Tuberculous meningitis as a complication of sarcoidosis

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SYNOPSIS In two patients with well established sarcoidosis, the acute onset of meningitis proved to be due to tuberculosis rather than to an extension of sarcoid granulomata to the meninges. The cerebrospinal fluid changes are very similar, and the differential diagnosis rests on a search for *Mycobacterium tuberculosis*.

The following two case histories are presented to show that the occurrence of a meningeal syndrome in sarcoidosis is not necessarily due to the presence of sarcoid granulomata in the meninges, as has been reported by a number of authors (For references, see Gaines *et al.*, 1970).

CASE 1

This girl was immunized with BCG at the age of 15 years. When she was 23 years old, a routine radiograph showed bilateral enlargement of the hilar lymph nodes. She did not react to 10 units of old tuberculin, and a diagnosis of sarcoidosis was made. Six months later she felt unwell, the hilar glands had further enlarged, and the erythrocyte sedimentation rate was elevated. She was started on prednisone, but soon developed erythema nodosum. A Kveim test and supraclavicular node biopsy both confirmed the diagnosis of sarcoidosis (Figure). Over the next two years, episodes of fever and of pain in the left hypochondrium occurred. The spleen was found to be enlarged. It was removed, found to weigh 3.6 kg, and to be full of multiple non-caseating nodules. Neither in this, nor in her sputum could *Mycobacterium tuberculosis* be demonstrated. Anterior uveitis followed this operation, and the lungs became progressively infiltrated. Her therapy was changed to chloroquine, indomethacin and corticotrophin (ACTH). Two and a half years after her first symptom she became febrile, drowsy, and developed a headache, and shortly after, a disturbance of sensation in the face and left arm which improved in the next three weeks. A month later she

again became febrile, and a radiograph of the chest showed consolidation of the right mid zone. *Staphylococcus aureus*, resistant to many antibiotics, was cultured from the sputum, but no tubercle bacilli

FIGURE Granulomata in supraclavicular node of case 1.

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were seen or cultured. She then became confused and developed a left hemiparesis. The cerebrospinal fluid (CSF) was under normal pressure, and contained no cells or organisms. The protein concentration was 110 mg/100 ml, sugar 60 mg/100 ml, and chloride 116 mEq/l. The presence of a staphylococcal cerebral abscess was suspected, but an isotope scan, carotid arteriogram, and ventriculogram were normal. The ventricular CSF, however, contained 36 lymphocytes/mm³. The lumbar fluid was therefore re-examined nine days after the first examination, and on this occasion there were 92 lymphocytes and 44 polymorphs/mm³, the protein concentration being 200 mg/100 ml and the sugar 9 mg/100 ml. The diagnosis of sarcoid meningitis was made, but shortly afterwards the laboratory found acid-alcohol-fast bacilli in the CSF. Streptomycin, PAS, and isoniazid were given and she rapidly became less confused, and the left hemiparesis improved. However, she continued to have severe morning headaches, and her memory was very poor. Three months after her acute illness, a lumbar pneumoencephalogram showed a communicating hydrocephalus, and the CSF at this examination still contained 30 lymphocytes/mm³, sugar 44 mg/100 ml. She then reacted to 10 units of old tuberculin. Intrathecal streptomycin was begun and the CSF gradually became normal.

Eighteen months after her acute illness she developed a uveitis, eosinophilia, and hypercalcaemia (7.5 mEq/l.). It was thought that the illness had reverted in pattern to the sarcoid form, steroids were recommenced, but antituberculous treatment was continued.

CASE 2

At the age of 27 years, this woman's routine radiograph of the chest showed extensive pulmonary fibrosis with some enlargement of the hilar lymph nodes. She did not react to 10 units of old tuberculin. A liver biopsy showed no definite evidence of sarcoid but, in view of the radiographic findings and tuberculin insensitivity, a confident diagnosis of sarcoidosis was made. The pulmonary changes responded to steroids, and nine years later the chest radiograph showed only some fine basal mottling. The next year, she rapidly lost 6 kg in weight, and developed severe headaches and vomiting. She then became febrile and confused and was admitted to hospital. Examination showed only irritability, confusion, photophobia, and neck stiffness. No lymph nodes were palpable, and the spleen was not enlarged. The CSF contained 152 lymphocytes/mm³ and 82 polymorphs/mm³. The protein concentration was 70 mg/100 ml and the sugar 50 mg/100 ml. Four

days later the CSF sugar was only 2 mg/100 ml. No acid-alcohol-fast bacilli could be seen, but in view of the very low concentration of sugar in the CSF it was decided to start antituberculous treatment. *Mycobacterium tuberculosis* was later grown on culture. She made an uneventful recovery, and continued antituberculous treatment for two years. At the end of that time her chest radiograph was normal.

DISCUSSION

The diagnosis of sarcoidosis was well established in both cases 1 and 2. Both had bilateral enlargement of the hilar lymph nodes, and both showed no response to 10 units of old tuberculin. The diagnosis was confirmed by a Kveim test and lymph node biopsy in case 1, and supported by the presence of pulmonary infiltrates in case 2. Although care must be taken, in the present state of knowledge, to avoid defining sarcoidosis in terms of aetiology, Scadding (1967) summarizes the evidence that suggests that in some patients, at least, sarcoidosis 'is a response to an antigen-antibody complex associated with the mycobacterial infection, in a subject with a special sort of alteration of reactivity'. If this is so, patients with illnesses intermediate between sarcoidosis and tuberculosis will occasionally be seen and, in rare instances, there will be a transition from one form of the disease to the other. Among Scadding's 275 personal patients with sarcoidosis there were five who showed a transition from pre-existing sarcoidosis to tuberculosis. The original diagnosis in all five was supported by bilateral hilar lymphadenopathy or pulmonary mottling, insensitivity to old tuberculin, and non-caseating granulomata in biopsies of lymph nodes or skin. In all, the character of the disease suddenly changed, lesions caseated, sensitivity to old tuberculin appeared, and tubercle bacilli could be found in the sputum.

The purpose of reporting the two patients is to draw the attention of neurologists to the possibility that the sudden appearance of meningitis in a patient with pre-existing sarcoidosis may be due to the presence of active tuberculosis. Chemical and cytological examination of the CSF is not necessarily of much help in distinguishing tuberculous from sarcoid meningitis. Gaines *et al.* (1970) have collected from the literature reports of 57 examinations of the CSF

in cases of sarcoid involvement of the nervous system. There was a pleocytosis in 41 cases, and an increased protein concentration in 40. In 10 the sugar concentration was reduced; it may occasionally be below 20 mg/100 ml. Therefore, the finding in the CSF of an increased number of cells, an increased concentration of protein, and a decreased concentration of sugar, does not distinguish between involvement of the meninges by non-caseating sarcoid granulomata, or by caseating tuberculous granulomata. Microscopical examination and culture of the CSF for *Mycobacterium tuberculosis* is essential, and if

any doubt remains, it will be necessary to treat the patient with antituberculous therapy.

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REFERENCES

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