Short reports

Hodgkin's disease with a granulomatous pulmonary presentation mimicking sarcoidosis

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ABSTRACT A prominent sarcoid like pulmonary granulomatous reaction to Hodgkin's disease was diagnosed six months before extrapulmonary Hodgkin's disease was confirmed histologically. It recurred with exacerbations of the lymphoma. The reaction is similar to that often seen at pathological staging of intra-abdominal organs not affected by Hodgkin's disease.

A sarcoid like granulomatous reaction to Hodgkin's disease is frequently found in lymph nodes, spleen, liver, and bone marrow whether or not these are affected by the neoplastic process.^{1,2} In contrast, granulomatous disease of lung parenchyma in the absence of Hodgkin's disease within the lung is unusual.¹⁻⁴ We report a patient with sarcoid like, granulomatous lung disease, which presented shortly before extrapulmonary Hodgkin's disease was diagnosed, and recurred when she relapsed with the lymphoma. This suggests that a pulmonary granulomatous disease simulating sarcoidosis may occur as a remote effect of Hodgkin's disease.

Case report

A 58 year old white woman presented with a two month history of weight loss (13 kg), lassitude, night sweats, and a dry cough. Examination showed late inspiratory crackles at both lung bases and a chest radiograph (fig 1) showed bilateral hilar lymphadenopathy and infiltration of both mid and lower zones. Transbronchial biopsy showed multiple non-necrotising granulomas composed of epithelioid and multinucleated giant cells in the peribronchial lung parenchyma (fig 2a). As mycobacterial and fungal studies gave negative results and no other cause of granulomatous disease was apparent, a diagnosis of pulmonary sarcoidosis was made. The result of a Kveim-Siltzbach test was negative. Her clinical condition improved slightly without treatment, but radiographic findings and the diffusion factor for carbon monoxide (TLCO) remained abnormal though stable. Six months after presentation hepatosplenomegaly and bilateral inguinal lymphadenopathy were noted. Inguinal lymph node biopsy showed lymphocyte depleted Hodgkin's disease (fig 2b). Six courses of ABVD (adriamycin, bleomycin, vinblastine, dacarbazine) produced considerable clinical improvement with resolution of the inguinal lymphadenopathy and organomegaly and reversion of the pulmonary infiltration and hilar lymphadenopathy.

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Fig 1 Chest radiograph at presentation showing bilateral hilar lymphadenopathy and pulmonary infiltration.

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Three months later she had a recurrence of her original symptoms and chest radiographic appearances. Transbronchial and bone marrow biopsy specimens showed non-necrotising granulomas without Hodgkin's disease and a repeat Kveim-Siltzbach test gave a negative result. Bronchoalveolar lavage fluid contained 70% T cells, 1% B cells, and 29% macrophages. The T cell helper-suppressor ratio was 2.5:1. Serum angiotensin converting enzyme activity was 139 (normal range 25-131) IU/l. Inguinal lymphadenopathy was again noted and biopsy showed mixed cellularity Hodgkin's disease. She received three courses of MOPP (nitrogen mustard, vincristine, procarbazine, prednisolone) and one course of ChlVPP (chlorambucil, vinblastine, procarbazine and prednisolone) but she developed pancytopenia and bone marrow biopsy showed infiltration by Hodgkin's disease. Chest radiography now showed shadowing throughout both lung fields without hilar lymphadenopathy. Considerable clearing occurred with corticosteroid treatment (prednisolone 1 mg/kg a day) but the Hodgkin's disease progressed, continued marrow infiltration, splenomegaly, and para-

(a)

(b)

Fig 2 (a) Transbronchial lung biopsy: granulomatous inflammation of peribronchial tissue with a discrete non-caseating granuloma. (Haematoxylin and eosin.)
(b) Inguinal lymph node: Hodgkin's disease showing pleomorphic Hodgkin's cells; a Reed-Sternberg cell is arrowed. (Haematoxylin and eosin.)

aortic and iliac lymphadenopathy being evident from computed tomography. She was treated with VM-26 but died shortly afterwards of pulmonary infection unresponsive to antimicrobial treatment.

Necropsy showed extensive pulmonary infection by the fungus *Rhodotorula rubra*, known to cause invasive disease in the immunocompromised host.⁵ Focal residual Hodgkin's disease was present in the lung, bone marrow, and spleen but no granulomatous reaction was seen at any site.

Discussion

The diagnosis of sarcoidosis is based on compatible clinical and radiological evidence, histological evidence of non-caseating granulomas, and negative results from microbiological studies, with support from the Kveim-Siltzbach test; serum angiotensin converting enzyme, lysozyme, transcobalamin II levels; gallium-67 lung scans; and bronchoalveolar lavage cell profiles.⁶ It is also based on exclusion of other causes of granulomatous disease, including granulomatous infections, usual interstitial pneumonia, and lymphoid interstitial pneumonia.⁷

In this case pulmonary sarcoidosis was suggested by the radiological features, the non-caseating granulomas in transbronchial biopsy specimens on two occasions, and the increase in T helper cells in lavage fluid. The clinical presentation suggested initially that this patient had sarcoidosis coexisting with Hodgkin's disease. The negative Kveim-Siltzbach test result in an older woman, however, the minimal increase in serum angiotensin converting enzyme activity, and the close temporal relationship to Hodgkin's disease on presentation and with each relapse and recurrence of the prodromal sarcoid like lung disease suggest an association with the lymphomatous process.

A sarcoid like granulomatous reaction to Hodgkin's disease in tissue unaffected by lymphoma is a frequent finding in spleen, liver, lymph nodes, and bone marrow at staging laparotomy.^{1,2} This reaction, much less evident at necropsy, has varied considerably in degree from patient to patient. As pulmonary and hilar lymph nodes are not sampled in Hodgkin's disease staging procedures, information on granulomatous lesions at presentation is not available but it probably does occur and may, as in the abdomen, occasionally be clinically important.

Several reports have documented an association between Hodgkin's disease and sarcoidosis,^{1,2,8} though these refer to episodes clearly separated in time and probably to the sequential occurrence of two not uncommon diseases. In the absence of a definitive test for sarcoidosis a similar concurrence cannot be disproved in this case. The temporal associations, however, and the similarity to the established intra-abdominal granulomatous reaction to Hodgkin's disease suggest that the pulmonary lesion was a granulomatous reaction to Hodgkin's disease.

Hodgkin's disease and sarcoidosis have several immunological similarities^{6,9,10}—namely, cutaneous anergy, peripheral lymphopenia, and prominent infiltration of helper T cells in diseased tissue. The unknown sarcoid antigen and Hodgkin's disease tissue can both provoke a granulomatous response, which in sarcoidosis is the major manifestation of the disease but in Hodgkin's disease is usually of minor importance. The intra-abdominal granulomas of Hodgkin's

disease, however, are occasionally prominent and our case suggests the same is true of pulmonary granulomas, which may simulate sarcoidosis. Low serum angiotensin converting enzyme activity and a negative Kveim-Siltzbach test result in the presence of Hodgkin's disease activity may help in distinguishing pulmonary granulomatous disease related to Hodgkin's disease from sarcoidosis.

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