MSCT Pulmonary Manifestations and Complications of Long Standing Sarcoidosis

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Abstract

Background: Sarcoidosis is a multisystem chronic inflammatory condition of unknown etiology. It is known to have mediastinal lymphadenopathy and parenchymal perilymphatic distribution of its granulomas. In long standing cases, however, fibrosis and honey combing described as fibrocystic changes with classic broncho-centric and upper zonal predilection are recognized. Mycetoma is a reported complication of fibrocystic sarcoidosis. Multi-slice computed tomography (MSCT) especially high-resolution technique (high resolution computed tomography, HRCT) play a very important role in diagnosing pulmonary manifestations and detect the possible complications of long standing sarcoidosis.

Aim of the Work: The purpose of this study is to depict the pulmonary parenchymal changes and the possible complications in long standing sarcoidosis and to explore the role of MSCT/HRCT in its diagnosis.

Patients and Methods: This study included 23 cases 20 females and 3 males, age range 45 to 62 years old (average 51.66 years). Cases were referred to the Radiology Department Kasr Al-Aini for MSCT/HRCT assessment of the chest. All patients were known cases of sarcoidosis with duration of illness ranging from five to seventeen years (5-17 years), all were subjected to thorough clinical evaluation, laboratory assessment. CT chest (with high resolution technique) done to all patients using MDCT (Toshiba- Aquillion, 64 detectors).

Results: In this study multi-slice and high resolution computed tomography (MSCT with high resolution technique; HRCT) detected various CT chest signs in long standing sarcoidosis patients.

Key Words: Multi-slice computed tomography – High resolution technique – Long standing sarcoidosis.

Introduction

SARCOIDOSIS is a multisystem disorder of unknown cause that is characterized by the presence of non caseating granulomas and the proliferation of epithelioid cells [1].

Although sarcoidosis can affect patients of any age, sex, or race, it typically affects adults less than 40 years old, and the incidence peaks in the 3rd decade of life, classically more in women than in men [2]. The diagnosis of sarcoidosis is commonly established based on clinical and radiological findings that are supported by histological findings [3].

The histological hallmark of sarcoidosis is non caseous granuloma [4]. Fibrotic changes usually begin at the periphery of a granuloma and extend centrally, leading to complete fibrosis and hyalinization, or both [5]. The upper lobes of the lung are most severely affected [6]. Vascular involvement is observed in more than half of patients with sarcoidosis who undergo an open lung biopsy or autopsy study [7].

The clinical signs and symptoms are non specific and include fatigue, general malaise, weight loss, and less commonly fever [3]. The characteristic radiological findings associated with sarcoidosis have been well described and the findings include bilateral hilar lymphadenopathy and parenchymal abnormalities [8]. Multiple small nodules in a perilymphatic distribution along with irregular thickening of the interstitium are typical CT findings of sarcoidosis [3].

The clinical course varies; nearly two-thirds of patients with sarcoidosis generally remain stable or experience a remission within a decade after diagnosis, with few or no consequences thereafter [8,9]. However, approximately 20% of patients develop chronic disease leading to pulmonary fibrosis [10]. Less than 5% of patients die of sarcoidosis; death from sarcoidosis is usually the result of extensive and irreversible lung fibrosis with respiratory failure or cardiac or neurological
involvement [11]. Sarcoidosis-associated pulmonary hypertension (SAPH) has been reported by several groups [12,13].

More than 40 years ago, Siltzbach developed a sarcoidosis staging system based on the pattern of plain chest radiographic findings [3] The Siltzbach classification system defines the following five stages of sarcoidosis in plain chest radiography: Stage 0, with a normal appearance at chest radiography; stage 1, with lymphadenopathy only; stage 2, with lymphadenopathy and parenchymal lung disease; stage 3, with parenchymal lung disease only; and stage 4, with pulmonary fibrosis [7]. Computed tomography added a great value in establishing diagnosis’, staging and detection of complications of long standing thoracic sarcoidosis, sometimes giving more anatomic and pathological details that were undetectable by conventional plain radiography. High resolution technique (HRCT) demonstrates normal and abnormal lung interstitium and morphologic characteristics of both localized and diffuse parenchymal abnormalities; in this regard, HRCT is clearly superior to plain radiographs and conventional CT. A role for high resolution computed tomography (HRCT) exists when patients present with atypical clinical or radiographic findings, for detection of complications, or in the context of a normal radiograph but clinical disease suspicion, thus changing the staging with plain radiography [6,14-17].

Parenchymal fibrotic changes: In most patients, sarcoid granulomas resolve with time [8]. However, in an estimated 20% of patients, fibrosis becomes more prominent over time, producing CT and radiographic findings of linear opacities, traction bronchiectasis, and architectural distortion (displacement of fissures and broncho-vascular bundles). Fibrosis is seen predominantly in the upper and middle zones, in broncho-centric pattern or in patchy distribution [18]. Extensive interstitial fibrosis can cause pulmonary arterial hypertension and resultant right side heart failure [19].

Fibrotic changes may manifest as conglomerate masses with broncho-centric distribution associated with marked traction bronchiectasis [20]. These processes are usually seen predominantly in the central and upper lung. Again, this distribution is typical of sarcoidosis but can also be seen in tuberculosis and silicosis. Extensive calcification may be encountered within fibrotic granulomas [3].

Fibrotic cysts, bullae, and paracatricial emphysema represent advanced-stage sarcoidoses which are irreversible changes [21]. Fibrotic and cystic lesions typically involve the upper and middle lung zones and follow the large airways in a peri-hilar distribution [22]. Posterior displacement of the main or upper-lobe bronchus and volume loss (particularly in the upper lobes) are characteristic features of chronic fibrosis [3] see Tables (1,2).

Honeycomb-like cysts in patients with sarcoidosis are most commonly distributed in the subpleural regions of the middle and upper lung zones, whereas the lung bases are usually spared [23]. Occasionally this pattern of fibrocystic change is seen in the lower lung zones, an atypical location that may cause pulmonary sarcoidosis to be mistaken for idiopathic pulmonary fibrosis [24,25].

The formation of mycetomas is a well-recognized complication of long standing sarcoidosis [26]. Fungal balls may develop when pre-existing bullae and cysts (typically in the upper lobes) are colonized by saprophytic fungi, usually Aspergillus species [27].

Aim of the work:

The purpose of this study is to depict the pulmonary parenchymal changes and the possible developed complications in long standing sarcoidosis and to explore the role of MSCT using the high resolution technique (HRCT) in its diagnosis.

Patients and Methods

This study included 23 cases 20 females and 3 males, age range 45 to 62 years old (average 51.66 years). Referred to the Radiology Department Kasr Al-Aini at the period from 2010 – 2011, till 2010 – 2012.

All patients were already known to be cases of sarcoidosis with duration of illness ranging from five to seventeen years (5-17 years), all were subjected to thorough clinical evaluation, laboratory assessment. CT chest (with high resolution technique) was done to all patients using MDCT (Toshiba-Aquillion, 64 detectors).

Thirteen out of them were under therapy by corticosteroids for periods ranging from five to fifteen years and were coming for follow-up.

All patients had progressive dyspnea and dry cough while two patients had hemoptysis.

Inclusion criteria:

Known cases of long standing sarcoidosis.
Exclusion criteria:

Recent onset of sarcoidosis.

Methods:

• Thorough clinical evaluation and laboratory assessment.

• CT chest done to all patients using multi-detector computed tomography MDCT (Toshiba Aquilion, 64 detectors). High-resolution CT was done in all patients for detection of chronic pulmonary parenchymal changes (Figs. 1-7), see Table (3).

• Pulmonary function tests:

Done to all patients and showed restrictive changes in 20 patients, mixed changes in two patients and no appreciable changes in one patient.

Results

This study included 23 cases with sarcoidosis.

HRCT chest results showing different parenchymal lesions, their distribution as well as the fibrotic changes Tables (4,5).

Table (1): Pulmonary manifestations and complications of chronic sarcoidosis at high-resolution CT [3].

Morphological changes

Fibrotic changes: Bronchocentric fibrosis, reticular opacities, architectural distortion, traction bronchiectasis, bronchiolectasis, volume loss.

Fibrocystic changes: Cysts, bullae, blebs, emphysema, honeycomb-like opacities.

Mycetoma, aspergilloma.

Distribution of changes

Bilateral predominant: Upper and middle-zone locations of parenchymal abnormalities with broncho-centric distribution of fibrotic changes.

Rarely: Unilateral.

Basal predominance.

Table (2): Irreversible abnormalities of pulmonary sarcoidosis at high-resolution CT [3].

Honeycomb-like opacities, cysts, bullae, emphysema.

Architectural distortion.

Traction bronchiectasis, bronchiolectasis.

Volume loss in upper lobes, retraction of hila.

Mycetoma (in 10% of patients with end-stage sarcoidosis and a pre-existing cavity).

Table (3): Helical HRCT protocol for Toshiba aquilion multislice 64 channels CT scanner at Kasr Al-Aini Hospital.

Preparation: Not needed.

IV contrast: Not needed.

CT scanning:

• CT scan examinations are performed using Toshiba Aquilion multislice 64 channels.

• The examination is done in supine position.

• A scout is taken with 120kV and 120mA, and then helical scanning is done in caudo-cranial direction to minimize respiration artifacts.

• Using 64 detector row.

• Slice thickness 1.0mm.

• Pitch 1.5:1.

• Speed (mm/rotation) 7.5mm.

• Detector configuration 64x1.

• Beam collimation 5mm.

• Interval 5mm.

• Gantry tilt 0.0.

• FOV depends on the patients’ body built, but is about 35cm.

• kV 120.

• mA 250-400.

• Total exposure time 7 seconds during breath hold in inspiration.

Table (4): Parenchymal lesions; number and percentage in studied cases.

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Upper-Lobe fibrotic changes</th>
<th>Fibrocystic/ emphysema/honeycomb</th>
<th>Architecture distortion</th>
<th>Mycetoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>14</td>
<td>7</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>% of cases</td>
<td>60.8%</td>
<td>30.4%</td>
<td>69.5%</td>
<td>8.7%</td>
</tr>
</tbody>
</table>

Table (5-a): Bilaterality Distribution of parenchymal lesions.

<table>
<thead>
<tr>
<th>No. of cases</th>
<th>% of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral with rather symmetry</td>
<td>21</td>
</tr>
<tr>
<td>Unilateral predominance</td>
<td>2</td>
</tr>
</tbody>
</table>

Table (5-b): Zonal distribution of parenchymal lesions (fibrotic changes).

<table>
<thead>
<tr>
<th>Fibrosis</th>
<th>No. of cases</th>
<th>% of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper and mid zonal predilection</td>
<td>21</td>
<td>91.39%</td>
</tr>
<tr>
<td>Mid and lower zonal</td>
<td>None</td>
<td>0%</td>
</tr>
<tr>
<td>Broncho-centric fibrotic changes</td>
<td>23</td>
<td>100%</td>
</tr>
<tr>
<td>Diffuse</td>
<td>23</td>
<td>100%</td>
</tr>
</tbody>
</table>
Fig. (1a,b): Female patient 55 years old with chronic sarcoidosis, HRCT (axial and coronal images) showing broncho-centric fibrosis in both lungs more on the right side (arrows).

Fig. (2a,b): Female patient 32 years old with sarcoidosis, HRCT (axial and sagittal images) showing broncho-centric fibrosis in both lungs more on the right side with reduced volume of the right upper lobe. Prominent interlobular septa are seen on the right upper lobe anterior segment with a nodule seen in the left upper lobe posterior segment (arrow).

Fig. (3a,b): Female patient 40 years old with sarcoidosis, HRCT (axial and coronal images) showing broncho-centric fibrosis (arrows) in both lungs and right upper lobar honeycombing (asterisk).
Fig. (4a-d): Female patient 40 years old known case of sarcoidosis coming for follow-up. Axial post IV contrast enhanced CT (mediastinal and lung windows). Mediastinal window shows right paratracheal, bilateral hilar and subcarinal lymphadenopathy, with punctuate calcification (arrows). Lung window (d) shows bilateral upper lobar nodules with bilateral upper lobar fibrosis (curved arrows).

Fig. (5a-d): Female patient 55 years old known case of sarcoidosis coming for follow-up. High resolution CT in axial, coronal and sagittal planes showing bilateral upper lobe fibrosis, volume loss with honeycombing (asterisk), multiple fibrocysts, and thickened distorted fissures (curved arrow).
Fig. (6a-c): Female patient 40 years old known case of sarcoidosis coming for follow-up after an attack of hemoptysis. High resolution CT in (a,b) coronal and sagittal planes (a,b) showing left cavitary lesion with mycetoma (curved arrow), and bibasal fibrosis with traction bronchiectasis. (c) Mediastinal window (c) shows bilateral hilar lymphadenopathy (arrows).

Fig. (7a-d): 52 year old male patient with eight year-history of sarcoidosis, CT in axial plane (lung window) (a,b) showing bilateral upper lobar fibrosis (arrows) with a left upper lobe cavity and mycetoma (open arrow). Mediastinal window (c,d) shows mediastinal and bilateral axillary lymph nodes (curved arrows).

**Discussion**

Sarcoidosis is a multisystem chronic inflammatory condition of unknown etiology in which lung and the mediastinal lymph nodes affection is most common, being seen in approximately 90% of patients [1,3] and accounts for most of the morbidity and mortality associated with the condition [28].

Plain films as a preliminary study is usually done with no evident changes detected in early stages or very subtle parenchymal changes, yet, it was helpful in staging of the disease process [29].

Computed tomography has a great value in establishing diagnosis of thoracic sarcoidosis. The rapid adoption of multi slice computed tomography (MSCT) technology testifies to its advantages over single slice computed tomography (SSCT). The principal basis of its advantages can be stated as follows: MSCT allows large anatomic ranges to be scanned while simultaneously producing both
thin and thick slices and consequently results in
lowered image noise. HRCT can demonstrate normal
and abnormal lung interstitium and morphologic
characteristics of both localized and diffuse
parenchymal abnormalities; in this regard, HRCT
is clearly superior to plain radiographs and con-
ventional CT. A role for high resolution computed
tomography (HRCT) exists when patients present
with atypical clinical or radiographic findings,
detection of complications, or in the context of a
normal radiograph but clinical disease suspicion
is still present. If biopsy is required, then HRCT
can be utilized to guide clinicians to potential high-
yield sites for transbronchial or surgical lung biop-
sy; this was also ensured by Hawtin et al., Whitten
et al., Taguchi and Anno, Flohr et al., Bartz and
Stern [6,14-17].

All of our patients were already known to be
cases of long standing sarcoidosis with duration
of illness ranging from five to seventeen years (5-
17 years).

In our study the broncho-centric fibrotic changes
were found in all patients (100%); compared to
20% found in Abehera et al., [30], this could be
attributed to that our study was concerned with
chronic patients of sarcoidosis where irreversible
pulmonary parenchymal architecture distortion
supervened with permanent fibrotic and cicatrical
changes. Their study was concerned with reversible
and irreversible parenchymal changes. Thus, like-
lihood of early and reversible fibrotic changes
were less expected to be seen in our study, on the
other hand chronic fibrotic sequale were more
prevalent in our targeted sample (chronic and
complicated cases).

Co-existence of pulmonary chronic fibrotic as
well as fibro cystic changes and mediastinal lymph-
phadenopathy (Figs. 4, 6, 7) was found in five of
our patients (21.7%), this agrees with Criado et
al., and Koyama et al., that Siltzbach classification
stands only for plain radiography, while MSCT
has changed this concept [3,9].

Honeycombing (Table 4) is less common com-
pared to other interstitial lung diseases, and if seen,
tends to distribute sub-pleurally in the mid-upper
zone, sparing the bases [31]. In our study, honey-
combing, (Figs. 3, 5) was found in seven of our
patients (30.4%) and was supleural and predomi-
nantly upper lobar in distribution, this was also
described by Abehera et al., [30] and by Nishino
et al., [31]. In the review of 80 consecutive patients
with pathologically proven sarcoidosis and radio-
graphic evidence of pulmonary fibrosis the honey-
comb pattern was seen in 23 patients (29%) [30,31].

According to Koyama et al., [9] pulmonary
carcinoid nodules rarely manifest with cavitation (in
<3% of patients with parenchymal opacities). In
our study fibrocysts, traction bronchiectasis and
blebs were found in seven of our patients (Figs. 3,5) (30.4%); putting such findings in the chronic
sequale of the disease process, this goes with Muller
et al., describing similar changes in long standing
sarcoidosis patients [24].

Mycetoma formation was noted in 1-3% by
Muller et al., and Hours et al., [24,25]. In our study
only two patients had mycetoma (8.7%); a higher
incidence in the current study, dealing with the
long standing sarcoidosis with fibrocystic changes
but not early or non complicated cases, pointing
to that it was atypical parenchymal manifestation
of chronic sarcoidosis; actually considering it as
a remote complication of long standing fibrocystic
sarcoidosis (Figs. 6,7).

Regarding the disease process distribution
Tables (5a-b):

Bilateral fairly symmetric distribution was
noted in twenty one of our cases (91.39%), with
the broncho-centric distribution found in all patients
(100%) Figs. (1-7), while unilateral predominance
was noted in two of our patients (8.7%), this greatly
matches with the literature considering bilaterality
and rather symmetry of the disease distribution
found in more than 90% of patients and the unilat-
eral predominance of distribution considered an
uncommonly encountered finding, (Fig. 4) [3].

For interstitial pattern of disease distribution,
upper and mid zonal predilection was depicted in
twenty one of our patients (91.3%) this goes with
that found by Nishino et al., and was not found in
mid/lower zonal or bi basal regions individually
as a separate distribution pattern [31].

Fibrotic changes were noted as diffuse changes
in all of our patients (100%), while in the upper
and mid-zones in twenty one out of them (91.3%),
Fig. (5), while in only one patient (4.3%); these
changes were present predominantly in the basal
zones.

Extensive calcification may be encountered
within fibrotic granulomas [3]. However, in our
study it was found in one patient (4.3%), being
smaller and non-extensive, Fig. (4).
Conclusion:
Long standing sarcoidosis with chronic irreversible fibrotic and fibrocystic changes have a classic broncho-centric distribution with classic predominant upper lobar distribution. This could be well demonstrated by multi-slice CT using the high resolution technique.

Honeycombing in long standing sarcoidosis is classically subpleural and upper lobar.

Mycetoma is a rare but recognizable complication of chronic sarcoidosis.

References


Youssriah Y. Sabri, et al.