



# Coexistence of Sarcoidosis and Silicosis: Case Series

## Sarkoidoz ve Silikozis Birlikteliği: Olgu Serisi

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### Abstract

The differential diagnosis of silicosis includes sarcoidosis, berylliosis, hypersensitivity pneumonia, malignancy, tuberculosis and other granulomatous infections. Sarcoidosis is a systemic granulomatous disease with an unknown etiology, although it is thought that occupational exposure to such substances as silica and beryllium may be a trigger. An incomplete occupational history may lead to a diagnosis of sarcoidosis rather than pneumoconiosis in many cases, although various associations of these two diseases, such as the coexistence and detection of one before or after the other, have been reported in literature. The coexistence of sarcoidosis and silicosis is discussed in the present study with reference to five cases who applied to the Occupational Diseases department of a university hospital. Active pulmonary tuberculosis and lung malignancy were excluded in all cases, and histopathologic examinations of all samples were reported as non-caseating granulomatous inflammation. In the specimen of one case, a birefringent body was identified upon polarized microscopy. In the light of these cases, it is aimed to draw attention to the usefulness of a well-received occupational history in the differential diagnosis and etiology of sarcoidosis and silicosis.

**Key words:** Sarcoidosis, Silicosis, differential diagnosis.

### Öz

Silikozisin ayırıcı tanısı sarkoidoz, berilyoz, hipersensitivite pnömonisi, malignite, tüberküloz ve diğer granülatöz enfeksiyonları içerir. Sarkoidoz etiyojisi tam olarak bilinmeyen sistemik granülatöz bir hastalıktır ve silika, berilyum gibi mesleki maruziyet faktörlerin tetikleyici ajan olarak rol oynayabileceği düşünülmektedir. Eksik ve dikkatsiz bir meslek öyküsü birçok olguda pnömokonyoz yerine sarkoidoz tanısına yol açabilir. Ek olarak bu iki hastalığın bir arada görülmesine veya bir diğerinin ötekenden önce saptaması gibi durumlara da çeşitli makalelerde dikkat çekilmiştir. Bu yazıda bir üniversite hastanesinin iş ve meslek hastalıkları bölümüne başvuran beş olgu üzerinden sarkoidoz ve silikozis birlikteliği tartışılmıştır. Tüm olgularda aktif akciğer tüberkülozu ve akciğer malignitesi dışlandı. Tüm olguların biyopsi materyallerinin histopatolojik incelemeleri kazeifiye olmayan granülatöz inflamasyon olarak rapor edildi. Bir olguda polarize mikroskopta ışığı çift kıran cisim gösterildi. Burada, bu olgular ışığında iyi alınmış bir meslek öyküsünün sarkoidoz ve silikozisin ayırıcı tanısı ve etiyojisini saptamadaki faydasına dikkat çekmek amaçlanmıştır.

**Anahtar Sözcükler:** Sarkoidoz, Silikoz, ayırıcı tanı.

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The differential diagnosis of silicosis includes sarcoidosis, berylliosis, hypersensitivity pneumonia, malignancy, tuberculosis and other granulomatous infections. Sarcoidosis is a systemic granulomatous disease of unknown etiology, although it is thought that occupational exposure to such substances as silica and beryllium may play a role, as well as infectious agents and genetic factors, as triggering agents. It is known that the interaction of silica particles with macrophage activation and IL-1, TNF, fibronectin, fibrogenic cytokine and free radicals leads to immunoactivation and fibrogenesis. The presence of similar clinical, laboratory, radiological and histopathological findings of silicosis and sarcoidosis may be challenging for clinicians in a differential diagnosis, and an incomplete and inattentive occupational history may lead to a diagnosis of sarcoidosis rather than pneumoconiosis in many cases (1). Furthermore, various associations of these two diseases, such as the coexistence and detection of one before or after the other have been reported on in literature. In the present study, the coexistence of sarcoidosis and silicosis is discussed with reference to five cases who applied to the Occupational Diseases Department of a university hospital.

## CASE

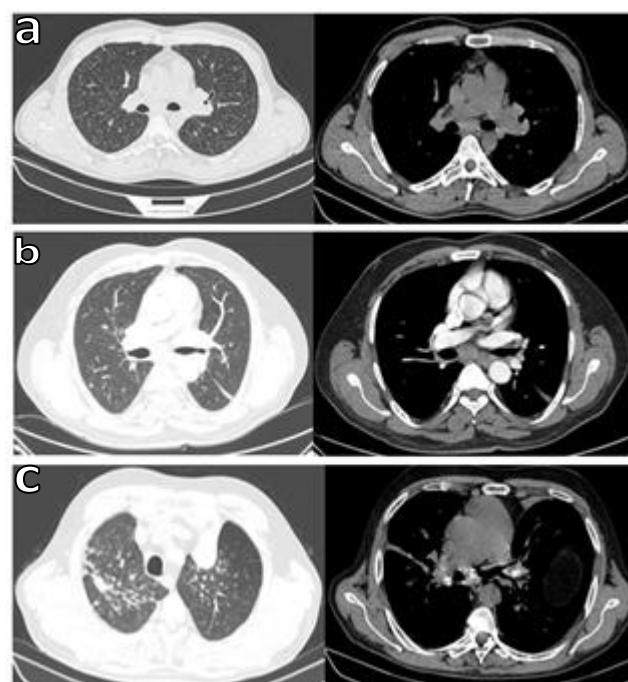
A total of five cases are described, all of whom are male, aged 27–51 years. Three of the cases were diagnosed initially with sarcoidosis and treated accordingly, in which sarcoidosis was diagnosed at the earliest in the first year and at the latest in the third year following admission. One case had been diagnosed with silicosis 6 years before their diagnosis of sarcoidosis.

Lymph node biopsies were performed by flexible bronchoscopy (FOB) in case-1, mediastinoscopy in case-2, both peripheral lymph node excisional biopsy and FOB in case-3, peripheral lymph node excisional biopsy in case-4 and by endobronchial ultrasonography (EBUS) in case-5. The histopathologic examinations of all samples reported non-caseating granulomatous inflammation. In the specimen of case 4, a birefringent body was revealed in a polarized microscopy.

Active pulmonary tuberculosis and lung malignancy were excluded in all cases. A fiberoptic bronchoscopy was performed in all cases, and the bronchial washing cytology results were found to be benign, and there was no reproduction of tuberculosis bacillus. Since the lymphocyte proliferation test could not be measured, sensitivity to exposures could not be investigated. Computed tomography (CT)/high resolution computed tomography (HRCT)

images of all cases revealed mediastinal lymph nodes associated with lung parenchymal nodules (Figure 1 and 2). While the radiological findings were stable at 3 and 4 years of follow-up in case-2 and case-3, whose final diagnosis was pneumoconiosis, mild progression was detected in case-1 in the third year of follow-up. Since the diagnoses of silicosis and sarcoidosis were new in case-4 and case-5, respectively, no specific follow-up could not be performed.

The demographics and clinical features of our cases are presented in Table-1, while their business lines and occupational dust exposures are presented in Table-2.



**Figure 1:** Thorax radiological images of cases 1, 2 and 3. (a) Thorax HRCT of Case 1, millimetric nodules and subcarinal lymphadenomegaly in bilateral lung parenchyma; (b) Thorax CT of Case 2, millimetric nodules and subcarinal lymphadenomegaly in bilateral lung parenchyma; (c) Thorax CT of Case 3, Right lung upper apical localized multiple nodules with radial borders, the largest reaching 2 cm in diameter, and subcarinal, hilar calcified lymphadenomegaly

## DISCUSSION

Of the five cases presented in this study, four were diagnosed initially with sarcoidosis, and silicosis was considered during follow-ups. One case previously diagnosed with silicosis was later confirmed to have sarcoidosis as well. Accurate occupational history taking is crucial for the differential diagnosis of silicosis in patients with sarcoidosis and for the detection of the etiology. As stated by Seaton, an incomplete history may result in a diagnosis of sarcoidosis rather than silicosis in the same patient (1).

Table 1: Demographics and clinical features of the cases

Cases	Age	ILO Evaluation	Thorax HRCT or CT	Spirometry	Sarcoidosis Features	Diagnosis Times
Case 1	27	Quality 2, 2/2, p/p ax	* 20- 25mm mediastinal lymphadenomegaly * Millimetric nodules observed more intensely in the upper zones of the bilateral parenchyma * Bilateral upper lobe apex and posterior peribronchial thickenings	FEV1: 3.13 ml %87 FVC: 3,50 ml %84 FEV1/FVC: %89	untreated follow-up	* Diagnosis of sarcoidosis 3 years before admission  * Diagnosis of silicosis on admission
Case 2	51	Quality 2, 1/1, p/s hi	* Largest subcarinal 2 cm, hilar lymphadenomegaly * Nodular pleural thickenings in bilateral upper lobes Right lung upper lobe 9 mm calcific granuloma * Millimetric nodule at the level of the right lung major fissure	FEV1: 2.57 ml %81 FVC: 3,36 ml %85 FEV1/FVC: %77	untreated follow-up	* Diagnosis of sarcoidosis 2 years before admission  * Diagnosis of silicosis on admission
Case 3	49	Quality 1, q/p 2/2 ax	* Lymphadenomegaly, the largest 13 mm, in the right axillary region * Bilateral upper lobe apical and lower lobe medial 2 cm multiple nodules with radial borders * Consolidation of right lung middle lobe laterally and left lung upper lobe anterior * Right pleural calcific focus Left hemidiaphragm elevated, left less pleural fluid	FEV1: 1.70 ml %48 FVC: 2.05 ml %47 FEV1/FVC: %77	long term oxygen therapy and corticosteroid therapy	* Diagnosis of sarcoidosis 3 years before admission  * Diagnosis of silicosis on admission
Case 4	33	Quality 2, q/q 2/2  A, hi, left pleural thickening	* Multiple calcified lymph nodes in the mediastinum, the largest of which is 30*14 mm * Millimetric multiple calcific nodules, diffuse in bilateral upper lobe and lower lobe superior, multiple micronodular areas in bilateral lower lobes	FEV1: 3.87 ml %87 FVC: 4.28ml %79 FEV1/FVC: 90.35	Methylprednisolone 4 mg, azathioprine 5 mg and hydroxychloroquine 200 mg for the last 1 year *  * After the diagnosis of sarcoidosis, due to joint pain and Anti-ribosomal P positivity, it was diagnosed by the rheumatology department.	* Diagnosis of sarcoidosis 3 years before admission  * Diagnosis of silicosis on admission
Case 5	44	Quality 1, r/r, 3/3 hi, ax	* Mediastinal and hilar lymph nodes, the largest of which is 20 mm in diameter in the subcarinal region * Multiple nodules with miliary distribution pattern in all lobes, bilaterally in the upper lobes, focal consolidations with local merging of nodules defined in the upper lobes and anterior segments	FEV1:12.07 ml %58,5 FVC: 2.67 ml %62 FEV1/FVC: %77.6	corticosteroid therapy  Serum ANA was weakly positive, and serum ACE level was 114.2 IU/L	* Diagnosis of sarcoidosis within the year of admission  * Diagnosed with silicosis 6 years ago

ILO: International Labour Organization, HRCT: High Resolution Computed Tomography, CT: High Resolution Computed Tomography, FEV1: Forced Expiratory Volume In 1 Second, FVC: Forced Vital Capacity

In a case-control study including 3,663 cases and 7,326 controls, it was stated that occupational silica exposure increased the incidence of sarcoidosis in men aged 20–

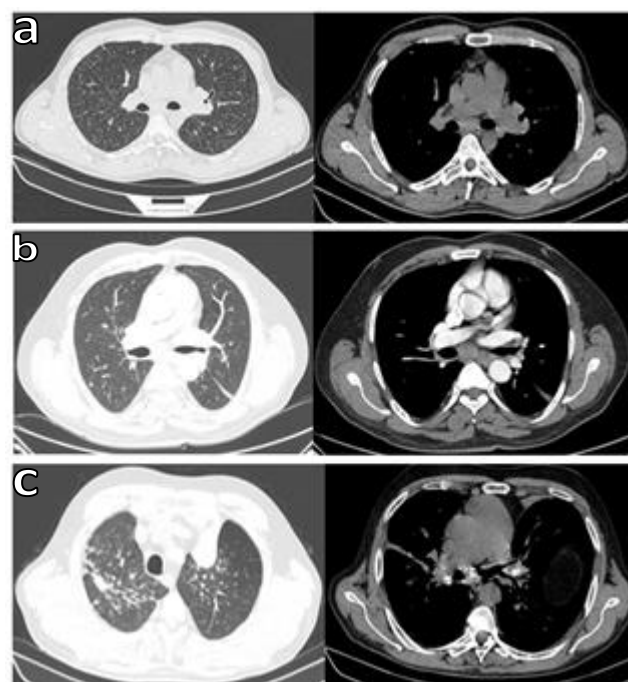
65 years, and sarcoidosis was reported at a higher rate in those who had been exposed to silica in the last 5 years of their occupation (2). The cases presented in the pre-

sent study had an average of 13.5 years of exposure to silica in various employment areas, and there was an average of 4.8 years (2–11 years) between the time of admission and the most recent exposure.

The prevalence of sarcoidosis has been shown to be higher in workers exposed to silica. In a retrospective cohort study conducted in 2017, a study of the medical records of workers in 10 iron foundries revealed that silica exposure increased the risk of sarcoidosis (SIR 3.94; 95% CI 1.07 to 10.08) (3). In the aftermath of the attacks against the World Trade Center, it was found that the incidence of sarcoidosis or sarcoidosis-like granulomatous lung disease increased in the 5-year observation period of the firefighters working in search and rescue teams when compared to the results of examinations carried out 15 years earlier (4). In a study from Sweden in 2019, 371 cases of sarcoidosis were identified among 297,917 male workers, and it was shown that smokers had an increased risk of developing sarcoidosis when exposed to high levels of silica dust when compared to non-smokers (5). In another case series, silica exposure was identified in six of eight sarcoidosis cases (6), while a study examining death records in the United States between 1988 and 1999, 3,393 of 7,118,535 recorded deaths were identified as being sarcoidosis-related and sarcoidosis was given as the underlying cause of death in 1,579 of these cases. It has also been reported that the risk of sarcoidosis mortality related to occupational exposure differs for those of different sexes and races (7).

**Table 2:** Work places and occupational dust exposures of the cases

Cases	Job/Work place	Task	Exposure	Time of Exposure
Case 1	Dental technician	Metal casting Metal leveling Sandblasting Porcelain polishing Skeleton making	Silica Plaster Wax Resin	14 years
Case 2	Ceramic Cement	Press-mill operator Machine maintainer	Silica Silica	21 years
Case 3	Rubber dough production	Production and Slaughter	Rubber Sulfur Kaulen	14 years
Case 4	Mining	Physical analysis - Elimination operator	Kuartz	9 years
Case 5	Foundry	Sandcore making	Silica Resin	8 years



**Figure 2:** Thorax radiological images of cases 4 and 5. (a) Thorax CT of Case 4, millimetric nodules up to 2 cm in diameter and subcranial, hilar calcified lymphadenomegaly in the right lung lobe superior; (b) Thorax CT of Case 5, millimetric multiple nodules with miliary distribution pattern in both lungs, predominantly in the upper lobes, in all lobes and accompanied by subpleural involvement, multiple mediastinal lymphadenomegaly; (c) 6 years ago Thorax CT of Case 5, millimetric nodules and subcranial lymphadenomegaly in bilateral lung parenchyma

In the cases in the present study, the coexistence of sarcoidosis and silicosis, or sequential associations of the two, can occur. In a case report, a 45-year-old man who had worked in metal molding and had been exposed to silica presented with symptoms for 3 years. The reported asteroid bodies, giant cells and granulomatous inflammation in the histopathological evaluation of an open lung biopsy were compatible with sarcoidosis, and silica particles were also found in the nodules (8). Roegel et al. (9) reported a case of rapidly progressive radiological findings of pseudotumoral silicosis during multivisceral exacerbation with iritis and erythema nodosum in a miner with pulmonary and nodal sarcoidosis treated with corticosteroids. The patient was biopsied by thoracotomy, and sarcoid granulomas with silicotic masses were found limited to the upper lobe, along with sarcoid granulomas in the middle lobe and hilar lymph nodes, and the patient was thus diagnosed with sarcoido-silicosis. The authors concluded that sarcoidosis promoted the rapid development of silicosis due to the changes in immunity, and was unexpected since the exposure had been moderate. They went on to speculate that this may be due to the deficiency in the elimination of silica particles from the lungs.

Clinician may not be able to give a definitive diagnosis of silicosis or sarcoidosis, but may diagnose patients with sarco-silicosis, silico-sarcoidosis or sarcoid-like granulomatous disease of the lung related to silica. The treatment modality of the patient may, therefore, change depending on which diagnosis is made. The “from treatment to diagnosis” method is frequently resorted to in these cases. A 67-year-old male patient who had been exposed to silica in a cement factory presented with bilateral centrilobular nodules, hilar and mediastinal lymphadenopathy with calcification on Thorax CT, and was diagnosed with suspected sarcoidosis. Upon the detection of birefringent material under polarized light microscopy in a mediastinal lymph node, EBUS and transbronchial needle biopsy were performed, and a diagnosis of silico-silicosis-related sarcoid-like granulomatous lung disease was made instead of sarcoidosis. After the replacement of the treatment modality with corticosteroid and azathioprine combination therapy, the patient’s radiological findings and clinical progress improved (10). Beijer et al. (11) reported on a 49-year-old patient who had been working as a plasterer in construction for 30 years. The patient was diagnosed with silicosis, and demonstrated silica sensitivity in a lymphocyte proliferation sensitivity test, along with birefringent material on a polarization microscopic examination of an open lung biopsy. His symptoms, however, persisted and fibrosis due to silicosis continued, even under prednisone and azathioprine treatment. Symptomatic and radiological improvement was detected in the 7th month after the patient was started on infliximab, and so his condition was rediagnosed as sarcoidosis. In the present study, two of the cases were treated for sarcoidosis and the other three were followed up without treatment. Furthermore, two of our patients who were treated for sarcoidosis experienced radiological progression and were recently rediagnosed with silicosis. There are some limitations to the present study. The lack of lymphocyte proliferation tests in our cases was the missing aspect in terms of showing sensitivity. Furthermore, the level of exposure was limited to what the subjects reported in their occupational histories, and there were no personal dust exposure measurements. If large tissue samples of the lung parenchyma were available, our prediction would be better supported. In addition, the lack of a standard follow-up approach to the cases was also a shortcoming.

Silica can activate the autoimmune mechanism and lead to the emergence of autoantibodies, and so it has been associated with SLE, scleroderma, rheumatoid arthritis

and sarcoidosis (12). The role of silica as a trigger of sarcoidosis has been recognized (13), although it has not yet been clarified whether inorganic dusts can trigger sarcoidosis in those with and without genetic predispositions. In 2021, an article entitled “Sarcoidosis: An Occupational Disease?” noted that silica exposure can be associated with sarcoidosis in various sectors, such as agriculture, construction, fire brigade, foundries, timber and mining (14). In the light of the cases presented in the present study, we suggest that a well-documented occupational history, including exposure levels, may be helpful in the differential diagnosis of sarcoidosis and silicosis, and the etiology of parenchymal lung disease.

## CONFLICTS OF INTEREST

None declared.

## AUTHOR CONTRIBUTIONS

Concept - M.Y.Y., Y.D.; Planning and Design - M.Y.Y., Y.D.; Supervision - M.Y.Y., Y.D.; Funding - M.Y.Y.; Materials - M.Y.Y.; Data Collection and/or Processing - M.Y.Y.; Analysis and/or Interpretation - M.Y.Y.; Literature Review - M.Y.Y.; Writing - M.Y.Y.; Critical Review - M.Y.Y., Y.D.

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