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Sarcoidosis in north African people: About 35 cases

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Abstract. *Background and aim:* Sarcoidosis is a systemic disease of unknown cause characterized by the formation of non-caseating granulomatous inflammation in various organs, mainly lungs and intrathoracic lymph nodes. Its clinical and paraclinical presentation can range widely. Our aim is to study the clinical, paraclinical and evolution of mediastino-pulmonary sarcoidosis. *Methods:* This is a retrospective, descriptive and analytic study conducted over a 20-year period (January 2002 to December 2022). It compiled records of patients who were followed up for confirmed mediastino-pulmonary sarcoidosis. *Results:* The study included 35 patients with a mean age of 56.69 ± 14.42. There was a clear predominance of female patients (sex ratio:0.346). The most common functional respiratory signs were dyspnea (82.9%) and dry cough (80%). Extra-respiratory functional symptoms were noted in 45.7% of cases, with the most common being arthralgia (28.6%), xerophthalmia (20%) and skin lesions (14.3%). The most common parenchymal lesions were micronodules (71.4%), nodules (51.4%), and peribronchovascular thickening (40%). The The right upper lobe (77.1%) and middle lobe (74.3%) were the most affected lobes. Hilar adenopathy (71.4%), paratracheal adenopathy (60%), and the aorto-pulmonary window (54.3%) were the most frequent lymph node involvements. Oral corticosteroids were initially administered in 60% of cases. Chronic respiratory failure was observed in 20% of cases. Factors significantly associated with an unfavorable outcome included hemoptysis (p=0.008), the need for systemic corticosteroid treatment (p=0.009), acute respiratory failure (p=0.05), and echographic dilation of the right cavities (p=0.002). *Conclusions*: Diverse presentations and potential complications in mediastino-pulmonary sarcoidosis require vigilant patient management.

Key words: sarcoidosis, intrathoracic lymph nodes, chest high resolution computed tomography, prognosis

Introduction

Sarcoidosis is a multisystem granulomatous disease of undetermined etiology and pathogenesis. The incidence is estimated at around 1 to 40 / 100,000 per year (1–3). The clinical presentation varies depending on the specific organ involved. The lung and thoracic lymphatic nodes are the most frequently affected sites (4).Clinical presentations range from asymptomatic form to to sub-acute and acute clinical manifestations (5). The diagnosis of sarcoidosis relies on compatible clinical and radiographic manifestations, the presence of noncaseating granuloma on histopathologic examination, and exclusion of other causes of granulomatous inflammation (6). While spontaneous resolution occurs in most cases, chronicity can be found in 10 to 30% (7). Pulmonary fibrosis is the predominant severe manifestation (8). Serious extra pulmonary complications occurs

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in 4 to7% of cases (7). Systemic glucocorticoids are the first-line therapy for pulmonary sarcoidosis when needed (9). Therefore, the present study aimed to describe the clinical and radiological characteristics of patients with mediastinopulmonary form and their evolution.

Methods

Subjects

Our study is retrospective, descriptive, and analytic about 35 cases of confirmed mediastinopulmonary sarcoidosis, conducted over a 20-year period.

Inclusion criteria

Only confirmed cases of mediastino-pulmonary sarcoidosis with a concordant clinical, radiological, and pathological profile were enrolled.

Exclusion criteria

Uncertain diagnosis and incomplete records were excluded.

Statistical analysis

Statistical analysis SPSS 2020 software was used. Continuous variables were presented as means medians and standard deviations (SDs). Simple and relative frequencies were calculated for the categorical variables. Pearson's chi-square test and Student t-test were used for comparison.

Results

General characteristics of the study participants

The study was about 35 patients. The mean age was 56.69 ± 14.42. There was a female predominance with a sex ratio M/F of 0.346. No family history of sarcoidosis was noted. The most frequent largest age group was adults over 40 years. Eight patients were identified as daily smokers (22,9%). The median pack-years was 47 P/A. The phototype was reported in the records of 10 patients. Using Fitzpatrick classification, Phototypes II and III were equally represented (4/10). A medical history was documented in 54.3%. Hypertension was the most prevalent comorbidity (25.7%).

Table 1. Symptoms of Sarcoidosis at Diagnosis

	Number of cases	Percentages
Constitutional symptoms		
Fever	2	5,7
Asthenia	19	54,3
Anorexia	10	28,6
Weight loss	16	45,7
Intrathoracic manifestations		
Cough	28	80
Dyspnea	29	82,9
Chest Pain	11	31,4
Palpitation	5	14,3
Hemoptysis	4	11,4
Extrathoracic manifestations	16	45,7

Clinical presentation

Sarcoidosis was asymptomatic in 2.9% of patients. On the other hand, functional complaints were identified and were summarized in the Table 1 below. The most frequent constitutional symptom was asthenia (54.3%). Thoracic symptoms were observed in 97.1%. The most frequently symptoms were dyspnea (82.9%) and dry cough (80%). Extra-respiratory symptoms were noted in 45,7%: the most frequent were arthralgia (28,6%), xerophthalmia (20%), and skin lesions (14.3%).

Thoracic investigations

Chest X-ray was abnormal in 88,58 % of cases. The most commonly noted radiological types, according to the Siltzbach classification, were type III (34.3%) and type II (28.6%). Chest high resolution computed tomography (HRCT) was performed in all patients at initial clinical presentation by using multislice CT systems. Radiological evidence of pulmonary parenchymal involvement was present in 91,4% of cases. Intrathoracic lymph node involvement was present in 85,7%. The most frequent parenchymal abnormalities were confluent micronodules (71.4%), nodules (51.4%) and peribronchovascular thickening (40%). Septal lines were observed (34.3%), and non-septal lines (20%) of cases. Pulmonary fibrosis was observed too (20%).

In terms of distribution of the pulmonary opacities, the upper and middle lobes were the most affected fields. The right lung was more frequently affected, with involvement of the upper right lobe in 77.1%, the lower right lobe in 51.4%, and the middle lobe in 74.3%. Typical diffuse bilateral symmetric nodular involvement predominantly in the upper and middle regions was found in 15 patients (75% of cases). When it comes to lymph nodes involvement, hilar lymphadenopathies were the most frequent findings (71.4%). Then paratracheal lymphadenopathies (60%) and the aortopulmonary window (54 ,3%) were the most common findings. Bronchial fibroscopy was performed in 31/35 patients (88.6%). Normal bronchial mucosa was noted in 48.4%, while it was inflammatory in 51.6%. white, sticky mucus was noted in half of the cases. Bronchoalveolar lavage (BAL) was performed in 27/31 patients (87.1%). The fluid analysis showed lymphocytosis in 55.5% of cases. Macrophagic predominance was noted in 44.4%. The CD4/CD8 ratio was performed on BAL in 6 cases, with CD4 predominance in 5 cases (83.3%). Histological study of biopsies that were taken by fibroscopy led to the diagnosis of sarcoidosis in 21 patients (67.8% of cases), demonstrating granulomatous inflammation without caseous necrosis. Chronic inflammation of the bronchial mucosa without tuberculoid granuloma was observed in 10 patients, (32.2%) of cases. Finally, the histological evidence was obtained in 33 patients (94.2%), showing a tuberculoid granuloma without caseous necrosis in 29 cases (87.9%). This result was obtained through bronchial biopsy in 60% of cases. The other cases were obtained from extra thoracic sarcoidosis sites.

Extrathoracic findings

Extra-thoracic manifestations were noted in 13 patients (37.1%). Involvement of the skin was the most common extrathoracic one (20%). Sarcoids were identified in 5 patients (14.3%). Two cases of erythema nodosum were identified. Only one patient presented with Löfgren's syndrome. Ophtalmological involvement affected 14.3% of patients. Two patients had ENT (ear nose throat) involvement. Peripheral adenopathies were present in 8.6%. Hepatomegaly was present in only one patient. Cardiac involvement was suspected based on chest pain (31,4 %).

Blood work and other findings

We conducted blood work and other investigations mostly to rule out some confusing diagnosis. Hypercalcemia was found in 20% of cases. Two patients exhibited hypercalciuria.Serum angiotensin converting enzyme was measured in 12 patients, and was increased in 66.7% of cases. Antinuclear antibodies were measured in 16 patients, with positive results in half cases.

Treatment

In 40% of cases, abstention was recommended. The main reasons for etiopathogenic prescription was pulmonary issue. Beyond it, 25.7% of treated patients had extra pulmonary indication too. The 21 treated patients had initially received systemic corticosteroids. Methotrexate was used to treat only one case after corticosteroid therapy failed. Two cases of corticoresistance were noted, and one of them resulted in a fatal outcome after methotrexate treatment.

Evolution and complications

Favorable clinical evolution was observed in 74.3% including 37.14% of corticosteroid treated and 40% of untreated patients. It is worth noting that all untreated patients showed improvement. Over 70% of patients experienced complications, mostly within the first two years of sarcoidosis evolution (80%). Infectious pneumonitis was the most prevalent complication (40%). Acute respiratory failure affected 22.85% in the acute phase, while chronic respiratory failure (20%) appeared mainly in the chronic phase (85.71%). Factors associated to a poor clinical outcome included hemoptysis, increased CRP levels, scan abnormalities, need of systemic corticosteroid therapy,complications, and Dilatation of the right cavities on ultrasound (Table 2).

Discussion

Our study reveals a striking female predominance (74%), which is similar to other studies (Table 3). Despite higher prevalence in Black individuals (2), our study showcased a diverse range of Fitzpatrick phenotypes (20% II, 40% III, 40% IV). The distribution of comorbidities in our study was compared with those in the literature, as shown in

table 3. While familial forms of sarcoidosis exist, reported in 3.6% to 9% of cases (10,11), no cases of familial clustering were observed in our study. Asymptomatic sarcoidosis was found in 15%, 6.66%, 26%, and 10.5% of the study populations reported in Aloulou (12), Youba (13) , Morimoto et al. (14), and Silva et al.(15) , respectively. Our study identified this form in only 2.9%. General symptoms may occur in approximately one-third of patients with sarcoidosis (16). Fatigue was the most frequent general symptom in both our study (54.3%) and the literature (ranging from 27% to 56.66%) in Youba(13),Morar and Feldman (17)and Nunes et al (18) studies. Mediastino-pulmonary involvement is present in 90% of sarcoidosis cases(7,19,20) . This is consistent with the results of our study, where this involvement was found in 97% of cases. We compared observed thoracic functional signs with established reference ranges and report the findings in Table 3.

Chest X-ray remains a key tool for sarcoidosis diagnosis (23). According to Nunes et al(18), Bart et al (16), and Morar and Feldman(17), stages I and II are the most common. In Our study population stage III was most frequent (34.4%), followed by II (25.7%).Consistent with prior studies (24,25), CT scans revealed high prevalence of parenchymal involvement (91.4%) and lymph node involvement (85.7%) in our study. Hilar and paratracheal lymph nodes were most frequently affected (71.4% and 60%, respectively), similar to Fourati et al. (24). Bronchial fibroscopy was performed in 31/35 patients (88.6%). The endoscopic appearance of the bronchial mucosa was normal in 48.4% of cases, whereas it was inflammatory in 51.6%. These data concur with those of other series (29,30).

BAL confirmed lymphocytosis in 55.5% of cases, consistent with previous studies (26,27). Notably, our study found a high CD4+/CD8+ ratio in 83.3% (compared to 21-57,4% in other studies) (26,27). Similarly, histological analysis from bronchial fibroscopy biopsies yielded a diagnostic rate of 67.8%, comparable to El Fadili et al. (60%) (26) but exceeding other reports, including Western ones like Navarre et al (28) (26%). Our study found that 60% of patients received systemic corticosteroids, whereas an Iranian study reported oral corticosteroid prescription in 47.4% of cases (22). Sarcoidosis often has a good prognosis, however, some patients develop chronic complications like fibrosis and respiratory failure (29).This study observed a higher rate of such complications (20%) compared to a study by

Table 2. Factors associated with poor outcomes

	Favorable outcome	Unfavorable outcome	P
Hemoptysis	1 (3,7)	3 (37,5)	**0,008**
Condensations	7 (25,9)	6 (75)	**0,01**
Increased parenchymal lesions on follow-up CT scan	4 (14,8)	6 (75)	**0,01**
Need for systemic corticosteroid therapy	13 (48,1)	8 (100)	**0,009**
The occurrence of complications	9 (33,3)	7 (87,5)	**0,007**
Infectious pneumopathies	8 (29,6)	6 (75)	**0,02**
Acute respiratory failure	1(3,7)	4 (50)	**0,05**
Dilatation of the right cavities on ultrasound	0	2(5,7)	**0,02**

Table 3. Comparison with other studies

Variable	Current study (Tunisia)	Morar et Feldman (17) (South Africa))	Koudache et Embarek (21) (Algéria)	Aloulou (12) (Tunisia)	Alavi et al (22) (Iran)
Sex ratio	0,346	0,478	0,375	0,17	0,303
Pathological antecedents	Diabetes 20%	15,7	9,09	-	-
	Hypertension25,7%	32,4	36,36	-	-
	Asthma 8,6%	11,8	-	-	2,3
	Tuberculosis 0%	16,7	-	-	0,05
Symptoms	Cough 80	84	Cough and/or Dyspnea: 54,5	-	77,3
	Dyspnea 82,9	53,9		-	61,7
	Chest pain 31,4	27,5		-	-
	Hemoptysis 11,4	2		-	1

Majdoub et al. (7%) (29).Sarcoidosis patients also face a higher risk of infections, as shown in this study (40%) which were higher than Winterbauer and colleagues study results (4,5%) (30).

Conclusion

Sarcoidosis is a granulomatous disease of unknown cause that primarily affects the lungs but can involve any organ, leading to diagnostic challenges. Our study described the clinical, paraclinical, and evolutionary profile of mediastino-pulmonary sarcoidosis in Tunisia which can help improve the diagnostic accuracy and management of the disease.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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