulomas; Warthin-Starry and other special stains were negative.

The abdominal pain resolved and he remained well throughout the

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FIGURE 1. Chest radiographs at presentation revealing bilateral basilar reticulonodular infiltrates.
first hospital week. Intravenous penicillin therapy was begun on hospital day 6 because neurosyphilis could not be excluded. Two hours after the first dose, chills, fever to 39.5°C, and right upper quadrant pain occurred, with tenderness and guarding. The white blood cell count was 15,300/mm³; the bilirubin was 6.3 mg/dl (direct 4.6 mg/dl), the ALP was 1,038 IU/L, and the aspartate aminotransferase was 288 U/L. Penicillin therapy was discontinued. Defervescence and resolution of abdominal pain occurred within 4 h. A DISHIDA scan was normal. The white blood cell count fell to 9,000/mm³ where it remained for the rest of the hospitalization. Sporadic episodes of right upper quadrant pain and fever (not exceeding 38.2°C) occurred over the next 5 days before complete resolution. Penicillin therapy was resumed, and a course for neurosyphilis was completed, without event.

Persistent ALP elevations (from 798 to 1,560 IU/L) prompted two unsuccessful attempts at retrograde cholangiography (sphincterotomy not performed), abdominal computed tomography (normal), and liver biopsy. The latter revealed mild periportal hepatitis and piece-meal necrosis with acute and chronic inflammation; granulomas were not seen, and special stains (including Warthin-Starry) were negative.

A month later he was asymptomatic and the physical examination findings were unremarkable. The RPR was positive at 1:128. All liver tests and the chest radiograph were normal. One year later, the RPR was positive at a 1:1 dilution.

**COMMENT**

This HIV-infected patient, clearly suffering from secondary syphilis, demonstrated bilateral pulmonary infiltrates that prompted bronchoscopic examination before the true origin of the pneumonitis was recognized. Similarly, the classically defined symptoms, signs, and biochemical abnormalities of syphilitic hepatitis were apparent; nevertheless, the flare of disease associated with the Jarisch-Herxheimer reaction so resembled acute cholangitis that he underwent aggressive investigative procedures before the true diagnosis was appreciated.

Pulmonary involvement by syphilis has been very rarely described, and it is traditionally manifested by either the parenchymal granums seen in tertiary disease or the interstitial pneumonia seen in overwhelming congenital syphilis. Earlier authors specifically denied the existence of parenchymal pulmonary disease in secondary syphilis; investigators once documented clear chest radiographs in as many as 1,500 patients with this stage of the disease (S. Landry, quoted in Biro et al.). The rarity and "clinical undemonstrability" of early pulmonary syphilis was bemoaned by Stokes et al. in their classic monograph.

However, five cases of radiologically apparent lung involvement in secondary syphilis have now been reported in the modern era, when alternative diagnoses could be more confidently excluded and the response to effective, specific antitreponemal therapy observed. Other infectious diagnoses that could have coexisted with secondary syphilis in our patient were adequately excluded by serologic testing, the clinical picture, and the response to specific antitreponemal therapy. The recognition of lung disease in our patient probably represents a combination of both an occasionally overlooked feature of this disease (chest radiographs are uncommonly requested in secondary syphilis) as well as the possible tendency for syphilis to present atypically in the HIV-infected patient. As an intact cell-mediated immune response is probably critical for the control of *Treponema pallidum* infection, subtle functional T-cell deficits seen even in early HIV infection may have been permissive for the evolution of the atypical pulmonary and hepatic presentations reported herein. As two of the previously reported pneumonitis cases were in homosexual men within the AIDS era, it is possible that undiagnosed HIV coinfection may have predisposed these patients, too, to more aggressive presentations, including syphilitic pneumonitis.

Liver involvement in secondary syphilis, although so rare that its existence has even been questioned, is characterized by abdominal or right upper quadrant pain, fever, hepatomegaly, and liver tenderness. Minimal elevations in the bilirubin and hepatocellular enzymes and marked elevations in the ALP value are seen. A delayed resolution following penicillin therapy is characteristic. The syndrome can mimic AIDS-related sclerosing cholangitis, a recently described entity that can nevertheless be excluded in our patient by its occurrence only in advanced immunodeficiency, the usual appearance of biliary tract abnormalities, and the persistence of abnormal results of liver function tests even following sphincterotomy.

To our knowledge, a Jarisch-Herxheimer reaction causing a flare of hepatitis symptoms has not been previously described. We suspect that worsening hepatic inflammation, caused by the local release of spirochetal antigens, was responsible for the flare of symptoms seen. If so, steroid prophylaxis against the Jarisch-Herxheimer reaction, as used for neurosyphilis, may also be appropriate for syphilitic hepatitis.

In summary, asymptomatic pulmonary infiltrates were seen in an HIV-infected patient with secondary syphilis, a previously unreported manifestation in this population. A Jarisch-Herxheimer reaction complicated coexistent syphilitic hepatitis, closely resembling acute cholangitis. We suggest that syphilis be excluded in any HIV-infected patient with rash and either pneumonitis or cholestatic hepatitis, as an appropriate response to therapy may obviate the need for more aggressive diagnostic procedures.

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**REFERENCES**

1. Fraser RG, Peter Pare JA, Pare PD, Fraser RS, Genereux GP. Diagnosis of diseases of the chest. Philadelphia: WB Saunders Co, 1989; 874-75
10. Geer LL, Warshauer DM, Delany DJ. Pulmonary nodule in syphilitic pneumonitis in HIV-infected Patient (Doolcy, Tomski)
Simultaneous Occurrence of Three Primary Lung Cancers*

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We present a patient with three lung cancers composed of adenosquamous carcinoma, adenocarcinoma, and squamous cell carcinoma. Marked response was obtained in squamous cell carcinoma components following chemotherapy, but not in adenocarcinoma components. Even multiple malignant lesions of the lung might have a chance to be controlled by a combination of chemotherapy and surgery. (Chest 1994; 105: 631-32)

CEA = carcinoembryonic antigen

In recent years, as a result of improvement in the diagnosis and the therapy for primary lung cancer, the number of patients suffering from multiple lung cancers has increased. We describe a patient with three simultaneous lung cancers composed of adenosquamous carcinoma, adenocarcinoma, and squamous cell carcinoma, which was successfully treated with neoadjuvant chemotherapy.

Case Report

A 63-year-old, apparently healthy man who had a routine medical checkup in October 1989 showed a rise in carcinoembryonic antigen (CEA) level. Chest radiograph then revealed a mass in the right lung. He was admitted to the hospital for further study free of symptoms in March 1990. His family history was positive for lung cancer in his brother. He had an 80-pack-year history of cigarette smoking. Results of physical examination were within normal limits. Laboratory data were noncontributory except for the CEA value, which was 18.1 ng/ml. At hospital admission, besides the known mass in the right lower lobe that measured 60 mm in diameter, a second mass 20 mm in diameter was detected in the left lower lobe. Flexible fiberoptic bronchoscopy with brushing cytologic studies revealed squamous cell carcinoma in both the larger tumor in the right lower lobe and the smaller tumor in the left lower lobe. Neoadjuvant treatment prior to surgery was performed. Three courses of chemotherapy were administered consisting of cisplatin, 100 mg/m², etoposide, 240 mg/m², and vindesine, 4 mg/m². Chest computed tomography then confirmed an 80 percent reduction of the right mass (partial response) with a disappearance of the left mass (complete response). His serum CEA fell to 5.3 ng/ml. On July 13, the patient underwent right lower lobectomy with hilar and mediastinal lymphadenectomy. There was no evidence of mediastinal lymph node metastasis. The histologic report revealed adenosquamous carcinoma composed of a tubular adenocarcinoma and a low-differentiated squamous carcinoma being predominant, only part of which consisted of degenerated cancer cells following preoperative chemotherapy. The patient's postoperative course was uneventful. He refused any further surgical intervention in the left lung. When he was discharged from the hospital on August 21, his serum CEA level was 3.4 ng/ml. One and a half months after hospital discharge, he agreed to an operation when the follow-up examination showed enlargement of a left mass, in spite of serum CEA level remaining low at 3.7 ng/ml. On October 12, a left thoracotomy was performed and revealed in addition to the known tumor in S8 measuring 12 mm in diameter, another tiny, hard separate mass just under the pleura. A frozen section of the latter revealed an adenosquamous carcinoma. A partial resection of the left lower lobe, including the two masses, and hilar lymphadenectomy were carried out. Microscopic examination demonstrated that the mass recognized preoperatively was a moderately differentiated squamous cell carcinoma with a slight degeneration of the cancer cells resulting from preoperative chemotherapy. The tiny mass that was found accidentally was a papillary adenocarcinoma that showed no effects of the therapy. The surgical margins and hilar lymph nodes were free of disease. The patient's postoperative course was uneventful. He left the hospital on November 10 with a serum CEA level of 3.7 ng/ml. He continues to do well, without recurrence more than 2 years after the final operation.

Discussion

This case raises three questions. First, did the three cancers have an independent origin? Second, did the effects of chemotherapy differ on the adenocarcinoma and the squamous cell carcinoma? Finally, how should one manage multiple malignant tumors?

Adenosquamous carcinoma was found in the patient's right lower lobe, while an adenocarcinoma and a squamous cell carcinoma were recognized separately in his left lower lobe. We questioned whether these tumors represented new primary or metastatic lesions. The criteria for the diagnosis of multiple