Sarcoidosis and lymphoma in the same patient

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Summary

A case of lymphocytic lymphoma in a patient with coincidental sarcoidosis is described, and the possible relationship of the two conditions is discussed. A revised set of diagnostic criteria is proposed to overcome previous difficulties encountered in validating such dual pathology.

KEY WORDS: sarcoidosis, lymphoma, hypogammaglobulinaemia.

Introduction

The coincidental occurrence of Hodgkin’s disease and sarcoidosis is very uncommon. Rarer still are descriptions of non-Hodgkin’s lymphoma and sarcoidosis in the same patient. We report a case of systemic sarcoidosis, confirmed histologically, where a well-differentiated lymphocytic lymphoma subsequently developed. We review the difficulties in validating such dual pathology and propose revised criteria for the acceptance of such cases. Furthermore, we discuss recent controversies concerning the nature of the relationship, if any, between sarcoidosis and lymphomatous disorders.

Case report

A 52-year-old nurse presented in August 1978 with dyspnoea and chest pain. Physical examination revealed splenomegaly and inguinal lymphadenopathy. Chest X-ray showed bilateral hilar adenopathy with diffuse pulmonary infiltrates. Investigations revealed the following abnormalities: forced vital capacity (FCV) 2.8 litres (90% predicted); forced expiratory volume in 1 min (FEV1) 1.95 litres (71% predicted); single breath diffusing capacity (transfer factor) 65% predicted; urinary calcium excretion 559 mg/24 hr; serum immunoglobulins IgG 520 mg/dl, IgA 80 mg/dl, IgM 67 mg/dl. The erythrocyte sedimentation rate was 9 mm/hr; other biochemical and haematological investigations proved normal. Histological examination of tissue obtained at mediastinoscopy revealed fragments of lymph-node which were extensively replaced by well-demarcated epithelioid cell and giant cell granulomata, without caseation, which were confluent in a few areas (Fig. 1). No micro-organisms were demonstrated and the appearances were regarded as highly consistent with sarcoidosis. On the basis of typical clinical, radiological, physiological, biochemical and histological features, the diagnosis of sarcoidosis was made. Treatment with 40 mg of prednisone on alternate days was instituted with a prompt and complete resolution of all clinical and radiological abnormalities.

The patient went to the United States where the prednisone was slowly reduced to zero without recurrence of lymphadenopathy or pulmonary infiltrates. In February 1980, 20 months after the diagnosis of sarcoidosis, she was found on routine review to have marked splenomegaly and inguinal lymphadenopathy. Her chest X-ray remained normal. An inguinal lymph node biopsy and bone marrow biopsy was carried out. These have been reviewed by us and revealed obliteration of the normal architecture of the lymph-node with replacement by a uniform sheet of round cells with small nuclei and rather indistinct cell boundaries, the appearances being those of a diffuse malignant lymphoma of well-differentiated type (Fig. 2). The bone-marrow showed somewhat hypercellular haemopoietic marrow with extensive replacement by diffuse malignant lymphoma similar to that in the node. No granulomata were seen on any of the sections of lymphoma tissue.

She was treated with prednisone, 30 mg daily, with partial reduction in the size of her spleen and lymph nodes. Subsequent relapse required treatment with combination chemotherapy but a further lymph node and liver biopsy in December 1980 both confirmed...
the presence of lymphoma. No stigmata of sarcoidosis could be detected in any of these additional biopsies. In view of the persistent disease, she received 2,500 rads to the paraortic and inguinal areas with a good response. The patient is living in the United States at the time of writing.

Discussion

This case of sarcoidosis with a coincidental lymphoma prompts discussion under 3 headings: firstly, a review of the difficulties in confirming both diagnoses in the same patient; secondly, suggested stricter criteria for the validation of such dual diagnoses; thirdly, a review of the nature of the relationship, if any, between the 2 disorders.

Diagnosis of sarcoidosis and lymphoma in the same patient may prove difficult to establish because the granulomatous lesion of sarcoid lacks specificity. Sarcoid-like granulomas have been reported in infectious diseases, following exposure to chemical agents in a variety of chronic inflammatory conditions and...
<table>
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<th>Reference</th>
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<th>Evidence for lymphoma</th>
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<tr>
<td>Buckle, 1960</td>
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<td>Reticulosarcoma</td>
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<td>Atwood et al., 1966</td>
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<td>Silver et al., 1967</td>
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<td>Goldfarb and Cohen, 1970</td>
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<td>Brincker, 1972</td>
<td>53 M</td>
<td>Lympho... 5 years</td>
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<td>42 M</td>
<td>Lympho... 17 years</td>
<td>Hodgkin’s disease</td>
<td>Fever, arthralgia, hilar adenopathy, skin and muscle (Bx)</td>
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<td>McFarland et al., 1978</td>
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<td>Ponticelli et al., 1981</td>
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<td>CXR: skin (Bx), liver (Bx), Scalene node (Bx)</td>
<td>Skin (Bx)</td>
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<td>16 M</td>
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<td>Brennan et al.</td>
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<td>Inguinal node (Bx), liver (Bx), bone marrow (Bx)</td>
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Abbreviations: Age = age at onset of sarcoidosis; CXR = chest radiograph suggestive of sarcoidosis; Bx = biopsy positive from this site; Aut = autopsy histology.
found that malignant lymphoma and lung cancer occurred respectively 11 and 3 times more frequently than expected. However, these data have recently been critically re-examined by Rømer (1980) and revised results failed to show any excess of tumour occurrence over that expected in the general population. On-going studies by Rømer have so far failed to reveal any evidence of an increased risk of malignancy (Rømer, 1982). Obviously, further independent epidemiological studies in other populations are needed.

Pathogenetically, shared features of sarcoidosis and lymphoma include the occurrence of granulomatous histology, and the occurrence of cellular and humoral immunological dysfunction in both disorders. In sarcoidosis, abnormal T cell function (James, Neville and Walker, 1975; Goodwin et al., 1979; Daniele, Dauber and Rossman, 1980) and the resultant impairment in delayed hypersensitivity (Israel and Sones, 1965; Sharma and Beresford, 1973) might predispose to malignancy (Brincker and Wilbeck, 1974). The role of humoral mechanisms is further raised in our case by the finding of low serum immunoglobulins. Lymphoma risk is known to be increased in patients with congenital immuno-deficiency (Kersey, Spector and Good, 1973), autoimmune disease (Tabal, Sokoloff and Barth, 1967; Lewis et al., 1975; Louie and Schwartz, 1979) and those receiving immunosuppressant therapy (Hogberg and Fraumeni, 1973). The observation that lymphoma occasionally precedes sarcoidosis (Brincker, 1972) and recent descriptions of sarcoidosis following immunosuppressive therapy of a variety of tumours (Sybert and Butler, 1978; Trump et al., 1981) have prompted the suggestion that sarcoidosis may represent a form of opportunistic infection (Israel, 1978). It remains possible that an, as yet, unidentified common immune abnormality or extrinsic factor, such as a virus, may predispose to both conditions.

Clearly, prospective epidemiological studies in a variety of populations are needed to ascertain whether or not sarcoidosis is associated with lymphoreticular and/or other malignancies. Careful documentation of clinical cases using strict diagnostic criteria will complement such epidemiological studies and may provide a clue to the nature of the relationship.

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References

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