Case Report

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# A case report of sarcoidosis overlapped with Sjogren's syndrome

Maysoun Kudsi, PhD, MD[a], Tasneem Drie, MD[b,*], Naram Khalayli, MD[c], Hashem Ammar Obaid hassnah, MD[d], Fatima alzahraa alghawe, MD[b], Leen alhham, MD[b]

**Introduction and importance:** The diagnosis of sarcoidosis and Sjögren's syndrome (SS) in the same patient is a challenge since sarcoidosis is considered an exclusion criterion for SS.

**Case presentation:** The authors described a 62-year-old woman, who had SS for 8 years and presented with dry mouth, dry eyes, dyspnoea, and erythema nodosum. High resolution computed tomography of the chest showed symmetrical pulmonary micronodules, interstitial changes, and enlarged mediastinal lymph nodes. Anti-nuclear antibodies and anti-SSA antibodies were positive. Schermer's test was also positive. A biopsy of lung nodules revealed non-caseous granuloma. Salivary gland biopsy showed focal lymphocyte infiltration. Diagnosis of sarcoidosis and SS were done according to the classification criteria in this patient.

**Clinical discussion:** Although the diagnosis of Sjogren requires the exclusion of conditions that cause dry eyes and mouth, such as sarcoidosis, Few studies have reported the coexistence of sarcoidosis and SS such as this case report.

**Conclusion:** This case extends our understanding of overlapped SS with sarcoidosis and provides a referential value for clinical diagnosis.

**Keywords:** sarcoidosis, Sjogren's syndrome, Shermer test, non-caseous granuloma

## Introduction

Sarcoidosis and primary Sjögren's syndrome (pSS) are systemic immune diseases with similar clinical features[1].

SS is a rare condition that affects exocrine glands, and other body systems. It is manifested by infiltration of lymphocytes, in particular lacrimal glands, the parotid gland, and the salivary glands, causing dryness of the mouth and eyes. SS is diagnosed according to the American College of Rheumatology, and the European League Against Rheumatism(ACR/EULAR) criteria (Table 1)[2,3].

Sarcoidosis is a non-caseating granulomas systemic disease of unknown aetiology. The lung and lymphatic systems are the frequently involved organs[4].

Its diagnosis is based on three major criteria: a compatible clinical presentation, non-necrotizing granulomatous inflammation in a tissue biopsy, and excluding other causes of granulomatous disease. There are no internationally accepted measurements to decide if each diagnostic criterion has been satisfied[5]. Sarcoidosis should be excluded before a diagnosis of Sjogren syndrome[3]. There are few reports of sarcoidosis coexisting with pSS[1,6]. A report from Taiwan in 2017, states that SS was significantly associated with sarcoidosis (adjusted odds ratio, 11.6; 95% CI, 4.36–31[1].

Here, we report the coexistence of sarcoidosis and pSS in a 62-year-old female.

### HIGHLIGHTS

- The diagnosis of sarcoidosis and Sjögren's syndrome (SS) in the same patient is a challenge since sarcoidosis is considered an exclusion criterion for SS.
- There are few reports of sarcoidosis coexisting with primary SS.
- There is a higher prevalence of articular and ocular involvement, anti-nuclear antibodies, rheumatoid factor, and positive anti-Ro/SSA antibodies in patients with coexisting sarcoidosis and SS.
- Knowing whether a patient has SS or sarcoidosis makes it easier for us to decide what points we should pay attention to during follow-ups.

### *Case presentation*

A 62-year-old Syrian female, non-smoker, who had SS for 8 years, presented with fatigue, dry mouth, dry eyes, dyspnoea, arthralgia, and erythema nodosum 4 weeks ago to the out-hospital clinic in April 2023.

[a]Damascus University, Departments of [b]Rheumatology, [c]Psychiatry, Faculty of Medicine, Damascus University and [d]Faculty of Medicine, Syrian Privet University, Daraa, Syrian Arab Republic

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*Corresponding author. Address: Al-Mouwasat Hospital: Al-Mouwasat University Hospital Damascus, Syrian Arab Republic. Tel.:/fax: +963 948 958 318. E-mail: samsomadrei@gmail.com (T. Drie).



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**Table 1**

**American College of Rheumatology, and European League Against Rheumatism(ACR/EULAR) criteria for Sjogren Syndrome**

**ACR-EULAR 2016 Classification Criteria for Sjögren's**

| Item# | Item to be Scored | Weight |
|---|---|---|
| 1 | Labial salivary gland with focal lymphocytic sialadenitis and focus score of $1 foci/4 mm | 3 |
| 2 | Anti-SSA/Ro-positive | 3 |
| 3 | Ocular Staining Score ≥ 5 (or van Bijsterveld score ≥ 4 in at least 1 eye | 1 |
| 4 | Schirmer's test ≤ 5 mm/5 min in at least 1 eye | 1 |
| 5 | Unstimulated whole saliva flow rate #0.1 ml/min | 1 |

Physical examination revealed tender firm subcutaneous nodules up to the size of a coin, symmetrically distributed, with the left side slightly more affected, on palpation. No purulent material, fluctuance, or crepitus. The remainder of the physical examination was unremarkable. She was under artificial tears for 8 years, and 200 mg/day hydroxychloroquine for 6 years.

Laboratory tests revealed: White blood cells 9.3 K/microl (normal: 4.0–11.0 ) with 69% of neutrophils (normal: 50–70%) and 39% of lymphocytes (normal: 25–40%). Haemoglobin was 11.3 g/dl (normal: 12–16), platelet count 350 000 K/ul (normal = 150 000–400 000), procalcitonin less than 0.5 ng/ml, albumin 3,8 gms/dl (normal) alanine transferase 37 U/L (normal:7–55), aspartate transferase 29U/l (normal:8–48), erythrocyte sedimentation rate 78 mm/h (normal: 0–20) and c-reactive protein at 11.2 mg/l (normal: <6). Urinalysis was normal. Blood and Urine cultures were negative.

The immunological profile included: anti-nuclear antibodies were positive at/80 (< 1/40, negative), Anti-La was positive at 4 U (< 1 U, negative), and anti-RO was positive at 2U (< 1 U, negative), the rest of the immune profile including rheumatoid factor, Anti-cyclic citrullinated peptide antibody, perinuclear anti-neutrophil cytoplasmic antibody, antineutrophil cytoplasmic antibody were negative. Complements were within normal limits. Viral serology of hepatitis B, hepatitis C, and human immune deficiency were non-reactive. Bacteria, fungi, and mycobacteria detected by Gram, Grocott methenamine silver, and AFB tissue stains were negative. A tissue culture was negative for all organisms. Schirmer's test was positive Echography of salivary glands revealed bilateral fibrosis changes.

Chest X-ray showed bilateral hilar lymphadenopathy, and interstitial lung disease (Fig. 1).

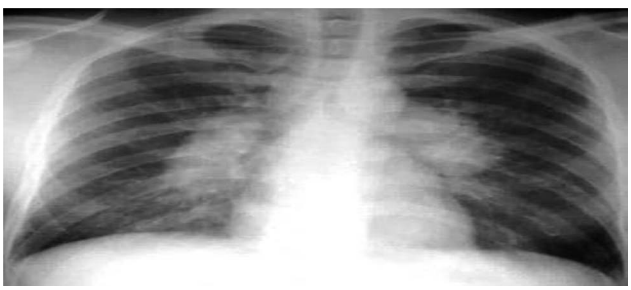

**Figure 1.** Bilateral hilar lymphadenopathy, and interstitial lung disease.

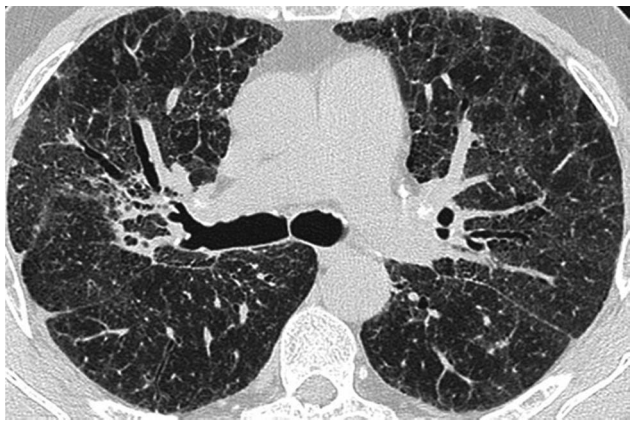

**Figure 2.** Symmetric pulmonary interstitial changes, and multiple enlarged lymph nodes in the mediastinum.

High resolution computed tomography of the chest showed symmetric pulmonary interstitial changes, and multiple enlarged lymph nodes in the mediastinum (Fig. 2).

Bronchoscopy showed that there were many small nodules under the bronchial mucosa. The percentage of lymphocytes (23%) increased in bronchoalveolar lavage fluid, and the CD 4 + / CD 8 + lymphocytes ratio was 12.32, which increased significantly. The histopathology of mediastinal lymph node biopsies was non-caseating granulomatous (Fig. 3).

A biopsy of the skin lesions was performed. Histology revealed septal panniculitis without evidence of vasculitis, with a mixed cellular infiltrate of lymphocytes, histiocytes, and giant cells, compatible with erythema nodosum (Figs. 4, 5).

Salivary gland biopsies were also positive showing a lymphocytic infiltration, scoring 4 using Chisholm's criteria (focus score > 1)[7].

Serum angiotensin-converting enzyme did not increase (3.4 U/l, normal 17–55 U/l).

She was diagnosed with sarcoidosis and coexisting primary SS. She received 80 mg/day(1 mg/kg) prednisolone, 200 mg/day hydroxychloroquine, and 150 mg/day(2 mg/kg) azathioprine. Two weeks later, the dyspnoea was improved; the erythema nodosum disappeared, so prednisolone was gradually reduced 5 mg/week Three months later, she was on 20 mg/day of prednisolone, 200 mg/day of hydroxychloroquine, and 150 mg/day of azathioprine without clinical symptoms. High resolution computed tomography of the chest returns to normal.

Our study is compatible with the SCARE 2020 checklist[8].

This case is submitted on the research registry dashboard[9].

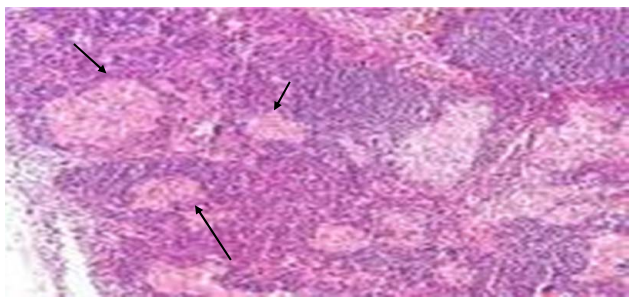

**Figure 3.** Non-caseating granulomatous.

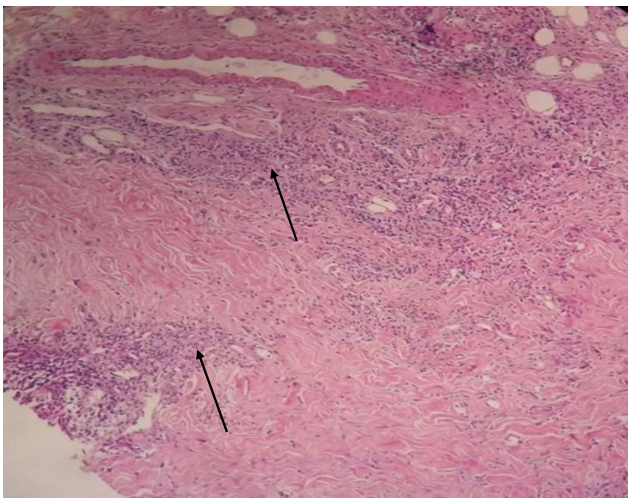

**Figure 4.** Septal panniculitis without evidence of vasculitis, with a mixed cellular infiltrate of lymphocytes black arrow.

## Discussion

pSS affects more women older than 40 years[1]. Our patient is a 62-year-old female. pSS symptoms include dry eye and mouth. dry skin, tiredness, muscle or joint pain, and sometimes rash, especially after sun exposure[10]. Our patient had dry eye and mouth, and joint pain. According to the 2002 and 2016 ACR/EULAR classification criteria for pSS. Sarcoidosis should be excluded before the diagnosis of pSS[3]. Our patient was diagnosed according to these criteria 8 years ago, without evidence of the presence of sarcoidosis at that time.

Sarcoidosis is a systemic granulomatous disease. CD4 + T cells interact with antigen-presenting cells to initiate the formation of granuloma plays a role in its pathogenesis[1]. Dyspnoea, which worsens with activity, persistent dry cough, chest pain; and wheezing are the manifestations of pulmonary sarcoidosis[11]. Our patient had dyspnoea. Its diagnosis is based on three major criteria: a compatible clinical presentation, non-necrotizing granulomatous inflammation in a tissue biopsy, and excluding other causes of granulomatous disease. There are no internationally accepted measurements to decide if each diagnostic criterion has been satisfied[5].

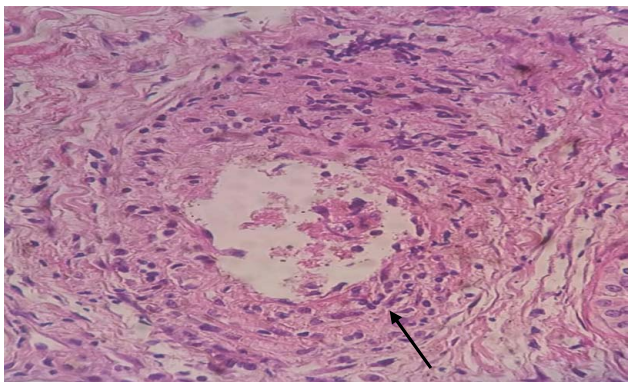

**Figure 5.** Histiocytes, and giant cells black arrow.

Few studies have reported the coexistence of sarcoidosis and SS[1,6,12,13] There is a higher prevalence of articular and ocular involvement, anti-nuclear antibodies, rheumatoid factor, and positive anti-Ro/SSA antibodies in patients with coexisting sarcoidosis and SS[10]. Although anti-nuclear antibodies could be detected in sarcoidosis, anti-Ro/SSA antibodies were uncommon. SS is diagnosed according to clinical findings, positive antibodies and tests, and histological findings of a gland biopsy[3], as in our patient. Sarcoidosis diagnosis is based on three major criteria: a compatible clinical presentation, non-necrotizing granulomatous inflammation in a tissue biopsy, and the exclusion of other causes of granulomatous disease[4], as in our case.

In sarcoidosis patients with positive anti-SSA/SSB antibodies and focal lymphocyte infiltration in a labial gland biopsy, can suggest a coexistence with SS.

The recommendations address the use of saliva substitutes and artificial tear drops, topical non-steroidal anti-inflammatory drugs, topical corticosteroids, topical CSA (cyclosporine A), serum tear drops, oral muscarinic agonists, hydroxychloroquine, oral glucocorticoids, immunosuppressive treatment, and biological therapies[14].

Sarcoidosis and SS should be considered in the differential diagnosis of non-productive coughs. In patients first diagnosed with SS or sarcoidosis, we should take the co-occurrence of both diseases into account as a differential diagnosis and the gum test should be used as a screening test because both diseases may present with Sicca symptoms such as the dry mouth[1].

Oral glucocorticoids with or without another immunosuppressive drug are the first-line therapy for symptomatic patients with abnormal pulmonary function test results and lung infiltrates[10]. Our patient was treated with glucocorticoids hydroxychloroquine, and azathioprine as an immunosuppressive agent.

Ramos-Casals and colleagues presented 54 cases of coexisting sarcoidosis and SS: 49 (83%) patients were female, with a mean age at diagnosis of 50 years. According to the histopathologic examination of the exocrine glands performed in 53 cases, we defined the coexistence of sarcoidosis and SS in 28 cases, while in the remaining 25 patients, sarcoidosis mimicked SS. Clues to identifying when sarcoidosis coexists with SS were a higher prevalence of systemic manifestations (arthritis and uveitis) and positive immunologic parameters (anti-nuclear antibodies, rheumatoid factor, and anti-Ro/SS-A), as well as the existence of a focal sialadenitis (Chisholm-Mason score grades III-IV, with a CD4 + lymphocytic infiltration) in the salivary gland biopsy. In patients first diagnosed with primary SS, the appearance of some clinical features such as hilar adenopathies, uveitis, or hypercalcemia leads to the diagnosis of coexisting sarcoidosis[12].

## Conclusions

This rare case revealed that sarcoidosis and SS can coexist simultaneously. It extends our understanding of the overlapped disorder and provides a referential value for clinical diagnosis. If sarcoidosis or SS is suspected, the possibility of both should be considered as a differential diagnosis. Knowing whether a patient has SS or sarcoidosis makes it easier for us to decide what points we should pay attention to during follow-ups.

## Ethical approval

It is waived at our institution.

## Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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None.

## Author contribution

M.K. described the case and collected the clinical data. reviewed and edited the manuscript. All authors have read and agreed to the published version of the manuscript.

## Conflicts of interest disclosure

None.

## Research registration unique identifying number (UIN)

1. Name of the registry: tasneem drie.
2. Unique Identifying number or registration ID: researchregistry9157.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.researchregistry.com/browse-theregistry#home\.

## Guarantor

Tasneem Drie.

## Data availability statement

None.

## Provenance and peer review

Not commissioned, externally peer-reviewed.

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