Bronchoalveolar Lavage in Gold Lung*

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We report the results of bronchoalveolar lavage in a patient with gold salt-induced interstitial pneumonitis. The presence of elevated numbers of lymphocytes in the lavage specimen supports a hypersensitivity-related pathogenesis of this disease. Such findings may help distinguish pulmonary complications of gold therapy from interstitial disease due to rheumatoid arthritis.

Therapeutic administration of gold salts in patients with rheumatic diseases has been associated with the development of interstitial pneumonitis and pulmonary fibrosis.1,8 Similar pathology may develop in patients with rheumatoid arthritis without exposure to gold; bronchoalveolar lavage (BAL) in such patients reveals an increase in the percentage of neutrophils, but no alteration in lymphocyte numbers.8 We present the case history of a woman with rheumatoid arthritis who developed interstitial pulmonary infiltrates while being treated with gold salts. BAL analysis showed an abnormal increase in the percentage of lymphocytes, and suggests that a pulmonary hypersensitivity response to gold is important in the pathogenesis of "gold lung."

CASE REPORT

A 42-year-old nonsmoking woman with a 12-year history of seropositive rheumatoid arthritis (rheumatoid factor titers ranged from 1:80 to 1:2,560) was admitted to the hospital in order to evaluate a chronic nonproductive cough and exertional dyspnea. Eight months prior to admission she started to receive weekly injections of 50 mg gold sodium thiomalate for symptomatic relief of joint pain. One month after initiation of therapy, gold administration had to be suspended for three weeks, due to the development of a macular pruritic skin rash. Gold therapy was subsequently resumed without dermatologic sequelae. The only other medication used by the patient was aspirin, taken only infrequently and in low doses (less than eight 325 mg tablets per day) since it caused gastric irritation. After three months of gold treatment, the patient developed a nonproductive cough. The cough became progressively worse over the next five months, and did not respond to antibiotic therapy. She developed dyspnea with minimal exertion and was admitted to the hospital. A chest roentgenogram showed diffuse interstitial infiltrates with a predominance in the upper lobes (Fig 1). Routine laboratory tests were normal; complete blood count showed a normal leukocyte count with no eosinophilia. Pulmonary function tests were consistent with a restrictive pulmonary process (see below). A tuberculin skin test gave negative results, but the skin test for Candida was positive. Bronchoalveolar lavage (BAL) was performed as previously described7 using a total of 120 ml of sterile saline solution (70 percent recovery). Differential cell analysis revealed 35 percent lymphocytes, 1 percent neutrophils, and 64 percent alveolar macrophages, with an increased absolute total cell count of 6.48 x 106 cells. (The normal BAL differential in our laboratory,7 as mean percent ± SEM, is: lymphocytes, 3.7 percent ± 0.3; neutrophils, 0.9 percent ± 0.3; alveolar macrophages, 95.4 percent ± 0.4; the normal absolute total cell count varies between 6 x 106 and 1 x 107 cells). A transbronchial biopsy revealed interstitial fibrosis and pneumocyte proliferation. Prednisone therapy (40 mg daily) was initiated. Marked symptomatic improvement was reported after a few days of steroid therapy, and dosage of the drug was tapered and discontinued after a total of three months of therapy. Pretreatment and post-treatment pulmonary function values, respectively, were: total lung capacity, 4.8 L and 5.9 L; vital capacity, 3.0 L and 3.5 L; forced expiratory volume in one second (FEV1), 2.4 L and 2.9 L; FEV1/forced vital capacity, 80 and 83 percent; and single breath carbon monoxide diffusion capacity, 23 and 27 ml/min/mm Hg. The appearance of chest roentgenogram returned to normal, and has remained normal after two years. An in vitro assay of lymphocyte transformation response to gold, performed after termination of steroid therapy, was negative.

DISCUSSION

Gold-related interstitial pulmonary disease typically occurs after one to four months of therapy,5 may resolve spontaneously with cessation of therapy,3,9 may exacerbate with re-exposure,2,5 and uniformly responds to steroid therapy when started early.4 This clinical picture suggests that pulmonary toxicity from gold is a manifestation of a hypersensitivity reaction to gold salts. The finding of an elevated percentage of lymphocytes on BAL of our patient is consistent with this interpretation.

Another explanation for the presence of lymphocytes on BAL is unlikely. The pulmonary diseases presently characterized by a "lymphocyte predominant" alveolitis include sarcoidosis, hypersensitivity pneumonitis from other causes, and granulomatous infectious diseases.4 These diseases were unlikely in the current case since previous findings on chest roentgenograms were normal, the patient had a negative tuberculin skin test reaction and was not anergic, and had never experienced any pulmonary symptom prior to her illness. Rheumatoid arthritis-associated pulmonary disease is also unlikely to explain this patient's illness, since "rheumatoid lung" typically occurs in male patients with very high rheumatoid factor titers, pleuropneumonitis, and other systemic involvement, not present in the current case.6 Our patient's clinical course, temporal association of pulmonary disease with initiation of gold therapy, good response to steroid therapy, and continued pulmonary health after ther-

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apy with steroids was discontinued are characteristic of gold-induced pulmonary disease.

Our patient's negative lymphocyte transformation response to gold does not rule out a hypersensitivity reaction. In other reports, assays of in vitro peripheral blood lymphocyte transformation responses to gold occasionally were positive, but frequently were negative. Even in the absence of a gold-induced lymphocyte transformation response, gold-exposed lymphocytes from patients with "gold lung" may elaborate lymphokines, which may be a more sensitive indicator of a cellular immune response than lymphocyte transformation.

To our knowledge, this is the first report of BAL in a patient experiencing a pulmonary reaction to gold. The presence of lymphocytic rather than the usual neutrophilic alveolitis of rheumatoid arthritis-associated pulmonary fibrosis may allow the clinician to diagnose a gold-induced hypersensitivity pneumonia by BAL and obviate the need for tissue biopsy. However, the absence of an increased percentage of lymphocytes on BAL may not rule out a gold-induced etiology, since it is conceivable that advanced cases may present with fibrosis without an active lymphocyte component. We hope that this report will encourage others to utilize BAL when patients experience pulmonary reactions while receiving gold therapy, in order to extend the observation reported in this isolated case.

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