Sarcoidosis with Involvement of the Nervous System

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The diverse manifestations of sarcoidosis have led to clinical interest in it by dermatologists, chest physicians, and occasionally neurologists and endocrinologists. Sarcoidosis is a systemic disease of unknown etiology and pathogenesis. The characteristic lesions are: epithelioid giant cell granuloma without caseations likely to be found in the liver, spleen, lymph nodes, phalanges of the hand, skin of limbs and the face, in the intestinal tract (regional ileitis), mucous membrane of the tonsils and conjunctiva. Eyes are involved in many ways resulting in papilledema, retinal lesions, secondary glaucoma or cataract, and exophthalmos. The combination of iridocyclitis with parotitis, Bell's palsy, polyneuritis, erythema nodosum, maculopapular eruption, peripheral and hilar lymph adenopathy are the first neurologic disorders. Sarcoidosis may involve any level of the nervous system. Meninges, brain substance, peripheral nerves, hypothalamus and hypophysis may be infiltrated with epithelioid and giant cell granuloma without caseation (Brain'). The subject has been reviewed by Colover'. Adhesive arachnoiditis may cause hydrocephalus. Hypophysis and hypothalamus are more frequently affected (Biggart').

Two interesting cases of pulmonary sarcoidosis with neurologic disorders are presented. One had, possibly, meningeal involvement with convulsions and the other developed spinal cord granuloma with acute paraplegia.

CASE 1
An English girl of 22 years was seen in December, 1954 at the Chest Consultant Clinic of North Lonsdale Hospital, Barrow-in-Furness, Lancs., England. She had no specific symptom except some lassitude. Her routine chest x-ray film revealed bilateral hilar adenopathy, basal macronodular and diffuse miliary pulmonary infiltrations. The radiologic appearances were suggestive of sarcoidosis of the lungs. Liver biopsy was done and histologic examination revealed epithelioid and giant cell granuloma (Fig. 1). A few months later she developed convulsions, suggestive of meningeal involvement. Neurologic examination revealed no focal sign. Her cerebrospinal fluid had increased protein. In view

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Figure 1: Liver histology showing sarcoid granuloma (December 14, 1955).
of the pulmonary and liver sarcoidosis, meningeval involvement by sarcoid process was suspected and she was put on cortisone 100 mg. daily with antituberculosis drugs, streptomycin 1 gm. and PAS 12 gm. daily for three months. She made remarkable recovery.

CASE 2

On July 15, 1960, a woman aged 35 was seen at the Zeal-Pak Clinic, Hyderabad (West Pakistan) for chronic paraplegia. History revealed that in December, 1952 she had pain in the right hypochondrium with cough and pyrexia for the past two weeks. She had been treated in one of the hospitals for liver disorder. In May, 1953 she developed complete paraplegia with a sensory loss to the upper abdominal level. She was unable to sit up, and was investigated and treated in another hospital. Myelography revealed some obstructive lesions at the level of the 10, 12 dorsal and the first lumbar vertebrae. X-ray films of the dorsal spine were normal. Exploration of the lower dorsal and upper lumbar spinal cord revealed a granulomatous tumor mass which was removed and decompression done. Biopsy of the tissue showed giant cells, epithelioid cells and lymphocytes. She was given a course of streptomycin and PAS. There was some gradual improvement in her sensory and motor symptoms. On October 17, 1955 she was able to sit up. She again complained of pain in the right lower chest and right hypochondrium, in association with cough and pyrexia. X-ray film of the chest showed diffuse bilateral micronodular lesion with confluent macronodules at the right base of the lung with hilar adenopathy (Fig. 2). On August 28, 1956 x-ray film of the chest showed considerable improvement with residual lesion at the right base (Fig. 3). She was seen by the author on July 15, 1960 for pyrexia, 102° F. and pain in the right hypochondrium. Examination revealed tender and enlarged liver up to four fingerbreadths. Her lungs were clear clinically and her old paraplegia was established with some residual weakness in both the legs. She was able to walk with support. Reflexes in the legs were normal. No sensory loss was noted, the sphincteric control was good.

Investigations: X-ray film of the chest revealed no evidence of pulmonary lesions except elevated right hemidiaphragm, possibly due to enlarged liver which was confirmed by right lateral view. Cholecystography revealed no abnormality. Liver function test showed thymol turbidity 6.5 units with negative Von den Bergh test. X-ray film of the dorsal spine showed no bony lesion except held up contrast media at the level of 10th, 11th and 12th dorsal spine. The erythrocyte sedimentation rate was 28 mm./hr., hemoglobin 12 gms., and white blood cell count, 6,550 per cmm. Stool and urine examinations revealed no abnormality. The Mantoux tuberculin test was negative. In view of a long course, with involvement of the liver, spinal meninges with granuloma, pulmonary lesions, negative Mantoux test, positive tissue biopsy of spinal cord granuloma revealing giant cells, and epithelioid cells suggestive of sarcoidosis. Liver biopsy was suggested, but refused.

![Figure 2: Chest x-ray film showing widespread micronodular lesions and right basal confluent macronodular lesions. Bilateral adenopathy is visible (October 17, 1955).](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21371/)
Vitamin D₃ (Ostocalcium),* three tablets daily was administered and her temperature subsided within a week. Cortisone, 100 mg. daily with INH 200 mg. and streptomycin 1 gm. daily were administered for three months. Her pain and heaviness in the right hypochondrium receded and the liver enlargement decreased to one fingerbreadth. She also noted some improvement in the motor power of her right leg and was able to walk with support.

Recently, some physicians have reported (International Conference on Sarcoidosis,* 1960) amelioration of the symptoms and signs, following treatment with chloroquine, in chronic and persistent cases of sarcoidosis. Therefore, she was put on chloroquine one tablet three times a day for three weeks, then two tablets daily, following three month course of cortisone, streptomycin and PAS. Since symptoms and signs were persistent in the liver and spinal meninges for the past eight years, prolonged therapy with chloroquine was worth a trial. She made remarkable improvement in the motor power of the legs and was able to walk with support and can stoop freely for her prayer without support. After two months on chloroquine treatment, she developed blurred vision and chloroquine was discontinued. She was again put on calciferol and short-term intermittent courses of corticosteroids.

**Discussion**

Pulmonary lesions in the presented cases were typical of sarcoidosis. In both cases, the liver was involved by the sarcoïd process. Case 2 had hepatomegaly for the past eight years with clinicopathologic evidence of acute episodes such as fever, cough, pain in the right hypochondrium, constitutional upset, and paraplegia. Diagnosis was confirmed by the histology of the spinal granulomata. Case 1 had no hepatomegaly or constitutional upset and the diagnosis was confirmed by the liver biopsy.

In Case 1, epileptic convulsions with increased cerebrospinal fluid protein were suggestive of meningeal involvement. In Case 2, recent x-ray inspection of the dorsolumbar spine, eight years following paraplegia, showed no bony involvement, which excludes spinal tuberculosis and her chest x-ray film, six years after the onset of pulmonary signs, was clear and showed no residual lesions. The sequence of events in these cases shows that the disease is of a systemic nature involving various organs successively.

The clinical course is variable and is usually chronic with minimum or no constitutional upset as in Case 1; however, there may be an acute phase with constitutional upset and fever as observed in Case 2. The course had been divided into three phases: acute, subacute and chronic. Sarcoidosis has been defined as subacute if the disease process is less than two years,

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*Calciferol 1500 units + Calcium phosphate 1.5 gm. daily.
and chronic if it is more than two years old. Case 2 presented all the phases and eventually merged into the chronic phase.

The prognosis in the subacute phase is better as there is a high incidence of remission within one year, while in the chronic phase the prognosis is poor as it leads to pulmonary fibrosis, cor pulmonale and nephrocalcinosis with hypercalciuria. None was observed in the presented cases.

Pulmonary lesions in sarcoidosis have been described as fine reticulation with bilateral hilar adenopathy, diffuse micro or macronodular lesions, involving the mid and basal zones. Other diagnostic features are negative tuberculin test, positive Kveim reaction, elevated serum gamma globulin, elevated serum calcium with calciumia and positive liver or gland biopsy, showing giant cell and epithelioid cell granuloma. Recently bronchial biopsy has been recommended. In the present cases, pulmonary lesions were nodular mostly midzonal, basal and bilateral with hilar adenopathy.

Steroids and antituberculosis drugs are recommended in acute progressive lesions of the lungs, in cases with persistent hypercalciuria, with involvement of the heart and central nervous system and in disfiguring of the skin. A minimum course of steroids is three months in subacute cases and long-term steroid therapy is indicated in the chronic cases. The dose is adjusted to the requirement of each case, so as to suppress the lesions without side effects. In cases of sarcoidosis with nervous system lesion, steroid therapy should be started as early as possible to avert any irreversible change. It was thought retrospectively in Case 2 that the steroids had been used at the onset of paraplegia, the results could have been much better. In spite of the delayed use of steroids, appreciable improvement was observed in the motor power of the legs.

ADDENDUM: A year after submission of this paper for publication, the patient's condition was reviewed on April 20, 1962. She was doing nicely on the intermittent short term courses of corticosteroids and Calciferol for six weeks and ACTH Gel 40 I.U. for three days after conclusion of each course. She showed further slow and steady improvement in the motor power of her legs.

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REFERENCES

INADEQUATE POSTANESTHETIC VENTILATION

Inadequate postoperative respiration happens according to the literature rather often. The most common cause seems to be the use of muscle relaxants. In the opinion of the authors, a valuable sign of returning muscle power is the "head-lift" test, which has been used for several years to the extent that no patient is moved from the operating table until he can lift the head from the pillow by flexing the neck, with the result that "re-curarization" never has happened. Thiopental alone causes only minimal respiratory depression in doses commonly used, but if opiates were added, a considerable degree of depression was always seen. We agree with other authors in the opinion that a routine use of opiate antagonists is not indicated. A condition of mild hypoxia may occur at the termination of nitrous oxide-oxygen anesthesias when the patient is breathing room air. The prophylactic treatment of this type of hypoxia must be administration of pure oxygen a few minutes after anesthesias with nitrous oxide.