Sarcoid-like lymphadenopathy in malignant teratoma

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Summary

The reported association between sarcoidosis and malignancy has relevance both to the diagnosis of the cause of lymphadenopathy and possibly also to the prognosis of the malignant disease. A case is reported in which mediastinal lymphadenopathy due to non-caseating epithelioid granulomata caused diagnostic difficulty in the staging investigation of a patient with malignant testicular teratoma.

KEY WORDS: sarcoidosis, lymphadenopathy, teratoma.

Introduction

Sarcoidosis is associated with a number of immunological abnormalities including depression of T-lymphocyte numbers and activity (Loehnen, Deremee and Tomasi, 1976), and thus immune surveillance theory (Burnet, 1957) might suggest a predisposition to neoplasia. Analysis of the Danish Cancer and Sarcoidosis Registries during the period 1962 to 1971 has confirmed an increased incidence of lymphomas occurring within 4 years of the diagnosis of sarcoidosis and has suggested an association between sarcoidosis and lung cancer (Brincker and Wilbek, 1974). Malignant lymphomata occurred 11 times, and lung cancer 3 times—more frequently than expected. A complicating factor in diagnosing this association is that 'sarcoid-like reactions' have been observed in patients with a variety of neoplastic disorders (Nadel and Ackerman, 1950; Brincker, 1972; O'Connell *et al.*, 1975).

Sarcoid lymphadenopathy is a potential cause of diagnostic confusion in patients with malignant disease when it may be interpreted as evidence of metastases. We describe a patient with malignant testicular teratoma, in whom mediastinal lymphadenopathy was found to be due to sarcoid-like granulo-

mata, though there was later relapse in the adjacent lung with metastatic disease.

Case report

A 33-year-old Caucasian man was referred in April 1979 following inguinal orchidectomy for an undifferentiated malignant teratoma of the left testis. Staging investigations including serum alpha-fetoprotein (AFP) and the beta sub-unit of human chorionic gonadotrophin (HCG), chest X-ray and bipedal lymphangiography were all within normal limits. A bulky left hilum shown on chest X-ray was demonstrated on mediastinal tomography to be vascular in origin. Computerized tomographic (CT) scans of the thorax and abdomen demonstrated enlarged mediastinal lymph nodes (Fig. 1) with no evidence of abdominal node enlargement. This was considered an atypical pattern of spread for metastasis from a malignant testicular teratoma (Peckham *et al.*, 1981) and therefore a mediastinal lymph node biopsy was performed at left thoracotomy in June 1979; this showed non-caseating epithelioid granulomata compatible with sarcoidosis.

The patient was therefore treated for Stage malignant teratoma with a protocol involving para-aortic and ipsi-lateral pelvic node irradiation and during the following 6 months, staging investigations remained normal. Subsequently, in February 1980 the patient became acutely ill with fever, weight loss, dysphagia, dyspnoea and an unproductive cough. Examination revealed evidence of mild superior vena caval obstruction and the chest X-ray showed a right paratracheal mass and a 2 cm rounded opacity in the left lung field above the hilum (Fig. 2). Serum AFP was raised at 41 µg/litre (normal less than 5 µg/litre) and the patient was treated for relapse of malignant teratoma with courses of combination chemotherapy consisting of cis-platinum, bleomycin, and VP16-213. Following the first course of this chemotherapy, there

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FIG. 1. CT scan at presentation demonstrating mediastinal lymphadenopathy (arrowed).

FIG. 2. Chest radiographs before and 3 weeks following the first course of chemotherapy for relapsed teratoma.

was rapid and almost complete regression of both the right paratracheal mass and the left lung opacity (Fig. 2). Additionally, the serum AFP fell to 9 $\mu\text{g/litre}$. Six courses of chemotherapy were administered. This was associated with a fall in serum AFP to within normal limits and a marked regression of the mediastinal nodes detected on CT scan. However, 2 months following completion of chemotherapy, constitutional symptoms recurred and a repeat CT scan showed that the mediastinal lymph nodes were enlarged. In November 1980, a median sternotomy was performed and biopsy of mediastinal nodes again demonstrated that in all nodes examined there was replacement of normal structures by non-caseating epithelioid granulomata. The lymphadenopathy

resolved spontaneously and on reassessment in December 1981 there had been no relapse of either his sarcoid lymphadenopathy or his teratoma.

Discussion

This case illustrates the possible hazard of ascribing guilt-by-association in the diagnosis of the cause of lymphadenopathy. The patient developed mediastinal lymphadenopathy on 3 occasions and on each occasion it was suspected this was caused by metastasis from his malignant testicular teratoma. Pathological examination of mediastinal lymph nodes was performed on the first and third time this lymphadenopathy was detected and non-caseating epithelioid

granulomata were revealed. Since the third occasion that lymphadenopathy developed followed successful treatment of teratoma relapse, it is unlikely to represent a reaction to adjacent malignancy. On the second occasion lymphadenopathy developed there was strong clinical evidence for relapse of teratoma with a raised alphafetoprotein and a rounded opacity in the left lung field. Appropriate chemotherapy was instituted with rapid response in both the left lung field and mediastinum.

Both malignant teratoma and the majority of other malignancies may relapse without production of a tumour marker substance, and thus, short of node biopsy relapse, may be difficult to distinguish from the development of sarcoid-like lymphadenopathy. Sarcoidosis may be suggested by the finding of typical granulomata on biopsy of distant sites such as the liver, or by a positive Kveim test. Recently, serum angiotensin-converting enzyme (SACE) activity has been found to be a useful marker of sarcoidosis (Studdy *et al.*, 1978), though this test is not entirely specific and raised SACE activity was also found in 4% of controls, 2 out of 5 patients with Hodgkin's disease, 14% of patients with primary biliary cirrhosis and 9% of patients with active tuberculosis. SACE activity has not been analysed in patients with the sarcoid-like lymphadenopathy associated with malignant disease, and in any event a high value in conjunction with lymphadenopathy would not exclude concomitant relapse of the malignancy.

The significance of non-caseating epithelioid granulomata in malignant disease has been most intensively analysed in the context of the pathological staging of Hodgkin's disease at laparotomy (Bagley *et al.*, 1972; Abt *et al.*, 1974; O'Connell *et al.*, 1975). The incidence in this disease appears to range

from 8 to 18%. The presence of granulomas did not correlate with malignant disease at the same site. Though the cause of the granulomas remains obscure, O'Connell *et al.* (1975) felt they may represent a host response to the tumour, and their preliminary analysis of 17 patients with 'sarcoid-like' granulomas was suggestive of an associated improved prognosis following treatment.

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