Nodular Sarcoidosis: An Unusual Radiographic Appearance*

*Om P. Sharma, M.D. F.C.C.P.,** Robert Hewlett, M.D.,† and Jay Gordonson, M.D.‡*

Six patients with histologically confirmed sarcoidosis and multiple pulmonary nodules on a chest x-ray film are described. This radiographic appearance, typical of neoplastic metastases, is seen rarely in sarcoidosis.

Multiple circular or oval pulmonary densities on chest roentgenogram most commonly represent neoplastic metastases. This radiographic picture may also be seen in other tumors (lymphoma, myeloma), infectious diseases (especially tuberculosis and fungal chest diseases), immunologic disorders (Wegener's granulomatosis and rheumatoid lung), mucoid impaction, pneumoconiosis, A-V fistulae, multiple bronchial adenomas, benign metastasizing leiomyomas, hydatid cysts, pulmonary infarcts, laryngeal-tracheal-bronchial papillomatosis, hamartomas, multiple hematomas, splenosis, extramedullary hematopoiesis and nonspecific lung impaction abscesses. Sarcoidosis rarely produced multiple pulmonary nodules.

The purpose of this report is to describe six cases of biopsy-proved sarcoidosis with this uncommon radiologic manifestation. These cases represent an incidence of 4.0 percent in a series comprising 150 patients.

Case Reports

Case 1

This 31-year-old Negro woman was admitted in May, 1970, with a two-week history of swelling and pain about the eyes, with an associated dry gritty feeling. She complained also of weakness, anorexia, night sweats, and a nonproductive cough. A nonpruritic right-sided facial rash had been present for a few days. Physical examination findings were normal, apart from bilateral lacrimal gland enlargement. A chest roentgenogram showed bilateral hilar adenopathy and numerous discrete nodules (Fig 1).

Tuberculin, histoplasmin, coccidioidin, and mumps skin test results were negative. Lacrimal gland, liver, and scalene node biopsies showed nonspecific changes. A Kveim test reaction was positive. Aspiration needle biopsy, under fluoroscopic control, of the left hilar node revealed noncaseating granulomata. Results of a Schirmer's test were positive. Results of studies for autoimmune disease were negative. She was treated with corticosteroids. She became asymptomatic, and the chest x-ray film findings cleared completely within nine months, at which time treatment was discontinued. Her condition is unchanged 18 months later.

Case 2

A 20-year-old Negro man was admitted in July, 1971, with cough, fever, dyspnea, chest pain, night sweats, and recent weight loss. He denied hemoptysis. Positive findings on examination were a temperature of 37.5°C, supraclavicular lymphadenopathy, and liver enlargement of 2 cm. The spleen was not palpable. A chest x-ray film showed bilateral hilar lymphadenopathy and numerous parenchymal nodules (Fig 2).

Sputum could not be obtained. Results of tuberculin, histoplasmin, and coccidioidin skin tests were negative. A Kveim test reaction was positive. Lymph node biopsies, scalene and inguinal, showed sinusoidal hyperplasia. An open-lung biopsy revealed noncaseating granulomata.

A course of corticosteroid therapy over four months produced no change radiologically.

In October, 1971, a pleural effusion appeared in the right hemithorax, but the serous exudate (protein 5.7 gm) revealed no evidence of any infection or malignancy. The Cope needle biopsy of the pleura showed chronic nonspecific fibrosis.

His extensive pulmonary disease currently has remained unchanged.

*From the Department of Pulmonary Medicine and the Department of Radiology, Los Angeles County, University of Southern California Medical Center, Los Angeles.
**Assistant Professor of Medicine.
†Barlow Fellow in Pulmonary Disease.
‡Assistant Professor of Radiology.
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Reprint requests: Dr. Sharma, 2025 Zonal Avenue, Los Angeles 90033

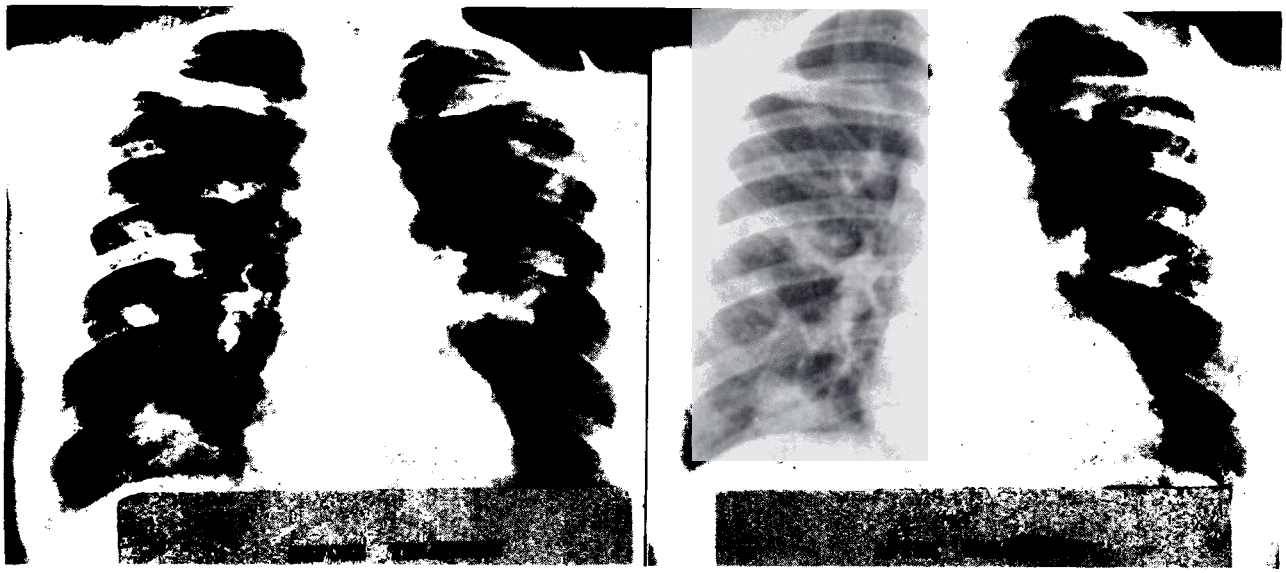

FIGURE 1. *Case 1.* Left hilar adenopathy and nodular shadows in both lung fields and right lower zone: Before and after treatment with corticosteroids.

CASE 3

This 21-year-old Negro woman presented in February, 1972, with erythema nodosum, fever, and arthralgia of both ankles and knees, of three weeks duration. She denied cough, dyspnea, hemoptysis, or chest pain. Personal and family histories were of no significance. A chest x-ray film showed bilateral hilar lymphadenopathy and multiple parenchymal nodules (Fig 3).

Results of tuberculin, mumps, histoplasmin, coccidioidin, streptokinase, streptodornase, trichophyton, and Candida skin tests were negative. Antistreptolysin O titers were normal. The VDRL was negative. A skin biopsy showed nonspecific changes. An open-lung biopsy was performed, which showed noncaseating granulomata.

In view of her systemic symptoms, a course of corticosteroids was given, but no improvement in chest x-ray film appearance has ensued in six months, although the erythema nodosum has resolved.

FIGURE 2. *Case 2.* Prominent bilateral hilar and paratracheal lymph node enlargement associated with multiple parenchymal nodules in 20-year-old Negro man.

CASE 4

A 28-year-old Negro man was admitted in March, 1970, following several days of testicular discomfort. His appetite was poor and he had lost some 6.78 kg in weight in the preceding two months. During this time, he had also noticed nonspecific chest pain. Physical examination revealed a small 2 mm swelling above the upper pole of the left testicle, considered to represent appendix epididymis. A chest x-ray film showed multiple pulmonary nodules (Fig 4).

Results of tuberculin, histoplasmin, and coccidioidin skin tests were negative. A Kveim test reaction was positive. Lymphangiography showed replacement and abnormal position of the nodes, consistent with a metastatic malignancy. A cervical node biopsy revealed numerous noncaseating granulomata. When closed-lung biopsy was nondiagnostic on two occasions, an open-lung biopsy was performed, which revealed noncaseating granulomata. Fungal and acid-fast bacil-

FIGURE 3. *Case 3.* Bilateral hilar and paratracheal node enlargement associated with scattered parenchymal nodules, both lung fields.

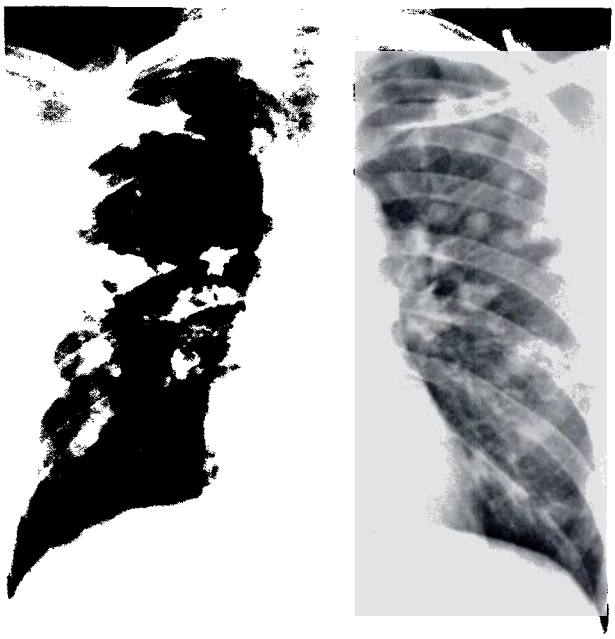

FIGURE 4. *Case 4.* Diffuse nodular involvement, both lung fields.

li stains of the tissue removed at biopsy were negative.

The patient was a known alcoholic. He did not take his medications, prednisolone and later chloroquine, faithfully. Currently, some 32 months since diagnosis, his clinical condition and abnormal x-ray film findings remain unchanged.

CASE 5

A 39-year-old Negro man presented in February, 1966, with acute pain and irritation of both eyes and photophobia. He had no other symptoms. Physical examination showed bilateral uveitis. A routine chest x-ray film revealed bilateral hilar adenopathy and multiple nodular parenchymal lesions (Fig 5).

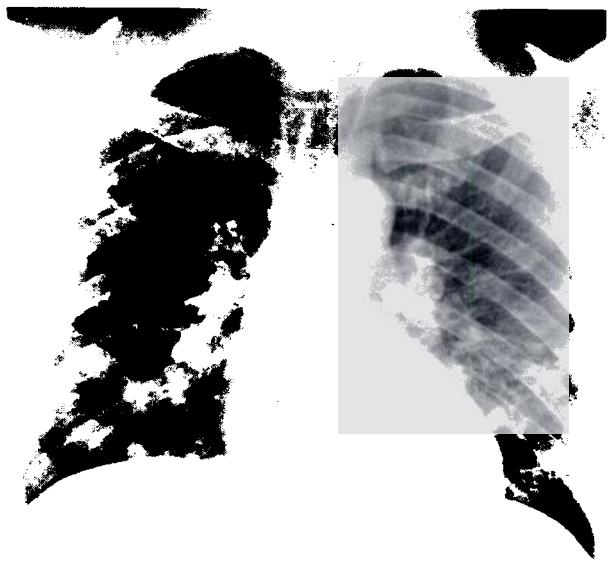

FIGURE 5. *Case 5.* Bilateral hilar lymph node enlargement and scattered parenchymal nodules in mid and lower lung fields.

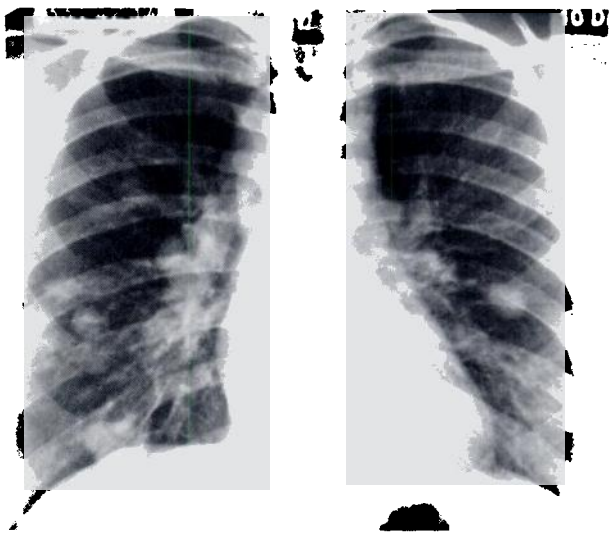

FIGURE 6. *Case 6.* Bilateral hilar lymphadenopathy and paratracheal adenopathy associated with parenchymal nodules in 21-year-old Negro woman.

Tuberculin and coccidioidin skin test results were positive. Gastric washings and nebulized sputa revealed a few acid-fast bacilli, although cultures remained negative. Sputum examination for abnormal cytology was negative. Scalene node liver and bronchial biopsies showed nonspecific changes. A conjunctival biopsy, however, revealed noncaseating granulomata, consistent with sarcoidosis.

The iridocyclitis has been controlled with topical corticosteroid eye drops. Antituberculous chemotherapy was administered for two years. No systemic corticosteroid therapy was given, as the patient remained asymptomatic. His chest x-ray film appearance has remained unchanged for the last five years.

CASE 6

A 21-year-old black woman presented in December, 1972, with a six-month history of chronic daily cough, productive of a small quantity of yellow sputum. There had been a 4.52 kg weight loss over this period. Findings at physical examination were within normal limits. A chest x-ray film showed bilateral hilar adenopathy and multiple pulmonary parenchymal nodules (Fig 6).

Tuberculin, histoplasmin, coccidioidin, and mumps skin test results were negative. Sputa examinations for pathogens, acid-fast bacilli and abnormal cytology were negative. Mediastinoscopy showed mediastinal lymph node enlargement, and biopsy revealed noncaseating granulomata.

Clinical and laboratory findings on these patients are briefly summarized (Table 1).

COMMENT

The varied radiologic appearances of sarcoidosis have been classified into four stages:

Stage 0–normal chest x-ray film

Stage 1–bilateral hilar lymph node enlargement

Stage 2–bilateral hilar lymph node enlargement with parenchymal infiltration

Stage 3–diffuse pulmonary infiltration without hilar adenopathy; this latter group, coalescing with a far

Table 1—*Brief Summary of Clinical and Laboratory Findings in Six Patients with Nodular Sarcoidosis*

Case, No.	Age, Yr.	Sex	Clinical Features	Chest X-Ray, Film	Histology (Noncaseating Granuloma)	Intermediate Tuberculin Skin Test, Results	Globulin 3-4 G/ 100Ml	Calcium 9-11 Mg/ 100Ml
1	31	F	fever, dryness of mouth & eyes; enlarged parotid & lacrimal glands.	BHL;* MPN**	hilar node	negative	4.2	9.2
2	20	M	fever, night sweats, weight loss	BHL;* MPN**	lung	negative	4.8	9.6
3	21	F	fever, erythema nodosum	BHL;* MPN**	lung	negative	4.6	10.6
4	38	M	weight loss, chest pain	MPN*	lung	negative	5.0	10.9
5	39	M	uveitis	BHL;* MPN**	conjunctiva	positive	4.2	10.8
6	21	F	cough, weight loss	BHL;* MPN**	mediastinal node	negative	4.4	10.2

*Bilateral hilar lymphadenopathy.
**Multiple pulmonary nodules.

advanced roentgenographic appearance of extensive pulmonary fibrosis with bullae formation. Atypical patterns are rare, well described in detail by Felson and Freundlich et al,[1-3] with particular reference to the differential diagnosis of the multicystic variety and the multinodular lesions. This latter type is conceded in Fraser and Pare, "An occasional case of sarcoid proved by biopsy or by a positive Kveim reaction shows large, dense, lesions simulating metastatic neoplasm."[4] In the cases presented, the multinodular lesions varied in size from less than 1 cm to 3-4 cm. Most of the lesions had well circumscribed borders, but in some (cases 1 and 2) there was coalescence, and the true margins became indistinct. In addition to multiple nodular parenchymal lesions, four of our cases demonstrated unequivocal hilar lymphadenopathy, which clearly alerted us to the possibility of sarcoidosis. It must be admitted, however, that a variety of other conditions may be consistent with these changes; infections, neoplasms, inhalation and idiopathic diseases; in the setting of additional diffuse nodules, metastatic neoplasia; and in the younger patient, lymphoma or leukemia must also be considered.

Several features demonstrated by the patients deserve comment. All were Negro, which is consistent with the predominance of this race with sarcoidosis in this country, and likewise, all six were under the age of 40 years at the age of onset, which parallels the experience of most reported series, that this is a disease of young adults.[5]

Many of the systemic effects of sarcoidosis are illustrated by these patients, *viz*, constitutional symptoms, pulmonary symptoms, ocular, rheumatologic, dermatologic, and reticuloendothelial manifestations. It is of interest that in the three patients in whom a Kveim reaction was sought, it was positive and may infer activity of the disease process, especially in the case without hilar adenopathy. A consistent finding in this group was the presence of hyperglobulinemia, although there can be no statistical conclusion drawn from such a small group.

It is further noted that in reporting what we believe may represent the first series of six patients with nodular sarcoidosis, that diagnosis was often delayed by inadequate attention to the need for exact tissue diagnosis of the pulmonary lesions. We would urge an active approach, including early open-lung biopsy when the diagnosis is at all in doubt.

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