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Clinical Presentation of Sarcoidosis in El-Minia Governorate (Egyptian Local Experience)

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Abstract
Background: *The exact course of sarcoidosis is still unknown, ranging from spontaneous remission with no treatment in 2/3 of cases and in the remaining 1/3 of the cases long-term treatment is needed. Chest computed tomography (CT); is beneficial to judge potentially reversible from irreversible (fibrotic) lung damages.*
Patients and Methods: *This work was a retrospective study included 30 patients with sarcoidosis who were presented as out-patients to chest clinic from 2012 to 2017.*
Results: *This study included 30 patients; 8 males and 22 females. Their age ranged from 32-62 years with mean and SD 45.1 ±10.49. Dyspnea grade 2 and 3 was the commonest symptom present in 28 patients, followed by cough in 24 patients. Ocular manifestations were also common, chest pain and CNS manifestation were found in 4 patients. Bilateral hilar lymph node enlargements (BHLs) were suspected in 25 patients at x ray film and detected in 24 patients on MDCT study. Also, on MDCT, nodular shadows were seen in 16 patients and ground glass opacities identified on 11 patients.17 cases were diagnosed by biopsy, Heerford syndrome in 2 cases and Lofgreen syndrome in 4 cases and 7 patients refused biopsy but had typical radiological and clinical scenario of sarcoidosis.*
Conclusion: *Diagnosis of sarcoidosis can be made by highly specific clinical and radiological manifestations with exclusion of other differential diagnosis, mainly TB and lymphoma. Radiological findings were more specific regarding their distribution that mostly preferred the middle and lower lung zones.*

Introduction

The exact course of sarcoidosis is still unknown; an abnormal immune response to airborne-transmitted antigen whether organic or inorganic is a strong theory in the causation of sarcoidosis. A genetic factor is usually there when speaking about sarcoidosis.(1)

Sarcoidosis is characterized by variable course ranging from spontaneous remission with no treatment in 2/3 of cases while in the remaining 1/3 of the cases long term treatment is needed.(2)

The chest radiograph findings are still the gold standard due to the limited radiation exposure and easy evaluation of disease regression or progression. However, inter-observer variability and lack of functional clinical parameters are limiting factors.(2)

Computed chest tomography (CT); is beneficial to judge potentially reversible from irreversible (fibrotic) lung damages.(3)

Treatment of sarcoidosis should be directed to the pulmonary and extra-pulmonary manifestations.

There are no guide lines for treatment; however, therapeutic options should include 1st line (glucocorticoids), 2nd line (disease modifying antisarcoid drugs) and 3rd line (biological agents) management protocols.(4&5)

The aim of this work to study the clinico-radiologic presentation of chest sarcoidosis in our locality.

Material and Methods

Design of work

The clinical study was a retrospective study included 30 patients with sarcoidosis who were presented as out-patients to chest clinic from 2012 to 2017.

Patients were diagnosed according to a constellation of clinical findings that are so specific for sarcoidosis that the diagnosis may be made empirically without the need for a confirmatory biopsy **(Baughman et al; 2011)**(6)**,** or tissue biopsy revealing granulomatous inflammation (usually non-caseating), with exclusion of alternative causes of granulomatous inflammation **(Mukhopadhyay et al; 2013).**(7)

All the patients had been subjected to the following

- Full detailed history taking included (age, sex, smoking status, other exposure, duration of illness and symptoms of different systems affection).
- Full general examination.
- Local chest examination: For any abnormality.

Investigations Included

1) Plain chest x- ray (PA view).
2) High Resolution Computed tomography.
3) Echocardiography for:
   - Ejection fraction.- Pulmonary artery systolic pressure
   - Diastolic dysfunction.- Pericardial effusion
4) Pulmonary function tests (PFT).

- Results were recorded for forced vital capacity (FVC), forced expiratory volume in 1st second (FEV1), FEV1/FVC percentage and forced expiratory flow at 25-75% of FVC (FEF25-75%). Absolute and percente predicted values were detected.

5) General laboratory evaluations as complete blood picture, ESR, CRP, liver function tests and renal function tests.
6) Laboratory tests known to be related to sarcoid as ACE and serum calcium.
7) Investigations for exclusion of TB: Ziehl-Neelsen sputum test, tuberculine test and Quanteferone TB Gold test.
8) Biopsy: End-bronchial ultrasound bronchoscopy. - Lymph node biopsy. - Other organs.
9) Treatment: - Steroid only. - Steroid and other agents.

Statistical Analysis

Data entry and analysis were done with IBM compatible computer using software called Statistical Package for Social Science (SPSS) for Windows version 19, and microstats program. Graphics were done using Excel. Quantitative data were presented by mean and standard deviation. Qualitative data were presented as number and percent. Mann Whitney test, Chi square test, z test of proportion, independent sample test and correlation test (Pearson's test) were used. The probability of <0.05 used as cutoff point for significant tests.

Results

This study included 30 patients; 8 males (26.7%) and 22 females (73.3%). Their age ranged from 32-62 years with mean and SD 45.1 ±10.49. Most of the patients were life-long non-smokers (70%); 3 were Ex-smoker (10%), 6 were passive smokers (20%) and none were active or current smokers.

Cough was found to be a frequent symptom, noted in 24 patients (80%). It was productive in 15 patients (50%) and dry in only 9 patients (30%). No cough at all was present in the remaining 6 patients (20%). Dyspnea grade 2 and 3 was a common symptom in the studied group and was found in 28 patients (93.4%). Majority of those

patients had a grade 2 dyspnea (86.7%). Only two patients had no breathing difficulty (6.7%). Chest pain and chest wheezes were present in 4 (13.3%) and 10 (33.3%) patients respectively (table 1).

We noted skin manifestations in the form of erythema nodosum in 6 patients (20%), but lupus pernio, keloid and skin papules each of them was present in 2 patients (6.7%).

CNS symptoms were present in 4(13%) patients, 2 of them had epileptic fits and other 2 patients had facial palsy.

Ocular manifestations were noted in the form of lacrimal gland swelling in 11 patients (36.7%), dryness of the eye in 7 patients (23.3%), itching in 5 patients (16.7%), eye redness in 5 patients (16.7%) and dropped eye lid in only two patients (6.7%). (table 2)

General symptoms were frequently noted and the commonest was fatigue in 21 patients (70%) followed by fever in 18 patients (60%), arthralgia in 15 patients (50%), weight loss in only 5 patients (16.7%) and peripheral lymphadenopathy in 5patients (16.7%). (table 3).

Regarding X-ray findings, bilateral hilar lymphadenopathy was the most common and found in 25 patients (83.4%). For the reticular, nodular patterns and pleural effusion, each of which was recorded in only two patients (6.7%). Veiling in chest radiograph was obvious in 9 patients (30.1%). Other chest X-ray findings were linear atelectatic bands in two patients (6.7%). (Table 4).

HRCT characteristics of studied patients revealed evident lymph node enlargements, most of them were bilateral hilar lymphadenopathy in 24 patients (80%), prevascular lymph nodes in 22 patients (73.3%), subcarinal nodes in 13 patients (43.3%), paratracheal nodes in 9 patients (30%). Other HRCT findings were nodular shadows in 16 patients (53.3%), air space shadows in 10 patients (33.3%), ground glass opacity in 11 patients (36.7%), reticular opacity in 5 patients (16.7%), pericardial effusion in 4 patients (13.3%) and pleural effusion in only two patients (6.7%). Many of the cases showed diffuse lung infiltrations that were evident in 17 patients (56.7%) but 11 patients showed localized lobar infiltrations (36.7%). (Table 5).

The diagnosis of our patients was made by various methods. The most important was biopsy in 17 patients (56.7%) in the form of cervical lymph node biopsy in 5 patients (16.7%), cutaneous biopsy in 2 patients (6.7%), ovarian and pelvic LN biopsy in two patients (6.7%), and mediastinal LN biopsy by EBUS in 8 patients (26.7%). Other diagnoses were made by Heerford syndrome in two patients (6.7%) and Lofgreen syndrome in 4 patients (13.3%). Seven patients (23.3%) refused biopsy but had typical radiological and clinical scenario of sarcoidosis. (table 6).

The most important laboratory investigation was ESR which was elevated in most patients with range (22-65). Another was ACE which was elevated in 18 patients (60%). Other lab investigations were shown in (table 7).

Table (1): Respiratory symptoms of the studied group:

		Frequency	Percent %
Cough	No	6	20.0
	Dry	9	30.0
	Productive	15	50.0
	Hemoptysis	0	0
Shortness of breath	Grade 0	2	6.7
	Grade I	0	0
	Grade II	26	86.7
	Grade III	2	6.7
	Grade Vl	0	0
Other symptoms	Wheeze	10	33.3
	Chest pain	4	13.3

Table (2): Extra pulmonary sarcoidosis among the studied group:

		Frequency	Percent %
Skin lesions:		12	38
	Erythematous nodosum	6	20
	Lupus pernio	2	6.7
	Kolloid	2	6.7
	Recurrent multiple bilateral papules	2	6.7
CNS manifestations		4	13
	History of facial palsy	2	6.7
	Epileptic fits	2	6.7
Ocular:		16	53
	Swelling of lacrimal gland	11	36.7
	Dryness of eye	7	23.3
	Itching	5	16.7
	Redness	5	16.7
	Dropped eye lid	2	6.7

N.B1. One patient may have more than one symptom

Table (3): General and local examination of the studied group:

			Frequency	Percent %
General Examination		Fever	18	60
		Weight loss	5	16.7
		Fatigue	21	70
		Peripheral lymphadenopathy	5	16.7
		Arthralgia	15	50
Local Examination	Shape	Normal	30	100
		Abnormal	0	0
	Presence of dullness	Positive	2	6.7
		Negative	28	93.3
	Auscultation	No abnormality	13	43.3
		Wheeze	10	33.3
		Bilateral crepitation more upper zone	2	6.7
		Bilateral crepitation more lower zone	5	16.7

Table (4): X-ray characters among the studied group:

		Frequency	Percent %
Hilar LN	No	5	16.7
	BHL	25	83.4
Nodular shadow	No	28	93.3
	Yes	2	6.7
Reticulonodular	No	28	93.3
	Yes	2	6.7
Distribution	Diffuse	2	6.7
	Rt lower zone	2	6.7
Effusion	No	28	93.3
	Yes	2	6.7
Vealing	No	21	90
	Bilateral basal	5	16.7
	Right lower	2	6.7
	Right middle	2	6.7
Other findings:	Linear atelectatic band	2	6.7

Table (5): HRCT characters among studied group (n=28)

		Frequency	Percent %
Hilar LN	No	4	13.3
	BHL	24	80
Paratracheal LN	No	19	63.3
	Yes	9	30.0
Retrocaval LN	No	16	53.3
	Yes	12	40.0
Prevascular LN	No	6	20.0
	Yes	22	73.3
Subcarinal LN	No	15	50.0
	Yes	13	43.3
Retrocardiac LN	No	21	70.0
	Yes	7	23.3
Nodular shadow	No	12	40.0
	Yes	16	53.3
Air space shadow	No	18	60
	Yes	10	33.3
Reticular	No	23	76.7
	Yes	5	16.7
Ground glass opacity	No	17	56.7
	Yes	11	36.7
Effusion	No	22	73.3
	Pericardial	4	13.3
	Pleural	2	6.7
Distribution:	Diffuse	17	56.7
	Middle lobe and lingual	7	23.3
	middle and lower lobes	4	13.3
Other findings:	Thick beaded right horizontal fissure	3	10.0

NB. Two cases without CT (total =28)

Table (6): Methods of diagnosis (biopsy or other):

	Frequency	Percent %
By biopsy:	17	56.7
Cervical lymph node biopsy (NCG) Cutanous biopsy (NCG) Ovarian and LN biopsy (NCG) Mediastinal biopsy (NCG) EBUS	5 2 2 8	16.7 6.7 6.7 26.7
Heerfordt syndrome	2	6.7
Lofgreen syndrome	4	13.3
Group refused biopsy had typical radiological and clinical scenario of sarciodosis	7	23.3

Table (7): Laboratory investigations of the studied group

		Minimum	Maximum	Mean	SD
Hemoglobin		10.0	15.8	13.243	1.5587
Total Leukocytic count		4100.0	7500.0	5956.667	997.1281
Eosinophils		1.0	2.1	1.400	.3301
Lymphocyte		32	39	34.73	1.964
Neutrophils		53	59	56.07	1.701
Erythrocyte Sedimentation Rate 1		11	121	39.60	33.521
Erythrocyte Sedimentation Rate 2		26	143	60.63	37.954
Aspartate amino transferase		22	65	39.27	15.739
Alanine amino transferase		25	53	36.90	9.597
Creatinine		.8	1.2	1.000	.1554
Urea		21	29	23.90	2.644
Calcium level		8.5	9.1	8.867	.2202
		Frequency		Percent%	
Angiotensin Converting Enzyme	Normal	12		40	
	Elevated >40nm/ml/minute	18		60	

Discussion

Sarcoidosis is a multi systemic disease of unknown etiology. It is responsible for 23-38% of chronic interstitial lung diseases **(Valeyre et al; 2015)**[8]**.**

In the present study, females were more affected (73.3%) than males (26.7%). This was supported by **Robert et al; 2016**[9] who found a higher incidence of sarcoidosis in females (75%) than males. While, **Elizabeth et al; 2016**[10] stated that male were more affected (56%) than females (44%).

The age of our patients was in the range of 32 to 62 year. Fifty % of them were below fourty. This comes in agreement with **Bresnitz and Strom; 1983**[11] who reported that sarcoidosis had a consistent predilection for adults below 40 year of age.

Many studies demoestrate a lower incidence of sarcoidosis in smokers[12,13,14]. This study comes in the same line with the above studies as only 20% of patients were smokers. Some higher incidence was reported by **Urbankowski et al; 2012**[15] who found that 42.6% of sarcoidosis patients were smokers. The exact cause behind this lower incidence of srcoidosis in smokers is not fully understood but may be caused by suppression of the phagocytic and the antigen presenting activites of alveolar macrophages[16].

Nasal symptoms were reported in nearly half of our patients. **Jill F et al; 2000**[17] reported nasal symptoms in 38% (60/159) of sarcoid patients but the incidence of biopsy-confirmed sarcoidosis in the same study was only 4% (6/159). Sorrly no nasal biopsies were available to prove or disprove the responsibility of sarcoidosis for the nasal symptoms in the present work. This in conjunction with the known high prevelance of allergic rhinitis worldwide approaching 41% in some studies should make us cautious in interpreting our result in this respect (Heinrich et al 2002).[18]

Gastro-esophageal reflux (GER) symptoms such as heart burn, regurgitation and sore throat were found in more than half of our patients (56.7%) and this comes in agreement with **Renato et al; 2011**[19] who reported a high prevalence of GER symptoms in patients with sarcoidosis (68%). Again the very high incidence of GER symptoms in the general population, reaching 31% in the middle east acoording to a systematic review by **(El-Serag et al 2014)**[20] should be taken into consideration.

In the present work, dyspnea was present in almost all patients (100%) and it was grade 2 by mMRC dyspnea scale in the majority of cases (86.7%). In a study done by **De Boer et al; 2014**[21], dyspnea was reported in 64% of patients. Although, dyspnea was still common in that study but it was far less than in the present work. A larger number of patients (56 patients) and different patient population (75% European) in **De Boer et al; 2014 study when** compared to the present study may give some explanation for the higher incidence of dyspnea in the present work.

Productive cough was found in 80% of patients and this incidence is much higher than the incidence reported by **Kiter et al; 2011** who reported cough in 53% of patients. Of note is the much higher number of patients in Kiter et al; 2011 study comprising 253 patients[22].

Chest pain was found in (13.3%) of our patients.JL Wait and A Movahead 1989, reported chest pain in 12 (28%) patients out of 43 sacroid patients. All these patients had negative coronary angiography. Chest pain in JL Wait and A Movahead 1989, study and in the present study might be myalgeic induced by cough. None of the patients in the present work had coronary angiography[23].

Chest wheeze was a frequent symptom in the present study (33.3%) which comes in agreement with **Mihailovic et al; 2008**[24] who found chest wheeze in up to (50%) of sarcoidosis patients. Airflow obstruction and airway hyper reactivity are common in sarcoidosis (Kalkanis A and Judson MA 2013)**(25)** and this can give some explanation for wheezing in the present work.

Eye involvement was present in more than half of our patients (53%) in the form of lachrymal gland

swelling and dry kerato conjunctivitis (60**%). Tugaland Tutkun; 2017**[26] reported eye involvement in up to 60% of sarcoidosis patients.

Neurological symptoms in the form of epileptic fits and facial palsy were present in this work in only 6.7% of patients. **Culver et al; 2017**[27] reported that less than 10% of sarcoidosis patients have neurological involvement.

In the present work skin involvement was present in 38% of the patients. **Velter and Lipsker 2016**[28] reported that skin involvement was found in about 30% of cases which comes in proximity to the present study.

Mild hepatosplenomegally was found in ultrasound examination in (30%) of our patients. **Ebert et al; 2008**[29] found about 40% of sarcoidosis patients had hepatosplenomegally in U/S examination. The very high prevelance of hepatitis C in Egypt reaching 40% in some areas (Elgharably et al 2016)[30] and the lack of histologiv proof of sarcoid in liver biopsies should be taken into consideration when evaluating the above results.

Doppler echocardiography of our patients showed left ventricular diastolic dysfunction as an early sign of granulomatous involvement of the myocardium in 13.3%. **Chapelon et al; 2004**[31] reported more than double the incidence (29%). Two factors must be considered when evaluating the present result, first is the lower number of patients in the present work and second is the very high prevalence of LV diastolic dysfunction in the general population reaching as high as 27.3% **(Tatiana et al 2009)**[32].

Pulmonary hypertension (PH) as a predictor of poor outcome in sarcoidosis was presented in 80% of patients. **Shorr et al; 2003**[33] reported that the frequency of PH was as high as 73.8%. Rates of PH in sarcoidosis patients in tertiary centres vary between 5–20 % **(Bourbonnais and Samavati 2008) (Alhamad et al 2013)**[34,35]. As a side note, the gold standard right heart catheterisation for diagnosing PH wasn't done neither in the present work nor in the other exhibited studies.

In the present work, the number of lymphocytes was normal in the majority of patients. **Gerke and Hunninghake; 2008**[36] reported peripheral blood lymphocytopenia. This may be caused by the accumulation of activated T-cells at disease areas, in addition to the effect of the increased serum anti-inflammatory cytokine interleukin IL-10 and increased circulating numbers of regulatory T-cells**.**

Most of our patients had normal serum urea and creatinine concentrations that coincide with **Berliner et al; 2006**[37] who reported infrequent renal disease except in longstanding hypercalcemia and hypercalciuria.

The ESR was seen elevated in our patients and correlated with **Rothkrantz et al; 2003**[38].

X-ray findings of our patients revealed multiple radiologic patterns in form of bilateral hilar lymphadenopathy in (25/30 cases), 83.4%. **Lynch et al; 1997**[39] stated that the bilateral hilar lymphadenopathy (BHL), was the classic radiographic feature of sarcoidosis and presented in nearly three quarters of patients. Also, in this work the pulmonary parenchymal infiltrates such as nodular, reticulonodular and vealing was present in 59% of cases. **Lynch et al; 2003**[40] who found that pulmonary parenchymal infiltrates (with or without BHL) were present in 20 to 50% of patients in form of patchy or diffuse and preferentially involve the upper and mid lung zones, our patients had pulmonary parenchymal infiltrates more common in diffuse pattern and in the lower zone (6.7%).

In the present study BHL was present in (83.4%), prevascular lymph nodes in (73.3%), subcarinal nodes in (43.3%) and paratracheal lymphadenopathy in (30%). ***Semin;* 2015**[41] reported that lymphadenopathy was detected in up to 98% of patients with sarcoidosis in chest CT.

Regarding the lung parenchyma, the most common feature found in CT was nodular shadow in 53.3% which comes in agreement with **Semin; 2015**[41] who foundsmall nodules in patients with parenchymal lung involvement in 80% of cases. These nodules were bilateral, symmetrical and

correlated with **Criado et al; 2010**[42] who mentioned that nodules were usually found bilateral and symmetrical, following a perilymphatic pattern of distribution**.**

In addition to the previous nodular shadows (53.3%), another (10%) of patients showed thick beaded horizontal fissure and was supported by **Criado et al; 2010**[42] who explained that nodules in sarcoidosis tend to be more abundant around the bronchovascular bundles and subpleurallyas well as to lesser extent along the interlobular septae.

The present study revealed ground glass opacities in 36.7% of cases and this near to the results obtained by **Criado et al; 2010**[42] **and Keijsers et al; 2015**[43] who found ground glass opacities in 40% of cases.

In the present study only 6.7% of patients had pleural effusion, corresponded to **Huggins et al; 2006**[44] who reported that pleural effusion was a rare manifestation of pulmonary sarcoidosis (5 of 181 patients).

The previous CT findings were mostly found in diffuse distribution in the lungs (56.7%). But when there was localized distribution in CT, 23.3% of cases were in the middle lung zone and lingula that corresponded to **Criado et al; 2010** [42] who found a higher incidence of findings in the middle lung zones. In contrast we found 13.3% of the CT findings in the lower lung zones corresponded to **Müller et al; 1989**[45] who found that sarcoidosis features in CT involving mainly the lower-lung zone and may mimic an appearance of idiopathic pulmonary fibrosis. **Spagnolo et al; 2014**[46] who reported that the main distribution of lung infiltration in sarcoidosis patients was middle and upper zones.

Ninety five percent of patients in the present study, had a restrictive ventilator defect with FEV1/FVC ratio above 70%. Most of them had only mild restrictive pattern with FVC above 70%. An obstructive ventilator defect was seen in only 5% of patients (FEV1/FVC ratio below 70%). Spirometry in this study comes in agreement with **Calaras et al; 2017**[47] study who found an obstructive pattern in only a minority of cases (9.7%). It was strange for the research group of the present work to see defective spirometry in all the cases and the cause of this is unclear but may be reasoned by the fact that most of our patients seek medical advice only when suffering. Of note is that most patients in this study had some degree of dyspnea.

In a study by **Baratto et al; 2017**[48] diagnosis of sarcoidosis was only made when some typical clinical and radiological findings are supported by histological evidence of non-necrotic granulomas. Here, the diagnosis of our patients was made by various methods. More than half of cases (56.7%) had a confirmatory tissue biopsy from various tissues and organs. End Bronchial Ultra Sound (EBUS) biopsy was done in 16.7% of cases. The others were in the form of cervical lymph node biopsy (26.6%), cutaneous biopsy (6.7%), ovarian biopsy (6.7%).

Carter et al; 2017[49] reported that a presumptive diagnosis not requiring a tissue biopsy may be acceptable in special conditions, for example for Lofgren or Heerfordt syndromes. In the present work 43.3% of patients were diagnosed without biopsy as they had Lofgreen syndrome in 13.3%, Heerfordt syndrome in 6.7% and another 23.3% refused biobsy but had typical radiological and clinical scenario of sarcoidosis.

In the present study and among the patients who performed tuberculin skin test, 88.2% were negative and 11.8% were positive. This comes in agreement with **Gupta et al; 2003**[50] who reported that up to (95%) of sarcoidosis patients fail to react to tuberculin skin test. This can be explained by **Ahmadzai et al; 2012**[51] who mentioned that despite having an exaggerated T helper-1 (TH1)-mediated immune response at sites of disease, patients with sarcoidosis usually have suppressed peripheral blood responses to common recall antigens and poor response to vaccinations.

Although not all cases of sarcoidosis require treatment, as the disease may cause no symptoms and may spontaneously remit **Judson; 2015**[52].

Corticosteroid therapy remains the mainstay of sarcoidosis treatment. In the present study (80%) of patients had good response to oral steroid.

Delphi study of sarcoid experts reached a consensus that methotrexate is the preferred second-line agent for pulmonary sarcoidosis **Schutt et al; 2010**[53]. Methotrexate was the second line agent used in 13.4% of patients included in the present work with good response in 50% of them. This come in agreement with **Cremers et al; 2013**[54] who reported that (20-40%) of sarcoidosis patients do not respond to methotrexate. The small number of patients in the present work besides the small fraction of patients using methotrexate should be considered when looking to this result.

Conclusion

Most of the clinical and radiologic features of sarcoidosis seen in the present work were consistent with what is common in the vast majority of papers tackling sarcoidosis. A relatively high proportion of patients had a lower and middle lobe predominace of their radiologic findings.

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List of Abbreviations

CT (Computed tompography)
FVC (Forced vital capacity)
FEV (Forced expiratory volume)
TB (tuberculosis)
SPSS (Statistical Backage for social science)
CNS (central nervous system)
HRCT (high resolution computed tomography)
EBUS (endobronchial ultrasound)
ESR (erythrocyte sedimentation rate)
ACE (angiotensine converting enzyme)
GER (gastro-esophageal reflux)
LV (left ventricular)
PH (pulmonary hypertension)
BHL (Bilateral hilar lymphadenopathy)
TH1 (T helper-1).