Gallium Scanning in Lymphoid Interstitial Pneumonitis of Children with AIDS

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Lymphoid interstitial pneumonitis (LIP) is a frequent pulmonary complication in the child with the acquired immune deficiency syndrome (AIDS) and human immunodeficiency virus (HIV) infection. We report the gallium scan findings in two children with AIDS and LIP. Gallium scintigraphy in both children demonstrated increased radionuclide concentration throughout the lungs, a pattern indistinguishable scintigraphically from that of *Pneumocystis carinii* pneumonia (PCP). This should alert nuclear medicine practitioners and referring physicians to another cause of diffusely increased gallium uptake in the lungs of patients with AIDS.

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Gallium scanning has become an important diagnostic tool in the evaluation of pulmonary complications in patients with acquired immune deficiency syndrome (AIDS) or the AIDS-related complex (ARC). It has been of particular value in the early identification of *Pneumocystis carinii* pneumonia (PCP) (*1–4*) and *Mycobacterium avium intracellulare* infection (*5,6*). This has allowed prompt definitive diagnosis using either open lung biopsy or fiberoptic bronchoscopy, and early institution of therapy.

In patients with AIDS, the finding of diffusely increased lung activity on the gallium scan has been commonly associated with PCP. We have recently examined gallium scans of two children with AIDS who exhibited this finding that was proven by biopsy to be secondary to lymphoid interstitial pneumonitis (LIP). This is the first report of the gallium scan findings of this entity.

CASE REPORTS

Patient 1

Patient 1 is a 5½-yr-old black male who presented with a 1-mo history of intermittent respiratory distress. He was the 2 lb, 5 oz product of a 28-wk gestation born to an intravenous (i.v.) drug-abusing mother. He had a past history of failure to thrive, cerebral palsy, hepatosplenomegaly, recurrent otitis media, and intermittent lymphadenopathy. Physical examination on admission showed a poorly nourished child with a weight and height below the fifth percentile for age. Pertinent findings included a respiratory rate of 44/min, finger clubbing, scattered rhonchi and rales bilaterally, hepatosplenomegaly, and generalized lymphadenopathy. Laboratory evaluation revealed polyclonal hypergammaglobulinemia with an IgG of 4,340 mg/dl, an IgA of 448 mg/dl, and an IgM of 86 mg/dl. A reversed helper-to-suppressor T cell ratio (T4/T8 ratio) of 0.3 was found. His serum was positive for antibody to human immunodeficiency virus (HIV), formerly HTLV-III/LAV, as detected by an ELISA assay and confirmed by Western Blot analysis. Arterial blood gases showed a pH 7.39, pO_2 71, and a pCO_2 30. Chest x-ray showed a diffuse interstitial nodular pattern in both lungs (Fig. 1). Despite therapy with i.v. trimethoprim-sulfamethoxazole, his respiratory status deteriorated, and he underwent open lung biopsy. Histologic examination revealed dense nodular infiltrates composed mostly of small lymphocytes, a few plasma cells, and reactive histiocytes predominantly in the interstitium consistent with a diagnosis of lymphoid interstitial pneumonitis (Fig. 2). Special stains for PCP and atypical mycobacteria were both negative. Gallium scanning was performed to evaluate its potential in the diagnosis or follow-up of LIP. The scintigraphy was performed 48 hr after the i.v. administration of 1.00 mCi (37.0 MBq) gallium-67 (^{67}Ga) citrate. Total-body images revealed diffuse uptake in both lungs. The lung activity was noted to be of greater intensity than the liver. Activity was also seen in the parotid glands, but none was found in the lymph nodes known to be enlarged (Fig. 3).

Patient 2

Patient 2 is a 9-mo-old white male infant who presented with a 4-day history of nonproductive cough and respiratory

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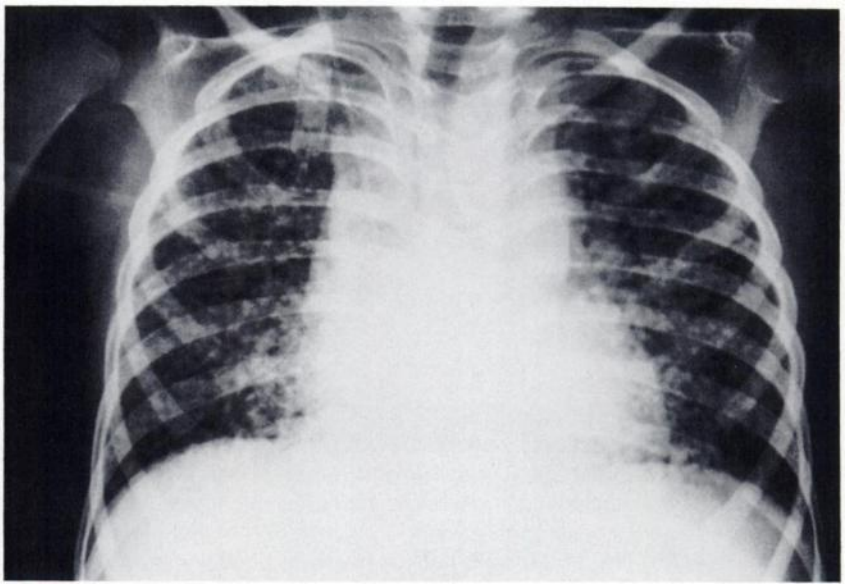

FIGURE 1
Patient 1: 5½-yr-old male with history of intermittent respiratory distress. Chest x-ray demonstrating diffuse nodular interstitial infiltration bilaterally.

distress. He was the 8 lb, 2 oz product of a full-term gestation born to an i.v. drug-abusing mother. His past history was significant for chronic otitis media, oral candidiasis, and two prior hospitalizations for presumed viral illnesses. Physical examination at the time of admission revealed generalized lymphadenopathy, hepatosplenomegaly, and diffuse bilateral wheezing and rales. Chest roentgenogram revealed diffuse bilateral infiltrates. Laboratory workup showed a T4/T8 ratio of 0.6; polyclonal hypergammaglobulinemia with an IgG of 3,480 mg/dl, IgA of 177 mg/dl, IgM of 282 mg/dl; and serum antibody to HIV by ELISA and Western Blot analysis. Despite therapy with i.v. trimethoprim-sulfamethoxazole and cefuroxime, his clinical condition continued to worsen with no detectable x-ray improvement. Open lung biopsy revealed histologic changes consistent with lymphoid interstitial pneumonitis. Over the next few weeks his respiratory status gradually improved off all antibiotic therapy, and he was discharged with a respiratory rate of 28/min and an unchanged chest x-ray. Gallium scanning was done at the time of a follow-up visit 3 wk later. Forty-eight hours after the administration of 0.75 mCi (27.75 MBq) of ^{67}Ga, total-body imaging revealed diffuse uptake in both lungs in a pattern similar to that of Patient 1. No uptake was seen in the parotid glands or the enlarged lymph nodes (Fig. 4).

DISCUSSION

Pneumocystis carinii pneumonitis has been recognized as a cause of diffuse gallium uptake in the lungs of immunosuppressed hosts. Positive scans were noted to precede severe clinical symptoms, and in many cases were present in patients with normal chest x-rays (*7,8*). The association of PCP and AIDS has sparked renewed interest in gallium scanning. In the study of Barron et al. on the use of gallium in AIDS patients with suspected PCP, the sensitivity was found to be 94%, and the specificity 74%. Thirty-five percent of patients with PCP had negative or equivocal x-rays (*3*). Other studies report a sensitivity of 100%, and specificities as high as 90% when the degree of gallium activity is graded (uptake equal to, or greater in intensity than that in the liver) (*4,9*).

The gallium scans reported in our patients show diffusely increased uptake of radiopharmaceutical in the lungs. A number of entities have been reported that occasionally may result in a similar picture. These include pulmonary toxicity secondary to chemotherapy, prior lymphangiography, IV drug abuse, previous radiation therapy, lymphangitic carcinomatosis, sarcoidosis, tuberculosis, diffuse interstitial fibrosis, and bronchogenic carcinoma (*1,10*). In the patient with AIDS, diffuse uptake of gallium has been reported in cytomegalovirus (CMV), CMV and cryptococcus, alveolar fibrosis, bleomycin toxicity, and interstitial fibrosis (*11*). PCP is unique in resulting in gross discordance between the gallium scan, and the chest x-ray and clinical symptoms (*7*). PCP was excluded in both our patients by the histologic findings on open lung biopsy and negative silver methenamine stains.

In this report, we identify lymphoid interstitial pneumonitis as a cause of diffuse pulmonary uptake of gallium in the child with AIDS and HIV infection. LIP was initially described in adults by Carrington et al. as a distinct clinicopathologic entity of obscure etiology. It was characterized histologically by a predominantly lymphoid infiltration of the pulmonary interstitium (*12*). Subsequently, it has been described in both adults

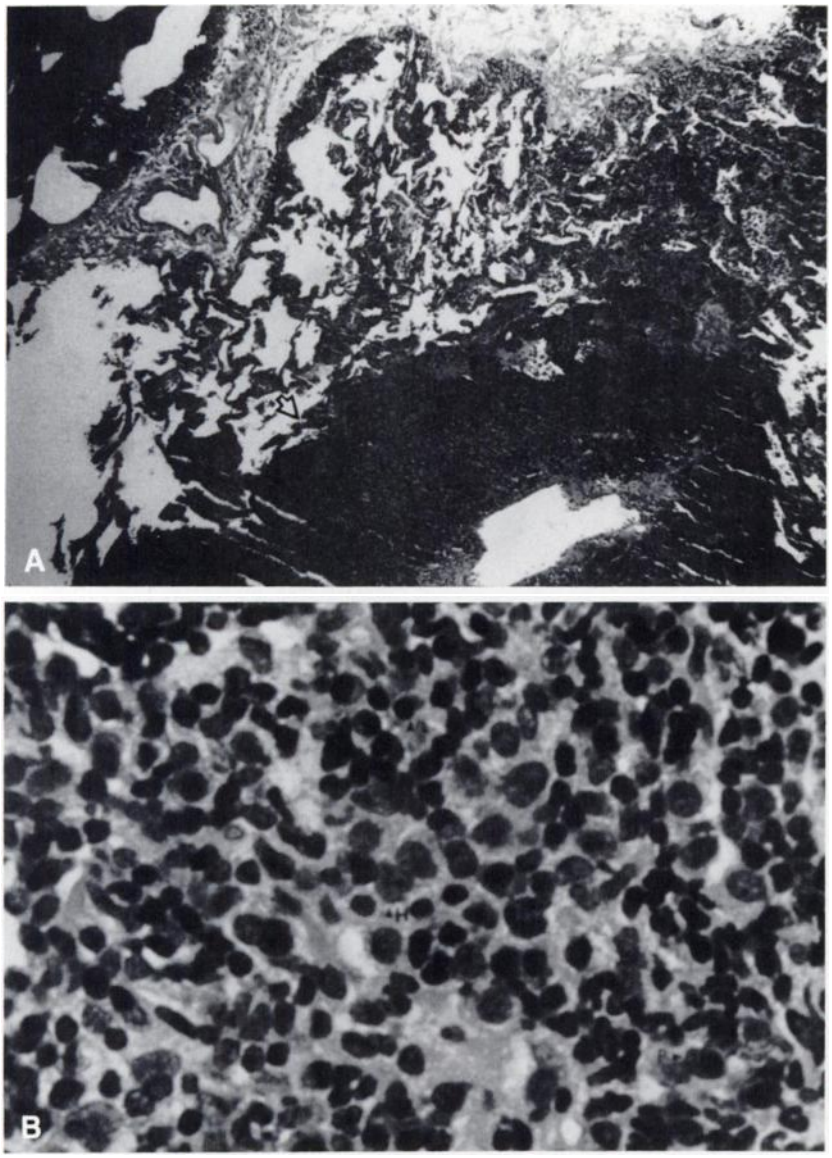

FIGURE 2
A: Section of lung biopsy from Patient 1 showing a diffuse, dense, nodular interstitial mononuclear cell infiltrate (clear arrow). (Hematoxylin-eosin stain × 100). B: Higher-power magnification of infiltrate shows predominance of small lymphocytes (L), occasional plasma cells (P), and scattered histiocytes (H). (Hematoxylin-eosin stain × 1,000).

and children in association with dysgammaglobulinemic states (*13,14*). Since LIP was first described in children with AIDS in 1983 (*15*), it has been recognized as an important and frequent pulmonary complication of HIV infection (*16*). Histologic analysis of lung tissue in these children reveals diffuse nodular aggregates of mononuclear cells consisting mostly of small lymphocytes and plasma cells throughout the lung parenchyma, and extending to the pleura and along the lymphatics. The marked hyperplasia of pulmonary lymphoid tissue seen in LIP may be triggered by Epstein-Barr virus (EBV) infection as suggested by the finding of EBV-specific DNA in most of the lung biopsy specimens from these patients (*16,17*). Many of these children also have generalized lymphadenopathy and hepatosplenomegaly. Enlargement of the parotid gland, which was demonstrated to accumulate gallium in our first patient, has been noted in association with pediatric AIDS. It is important to distinguish LIP from PCP because the former generally follows a more benign course and is managed differently (*18*).

Although chest roentgenograms in LIP characteristically show diffuse bilateral nodular infiltrates in the pulmonary parenchyma (*19*), other pulmonary complications of AIDS such as PCP may show such diverse roentgenographic patterns that the diagnosis on the basis of the x-ray alone can be difficult.

To our knowledge, this is the first report of the gallium scan findings of LIP. In both of our patients the findings were indistinguishable from those of *Pneumocystis carinii* pneumonia. This should serve to alert both nuclear medicine practitioners and referring physicians to another possible cause of diffusely increased lung uptake in the patient with AIDS.

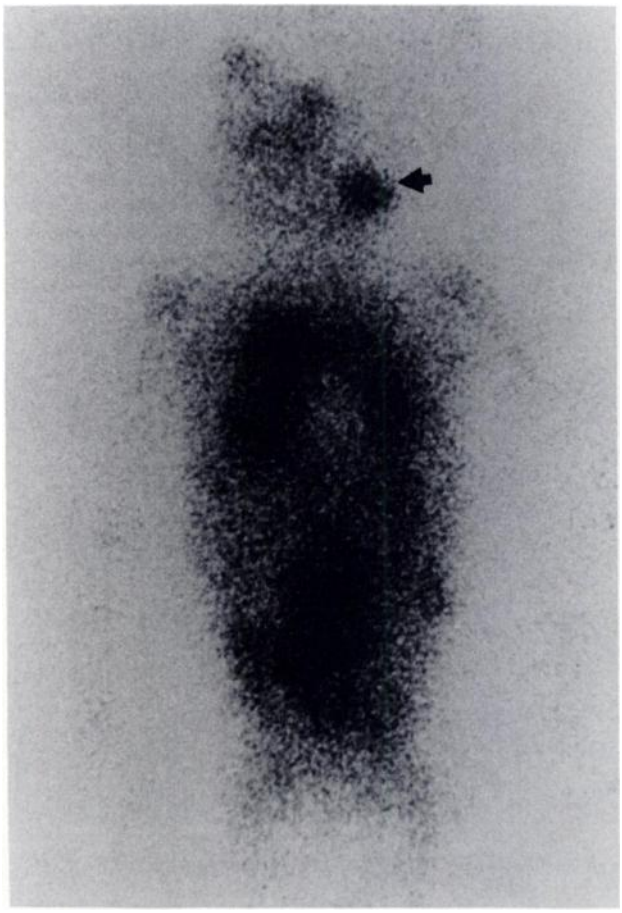

FIGURE 3
Patient 1: Anterior gallium scan revealing diffusely increased uptake in both lungs. Also note increased uptake in left parotid gland, which was enlarged in this patient (arrow). Other views (not shown) show similar activity on the right. Abdominal activity was of uncertain etiology, but because the patient had no known pathology in this area it was attributed to excretion of the radiopharmaceutical by the GI tract.

FIGURE 4
Patient 2: 9-mo-old male with history of nonproductive cough and respiratory distress. Posterior scan again shows diffuse gallium uptake in both lungs. No parotid gland uptake was found in this patient who did not have clinically enlarged glands.

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