Radiological Findings in Sarcoidosis

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Abstract

Background: Sarcoidosis is a multisystemic disorder of unknown cause that primarily affects the lungs. The diagnosis is based on the clinical manifestations, radiological findings and histological examination.

Objectives: To review and illustrate the typical and atypical radiological findings of sarcoidosis in the chest.

Methods: We analyzed the radiographic thoracic findings of all patients who had biopsy-proven sarcoidosis over the last 10 years.

Results: There were 100 consecutive patients (36 men and 64 women, age 20–84 years) with an established diagnosis of sarcoidosis. Thoracic lymphadenopathy was detected in 89 patients (89%). Lung parenchyma involvement was found in 60 patients. These changes were variable and included: ground-glass attenuation (n=39), multiple small nodules (n=44) and irregular thickening of the interlobular septa (n=16). Larger nodules (1–3 cm) were identified in 12 patients and frank consolidations were seen in 12 patients. Pleural thickening with subpleural nodules was identified in 17 patients.

Conclusions: Sarcoidosis has a wide variety of radiological manifestations in the chest. Familiarity with the various radiographic findings is important for diagnosis and management.

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Sarcoidosis is a systemic disease of unknown etiology with a wide variety of clinical and radiological manifestations [1]. This disease is characterized by non-caseating granulomas with proliferation of epitheloid cells. Morbidity and mortality are closely related to pulmonary manifestations. There is spontaneous remission in about two-thirds of the patients and progression in 10–30%. Fatalities occur in 1–5% owing to respiratory insufficiency, central nervous system involvement or myocardial involvement. Almost all organs may be affected, however intrathoracic involvement is the most common, affecting up to 90% of patients [1,2]. Certain radiographic findings, although not diagnostic, are highly suggestive of sarcoidosis. The finding of enlarged bilateral and symmetric bronchopulmonary and paratracheal lymph nodes has been recognized in sarcoidosis since at least 1940 [3]. The parenchyma of the lung may be normal or may demonstrate a variety of abnormalities [4]. The typical radiographic manifestations of sarcoidosis are generally recognized, however, there are many unusual manifestations, which are presented in this study.

Patients and Methods

In a retrospective study of the period 1994–2004, 100 consecutive patients with biopsy-proven, newly diagnosed pulmonary sarcoidosis were studied for their clinical symptoms, X-ray findings and pulmonary function. The diagnosis was made in 98 patients in our institution, based on mediastinoscopy and mediastinal lymph node biopsy, bronchoscopy and transbronchial biopsy, computed tomography-guided biopsy from lung nodules and ultrasound-guided biopsy from enlarged periportal lymph nodes. The remaining two patients had been diagnosed by bronchoscopy elsewhere prior to admission. We reviewed the chest radiographs and CT examinations of all the patients.

Results

The group consisted of 36 male and 64 female patients aged 20–84 years. At the time of diagnosis, 21% patients in our group presented with respiratory symptoms (dyspnea, chest pain) and 17% presented with constitutional symptoms (fever, weight loss). Sixty-two percent of our patients were asymptomatic but had chest X-ray abnormalities. Extrapulmonary manifestations were found in 11%.

Lung function test was retrieved in 10 patients, and revealed a restrictive pattern in one (total lung capacity 70%) and airway obstruction in five patients (forced expiratory volume in 1 second 52 ± 23%, mean ± SD). In the other four, lung function tests were normal [Table 1].

Thoracic lymphadenopathy was the most common finding

Table 1. Lung function test of 10 patients with pulmonary sarcoidosis

Patient #	FEV1	Post-BD FEV1	TLC	DLCO/VA
1	47	16%	90	81
2	97	8%	116	104
3	82	ND	70	33
4	47	14%	83	78
5	37	20%	92	67
6	61	18%	85	ND
7	87	1%	89	101
8	70	22%	92	87
9	106	ND	116	97
10	80	4%	88	118

FEV1, TLC and DLCO/VA are expressed as % of predicted values.

Post-bronchodilator FEV1 is expressed as % improvement after BD, as compared to pre-BD value.

FEV1 = forced expiratory volume in 1 second, TLC = total lung capacity, DLCO/VA = Diffusion capacity of the lung for carbon monoxide corrected for alveolar volume, ND = not done

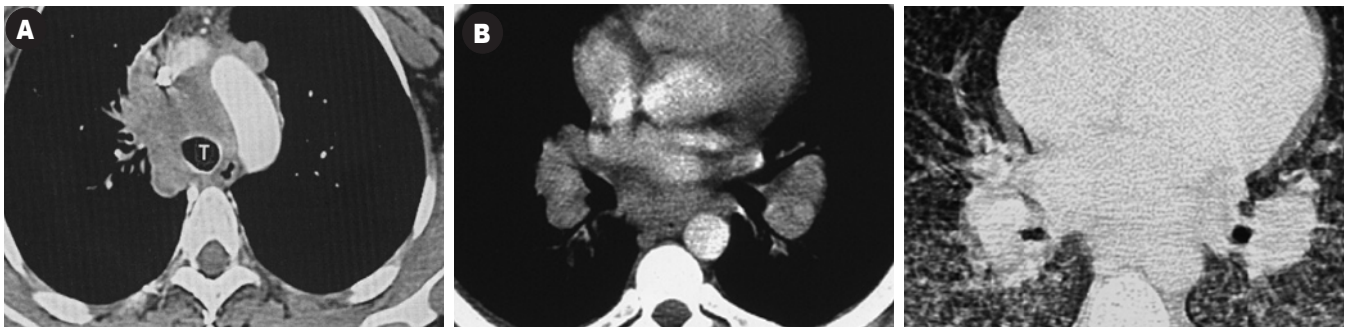

Figure 1. [A] Mediastinal lymphadenopathy in a 43 year old woman. Figure 1. **[B]** Mediastinal lymphadenopathy in a 55 year old man. Enlarged bilateral hilar and subcarinal lymph nodes are seen.

Figure 2. Pulmonary sarcoidosis. CT demonstrates multiple miliary nodules with perivascular distribution, reflecting the distribution of sarcoid granulomas along the lymphatic vessels within the interstitium.

in our patients, detected in 89 (89%). CT revealed bilateral hilar, paratracheal and aortic pulmonary window lymph node enlargement. Bilateral hilar with right paratracheal was the most frequent nodal enlargement, demonstrated in 66% of the patients [Figures 1A and B]. Lymph node calcifications were rare, detected in only three patients.

Lung parenchyma involvement was seen in 60 patients (60%). These changes were variable and included: ground-glass attenuation (n=39), multiple small nodules typically in a peribronchovascular distribution (n= 44), irregular thickening of the interlobular septa (n=16) [Figure 2], larger nodules (1–3 cm) (n=12), and frank consolidations larger than 3 cm (n=12) [Figure 3A]. In the majority of cases with lung parenchymal changes theirs was an upper lobe predominance (83%). Three of the patients with consolidations presented with cavitary masses [Figure 3B]. Forty-one patients (41%) had both, lymphadenopathy and lung parenchymal changes. Pleural thickening with subpleural nodules was identified in 17 patients.

Discussion

Pulmonary involvement is reported in as many as 90% of patients with sarcoidosis. The presence of bilateral and symmetric paratracheal and hilar lymph nodes enlargement, with or without parenchyma abnormality, is highly suggestive, although not diagnostic, of sarcoidosis. There is often an apparent predominance of right hilar and paratracheal lymph nodes, as left-sided nodes are obscured by other structures. The lateral chest X-ray may be helpful in identifying the presence of increased densities in the hilar area. In a Swedish study covering the years 1966 to 1980, a total of 57% of cases were detected by mass chest radiographs. In a Japanese survey, a 50% prevalence rate of asymptomatic cases was found [5]. The findings on chest X-ray form the base for staging, which relates to prognosis. The outcome, expressed either as spontaneous remission or as 5 year mortality, is closely related to the radiological stage: the 5 year mortality being 0% in stage 1, 11% in stage 2, 18% in stage 3, and more than 50% in stage 4 [6]. The ACCESS study [7], a case-controlled, multicenter study, involved 10 centers in the United States between 1997 and 1999. Incident cases and matched controls were compared regarding the prevalence of various exposures. Cases were confirmed by tissue diagnosis, compatible clinical course, and exclusion of other possible causes of granulomas. Altogether, 736 patients were enrolled, 63.6% female, 36.4% male, 53.4% white and 44.2% black. The peak age and gender affected were females aged 35–39 years. Lung involvement was seen in 95% of patients, skin involvement other than erythema nodosum in 16%, extrathoracic lymph node involvement in 15%, eye involvement in 11.8%, and liver involvement in 11.5%. Among the characteristics of lung involvement in patients enrolled in the study was the fact that 8% of the patients had stage 0, 40% stage 1, 36% stage 2, 10% stage 3, and 5% stage 4.

Sarcoidosis accounts for a wide variety of radiological manifestations [8-11]. High resolution CT is performed in most cases as it is highly sensitive for adenopathy and parenchymal changes. In our group of patients, mediastinal and bilateral hilar adenopathy with or without parenchymal changes were the most frequent finding (89%), correlating with the findings reported in the literature [2,4,7]. The most common nodes were the hilar and right paratracheal, observed in 66% of cases. Parenchymal findings con-

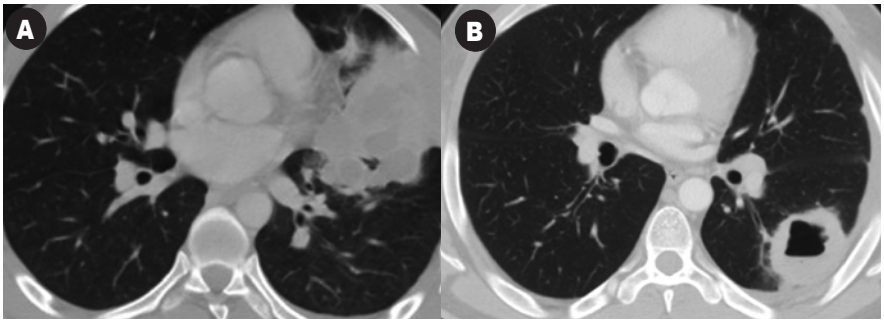

Figure 3. [A] Pulmonary sarcoidosis in a 48 year old man. CT demonstrates large consolidation in the left upper lobe. Note the presence of air bronchogram, which may also be seen in sarcoidosis. **[B]** Pulmonary cavitary sarcoidosis. A cavitary mass is demonstrated in this CT of a 50 year old man.

stitute a large spectrum and have a tendency to involve mostly the upper lobes (83%). The sarcoid granulomas are distributed along the lymphatic vessels and this is well demonstrated by high resolution CT. CT revealed widespread small nodules with a perivascular distribution in 44%. Nodules may also be evenly distributed throughout both lungs with predominance of the upper and middle lung zones or, more commonly, in the perihilar and peribronchovascular region. Thickened interlobular septum, seen in 16% of our patients, is a characteristic finding [5,9]. Large nodules or conglomerate masses are much less common, resulting from coalescence of granulomas [12]. Attention should be paid to the cavitary nodes which present a rare form of the disease – in our study 3%. Ground-glass attenuation, although not common in sarcoidosis, was demonstrated in 39% of our patients. Approximately 20% of patients develop some pulmonary fibrosis, which may lead to honeycombing and parenchymal distortion [1]. Our cases, as well as those described in the literature, demonstrate the variability of sarcoidosis patterns and the resemblance – in many cases – to other diseases like tuberculosis, lung malignancies or lymphoproliferative diseases. It is especially confusing in patients who already suffer from malignancy, as occurred in some of our cases with breast carcinoma or lymphoma who developed lung nodules, interlobular septal thickening or mediastinal lymphadenopathy. The radiographic findings were suggestive of sarcoidosis, however metastatic disease could not be excluded and histological diagnosis was therefore necessary. The diagnosis of sarcoidosis can be suggested radiologically; however, in many cases a histopathological examination is required in order to demonstrate the typical non-caseating epitheloid cell granulomas and exclude other disorders. This can be done by endobronchial and transbronchial biopsy as the airways mucosa is often infiltrated by sarcoid cells, even in radiological stage 1. Lymph node biopsy can be performed whenever adenopathy is present, either by bronchoscopic transbronchial needle aspiration and biopsies or by mediastinoscopic biopsies. In some cases, especially where peripheral lung nodules or consolidations are present, imaging-guided percutaneous biopsy is the preferred procedure.

Familiarity with the common and rare manifestations of pulmonary sarcoidosis and with the variable combinations of the radiographic signs may assist in diagnosing this disease and may reduce the delay to diagnosis and, if necessary, treatment.

References

1. Schaefer-Prokop C, Prokop M, Fleischmann D, Herold C. High-resolution CT of diffuse interstitial lung disease: key findings in common disorders. *Eur Radiol* 2001;11:373–92.
2. Aladesanmi OA. Sarcoidosis: an update for the primary care physician [Review]. MedGenMed 2004;6:1–11. www.medscape.com/viewarticle/470113
3. Meisels E. The course of Bersnier-Boeck's disease of the lungs in serial rontgenograms. *Am J Radiol* 1940;44:564–7.
4. ATS, ERS, WASOG: Statement on Sarcoidosis. *Am J Respir Crit Care Med* 1999;160:736–55.
5. Hosoda Y, Yamaguchi M, Hiraga Y. Global epidemiology of sarcoidosis. What story do prevalence and incidence tell us? *Clin Chest Med* 1997;18:681–94.
6. Reed HM. Sarcoidosis: a multisystem disease. *Minority Health Today* 2000;2:9–14.
7. Baughman RP, Teirstein AS, Judson MA, et al. A Case Control Etiologic Study of Sarcoidosis (ACCESS) research group. Clinical characteristics of patients in a case control study of sarcoidosis. *Am J Respir Crit Care Med* 2001;164:1885–9.
8. Takashi K, Hiroyuki U, kaori T, et al. Radiologic manifestations of sarcoidosis in various organs. *Radiographics* 2004;24:87–104.
9. Mul ler NL, Kullnig P, Miller RR. The CT findings of pulmonary sarcoidosis: analysis of 25 patients. *Am J Roentgenol* 1989;152:1179–82.
10. Miller BH, Rosado-de-Christenson ML, McAdams HP, Fishback NF. Thoracic sarcoidosis: radiologic-pathologic correlation. *Radiographics* 1995;15;421–37.
11. Nishimura K, Itoh H, Kitaichi M, Nagai S, Izumi T. Pulmonary sarcoidosis: correlation of CT and histopathologic findings. *Radiology* 1993;189:105-9.
12. Niimi H, Hartman TE, Muller NL. Necrotizing sarcoid granulomatosis: computed tomography and pathologic findings. *J Comput Assist Tomogr* 1995;19:920–3.

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