Thorax 1996;51:448–449

Commentary

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One report in a recent issue of *Thorax*[1] and a further two in this issue of single cases in which a diagnosis of sarcoidosis established by acceptable criteria was accompanied by evidence of other diseases, provide an opportunity for drawing attention to logical elements in interpretation of such cases.

In colloquial discourse the names of diseases are commonly used as if they refer to some sort of agent causing the illness.[2] This is mistaken, even for diseases definable aetiologically. For instance, tuberculosis is now definable as a disease caused by a specified mycobacterium, and a diagnosis of tuberculosis asserts that the observed symptoms and signs result from a complicated interaction between mycobacteria and the host leading to tuberculoid inflammatory changes in affected tissues; but we should not confuse the disease tuberculosis with the causal agent by which it is defined. In informed medical discourse it should be recognised that the names of diseases are a device by which we can refer succinctly to the conclusions of a diagnostic process which aims at elucidation of causation, but may stop short at various points; in current nosology the names of diseases convey very varied causal implications.[3] A diagnosis of sarcoidosis claims no more than that a granulomatous process, about whose cellular and immunological pathogenesis we have some knowledge, underlies the symptoms and signs, but admits ignorance of the cause of this process. When clinical and investigational findings include features of sarcoidosis together with those of some other disease, possible interpretations depend upon our knowledge of the causation of this disease.

The case of sarcoidosis with chylothorax as a presenting feature reported by Jarman *et al*[1] presented a straightforward diagnostic problem: could the accumulation of chyle in the pleura be attributed to obstruction of the thoracic duct by mediastinal lymph nodes enlarged by sarcoid granulomas or should one of the recognised and less benign causes of chylothorax be considered? In view of the remarkable infrequency of symptoms arising from local effects of the sometimes massively enlarged hilar and mediastinal nodes in sarcoidosis, there must initially have been serious doubt, happily resolved by the observed course to resolution. This report will be helpful in assuring clinicians faced with a similar case that a benign interpretation of an alarming situation is possible.

Diagnosis of sarcoidosis and lymphoma in the same patient raises the question of whether there may be some pathogenetic link between these two diseases, both defined in terms of histopathology. In the case reported by Ryan *et al* (pp 444–5) a patient with non-Hodgkin's lymphoma localised to the conjunctiva was found to have an asymptomatic lung infiltration, shown by biopsy to have the histological pattern of sarcoidosis and confirmed by a granulomatous reaction to a Kveim test. In view of the known frequency of asymptomatic pulmonary sarcoidosis this association may be expected to occur occasionally by chance but, because there are some similarities between the immunological abnormalities observed in sarcoidosis and in lymphoma, the question of some pathogenetic link arises. How seriously this question should be examined depends upon whether the frequency of this association is greater than would be expected from the incidence of the two diseases. Attempts to quantify this are complicated by two difficulties: local sarcoid reactions in tissues affected by lymphoma, and cases in which the diagnosis of sarcoidosis which would otherwise have remained undetected and followed a symptomless course to resolution was made only because of the supervention of lymphoma. Taking these factors into consideration, the available evidence is equivocal and does not support the idea of any important pathogenetic link between systemic sarcoidosis and lymphoma.

Sinicco *et al* (pp 446–7) report another case in which asymptomatic pulmonary sarcoidosis was associated with other diseases – namely, CD4 lymphocytopenia whose cause was undetermined, oral candidiasis, and pulmonary *Pneumocystis carinii* infection. Questions of several sorts arise. What was the relation between the causal agents of those defined aetiologically and sarcoidosis? There is no reason to suppose that either of them played any part in the pathogenesis of sarcoidosis, and no evidence that either of them occurs unexpectedly frequently in patients with sarcoidosis in whom humoral immunity is well maintained, and the peripheral lymphocytopenia in the active stages is due to sequestration of activated lymphocytes at sites of active granulomatous inflammation rather than a deficiency of lymphocyte function.

Leaving aside the question of the cause of the CD4 lymphocytopenia in this HIV negative homosexual man, what was its role in the pathogenesis of these infections, and was it related in any way to the sarcoidosis? There is good reason to suppose that it predisposed to the infections, but important questions about sarcoidosis and CD4 lymphopenia await answers. What is the effect of pre-existing CD4 lymphocytopenia on susceptibility to sarcoidosis, and what is the effect of the development of this condition on the course of established sarcoidosis? It is generally accepted that CD4 lymphocytes play an important part in the pathogenesis of the granulomatous process in sarcoidosis, and a plausible hypothesis is that this process may be a response to some sort of replicating agent. If there is such an agent, several interesting interactions between CD4 cell suppression and sarcoidosis might be expected. In an individual with established sarcoidosis, CD4 suppression might lead to the disappearance of some of the clinical manifestations of sarcoidosis and replacement of granulomatous inflammation by more active inflammatory changes. Among those with es-

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tablished CD4 suppression the incidence of new cases of sarcoidosis might be low. The current epidemic of HIV infection should provide an opportunity for the study of these questions. The number of reports of cases in which both diseases have been diagnosed (about a dozen) is smaller than might be expected from their incidences and in view of the interest of the association between them. It is difficult to draw conclusions from these cases: many provide no information about the long term course and in two which ended fatally[4 5] no necroscopic examination was performed.

Answers to several questions are desirable. Does the incidence of new cases of clinical sarcoidosis in those with established HIV infection differ from that in the general population? An epidemiological study to answer this question would be difficult to organise, expensive, and an unjustifiable addition to the burden of those dealing with the AIDS epidemic. What is the clinical course of such patients? What happens to patients with established sarcoidosis who acquire HIV infection as their lymphocyte counts fall? These questions might be answered by central collation and follow up of all detected cases so that they could be critically analysed as a group. It should not be impossible to organise such a study.

1 Jarman PR, Whyte MKB, Sabroe I, Hughes JMB. Sarcoidosis presenting with chylothorax. *Thorax* 1995;**50**:1324–5.
2 Campbell EJM, Scadding JG, Roberts RS. The concept of disease. *BMJ* 1979;**2**:757–62.
3 Scadding JG. Health and disease: what can medicine do for philosophy? *J Med Ethics* 1988;**14**:118–24.
4 Lowery WS, Whitlock WL, Dietrich RA, Fine JM. Sarcoidosis complicated by HIV infection: three case reports and a review of the literature. *Am Rev Respir Dis* 1990;**142**:887–9.
5 Amin DN, Sperber K, Broen LK, Chusid ED, Tierstein AS. Positive Kveim test in patients with coexisting sarcoidosis and human immunodeficiency virus infection. *Chest* 1992; **101**:1454–6.

Thorax 1996;**51**:449–450

Transphrenic dissemination of actinomycosis

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Received 29 July 1994
Returned to authors 19 October 1994
Revised version received 7 December 1994
Accepted for publication 31 January 1995

Abstract

Thoracic actinomycosis is an uncommon disease and often presents difficulty in diagnosis. Two cases are presented in which thoracic actinomycosis produced fistulae between the thoracic and abdominal cavities. Surgical drainage and high dose penicillin for at least 4–6 months was the treatment of choice.

(*Thorax* 1996;**51**:449–450)

Keywords: actinomycosis, transphrenic spread.

Actinomycosis is an infectious disease caused by a facultative anaerobic Gram positive micro-organism, usually *Actinomyces israelii*. We describe two patients with thoracic actinomycosis in which transphrenic spread of the disease played a major part.

Case histories

CASE 1

This patient, a 50-year old man, was seen with a four month history of pain in the right side of the chest. Physical examination and chest radiography showed no abnormalities. An abscess developed just below the right nipple. No healing was seen after several drainage procedures and the patient became increasingly unwell. Bronchoscopic examination repeatedly showed white tissue fragments in the medial segment of the middle lobe. A computed tomographic scan showed a right hilar mass with extension into the chest wall and a connection to a mass situated ventrally to the liver. Multiple fistulae later occurred in the right chest and abdominal walls. The liver showed indentation with a subphrenic abscess (fig 1).

Actinomyces israelii was isolated from cultures from the second bronchoscopic examination. Antimicrobial therapy was started with penicillin G (12 megaunits intravenously every 24 hours). The subphrenic abscess was opened through a right subcostal incision and the various fistulae were extensively cleansed and an irrigation system inserted into the phrenic cavity. Daily washings were performed and 0·5 megaunits of penicillin were instilled on each occasion.

After a postoperative period of two weeks the patient was discharged with continued anti-

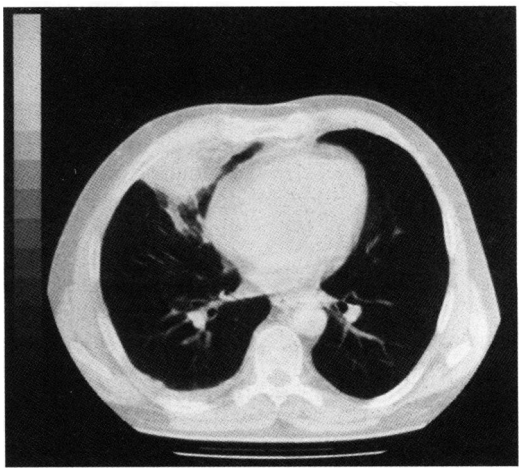

Figure 1 Computed tomographic scan of case 1 showing a subphrenic abscess along with infiltrative defects of the right chest wall.