

Is the coexistence of pulmonary sarcoidosis and multiple sclerosis possible? An unusual case report

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Abstract

Neurosarcoidosis and Multiple Sclerosis (MS) are both inflammatory disorders of the Central Nervous System (CNS), often presenting with overlapping clinical features, making differential diagnosis challenging. Neurosarcoidosis affects approximately 5-15% of systemic sarcoidosis patients and can mimic MS due to similar CNS involvement. Differentiation is critical, as treatment strategies vary significantly. Recent studies highlight that Cerebrospinal Fluid (CSF) analysis can aid in distinguishing these conditions. Key markers include elevated CSF white cell count, CSF lactate levels, and the absence of oligoclonal bands specific to MS. Radiological differences, such as distinct Magnetic Resonance Imaging (MRI) findings, also contribute to accurate diagnosis. While neurosarcoidosis is less common than MS, it remains a crucial differential diagnosis due to its potential for severe neurological outcomes. Further research is needed to refine non-invasive diagnostic criteria, potentially reducing reliance on CNS biopsy for definitive diagnosis.

Key words: right, aortic, arch, asthma, pulmonology, airflow, intrathoracic, obstruction.

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Introduction

Sarcoidosis and Multiple Sclerosis (MS) are both chronic, immune-mediated diseases that primarily affect different systems; sarcoidosis mainly involves the lungs, while MS targets the Central Nervous System (CNS). However, there have been cases reported where these two diseases coexist, raising questions about potential correlations, coexistence, and mimicry between the two conditions. Sarcoidosis is characterized by the formation of non-caseating granulomas in various organs, most frequently the lungs, and its manifestations can be detected through imaging techniques such as High-Resolution Computed Tomography (HRCT).¹ On the other hand, MS is known for demyelination and neurodegeneration within the CNS, presenting with a variety of neurological symptoms and lesions identifiable via Magnetic Resonance Imaging (MRI).² This article aims to explore the relationship between sarcoidosis and MS, examining whether these diseases can coexist, and if MS can mimic sarcoidosis in clinical presentation.

Case Report

A 40-year-old male was recently discharged from the Neurology Department at the Riuniti Hospital, Reggio Calabria

(Italy), with a diagnosis of Relapsing-Remitting Multiple Sclerosis (RRMS), and therapy with ofatumumab was recommended. He presented at my pulmonology clinic with a history of significant smoking (25 cigarettes/day), neurogenic bladder, and allergies to Parietaria and Graminaceae. The symptoms presentation are low-grade fevers and yellow-green sputum. A chest Computed Tomography (CT) scan on April 17, 2024, showed no pleural effusion but revealed fine thickening of bronchiolar walls, subpleural pseudonodules in the right upper lobe, and enlarged lymph nodes (~15 mm) in the right paratracheal region, Baret's lodge, aortopulmonary window, and along the aortic arch (Figure 1). The global spirometry with bronchoreversibility test and execution of capillary alveolar diffusion of carbon monoxide, performed with the PulmOne MiniBox+ Spirometer (Medical Graphics Italia; Milan, Italy) highlighted the presence of examination within normal limits (Table 1), with normal alveolocapillary diffusion and negative bronchoreversibility test for asthma. Evoked potentials indicated increased central motor conduction time, suggesting pyramidal tract impairment. The analysis of cerebrospinal fluid highlighted the presence of normal values, with the exception of granulocytes, type II oligoclonal bands, and negative anti-aquaporin 4 antibodies. Laboratory tests revealed an ACE level of <9 and elevated serum lysozyme (12.5), supporting a diagnosis of sarcoidosis. Imaging findings consistent with sarcoidosis included the galaxy sign, reversed halo sign, mosaic perfusion patterns, and perilym-

phatic and scissural nodule distribution. These findings suggest sarcoidosis with pulmonary and neurological involvement. The initial diagnosis was MS, but should be reevaluated due to possible neurosarcoidosis by neurologist. Additionally, a chest CT scan revealed Chronic Obstructive Pulmonary Disorder (COPD) with bronchiectatic, requiring Long-Acting Beta-Antagonists (LABA)/Long-Acting Muscarinic Antagonist (LAMA), antibiotics, and steroids, with collateral evidence of hypoplasia of the right thyroid lobe.

Discussion

Several studies suggest a possible association between sarcoidosis and MS. Both diseases share similarities in their underlying immune-mediated mechanisms. For instance, T-cell-mediated inflammation is a common feature, with an increased presence of activated CD4+ T cells seen in sarcoidosis and MS lesions.³ The coexistence of sarcoidosis and MS has been documented in multiple case reports and clinical studies, indicating that while rare, it is not unheard of for patients to present with both conditions simultaneously.⁴ The pathophysiological links between these diseases are still under investigation. Genetic predispositions and environmental triggers may play a role in their co-occurrence. Shared genetic markers, such as certain Human Leukocyte Antigen (HLA) types, have been implicated in both diseases, suggesting a common genetic susceptibility.⁵ The coexistence of sarcoidosis and MS can complicate the diagnostic process due to overlapping symptoms and the potential for one disease to mask the other. For example, neurological manifestations of sarcoidosis, referred to as neurosarcoidosis, can mimic MS both clinically and radiologically.⁶ Neurosarcoidosis can present with demyelinating lesions in the CNS, which are also characteristic of MS, making differential diagnosis challenging.⁷ A significant diagnostic challenge arises from the presence of oligoclonal bands in the CSF. While oligoclonal bands are a hallmark of MS, they are not exclusive to this

disease and can also be found in other autoimmune conditions, including neurosarcoidosis. This finding underscores the necessity of considering the broader clinical and radiological context when diagnosing MS, as relying solely on CSF oligoclonal bands can lead to misdiagnosis.⁸ Diagnostic criteria for each disease must be rigorously applied to avoid misdiagnosis. For sarcoidosis, imaging findings from CT scans, such as bilateral hilar lymphadenopathy and pulmonary infiltrates, combined with histological evidence of non-caseating granulomas, are critical.⁹ For MS, MRI findings showing typical demyelinating plaques, along with clinical symptoms of neurological deficits and the exclusion of other causes, are essential.¹⁰ MS can present with a range of neurological symptoms that overlap with those of neurosarcoidosis, including optic neuritis, cranial neuropathies, and transverse myelitis. This overlap can lead to diagnostic confusion. Moreover, certain therapies used to treat MS, such as interferon-beta, have been reported to induce sarcoid-like granulomatous reactions, further complicating the clinical picture.¹¹ High-resolution imaging and careful interpretation of radiologic findings are crucial. For instance, MS lesions typically have a periventricular and juxtacortical distribution, while neurosarcoidosis lesions may be more diffuse and can involve the meninges and cranial nerves.¹² Advanced imaging techniques, including Positron Emission Tomography (PET) and specific MRI sequences, may help differentiate between these entities by highlighting different patterns of inflammation and lesion distribution.¹³ While sarcoidosis and multiple sclerosis are distinct diseases with separate primary targets and typical presentations, evidence suggests they can coexist and may share underlying immunopathological mechanisms. This coexistence can complicate diagnosis and management, as overlapping symptoms might lead to diagnostic confusion and potentially inappropriate treatments. A multidisciplinary approach involving pulmonologists, neurologists, radiologists, and pathologists is essential to ensure a comprehensive evaluation of the patient's symptoms and imaging findings. Diagnostic criteria must be carefully applied to distinguish between sarcoidosis and MS. Advanced imaging techniques, such as high-resolution CT for sarcoidosis and MRI for MS, along

Table 1. Global Spirometry with PulmOne MiniBox+ (Medical Graphics Italia; Milan, Italy). Global Spirometric values indicate hyper-reactivity response to salbutamol 400 mcg (+230 ml FEV₁ and +270 ml FVC) with bronchoreversibility test negative. It indicates the presence of bronchiectasis. DLCO values results are negative. Total Lung Capacity (TLC) is at limit for diagnosis of restrictive pattern.

Spirometric parameters calculated	Predicted value and measurement value (pre-BD)	Predicted value and measurement value (post-BD)	Percentage change from predicted value
FEV ₁	3,55 L - 87%	3,78 L - 93%	+6%
FVC	4,32 L - 103%	4,59 L - 91%	+6%
FEV ₁ /FVC	82,16% - 101% predicted value	82,30% - 102% of predicted value	0%
FEF 25-75	3,79 L/sec - 95%	4,18 L/sec - 105%	+10%
PEF	8,76 L/sec - 96%	7,72 L/sec - 84%	-12%
TLC	5,51 L - 80%	/	/
RV	1,19 L - 76%	/	/
RV/TLC	21,52% - 96%	/	/
IC	2,77L - 74%	/	/
DLCO	95%	/	/
KCO-C	86%	/	/
DLCO/VA	86%	/	/

FEV₁, Forced Expiratory Volume in one second; FVC, Forced Vital Capacity; FEV1/FVC, Forced Expiratory Volume in one second/Forced Vital Capacity ratio; FEF 25-75, Forced Expiratory Flow 25-75%; PEF, Peak Expiratory Flow; TLC, Total Lung Capacity; RV, Residual Volume; RV/TLC Residual Volume To Total Lung Capacity ratio; IC, Inspiratory Capacity; BD, Bronchodilator; DLCO, Carbon Monoxide Capillary Alveolus Diffusion; KCO-C, Calculated Carbon Monoxide Collection Capacity Or Diffusion Coefficient; DLCO/VA, Carbon Monoxide Capillary Alveolus Diffusion/Alveolar Ventilation.

with histopathological analysis, are critical. These methods help identify characteristic features, such as non-caseating granulomas in sarcoidosis and demyelinating plaques in MS. Employing these diagnostic tools effectively can prevent misdiagnosis and ensure

that patients receive appropriate and targeted therapies. Recognizing the potential for these diseases to mimic each other can significantly improve diagnostic accuracy and patient outcomes.

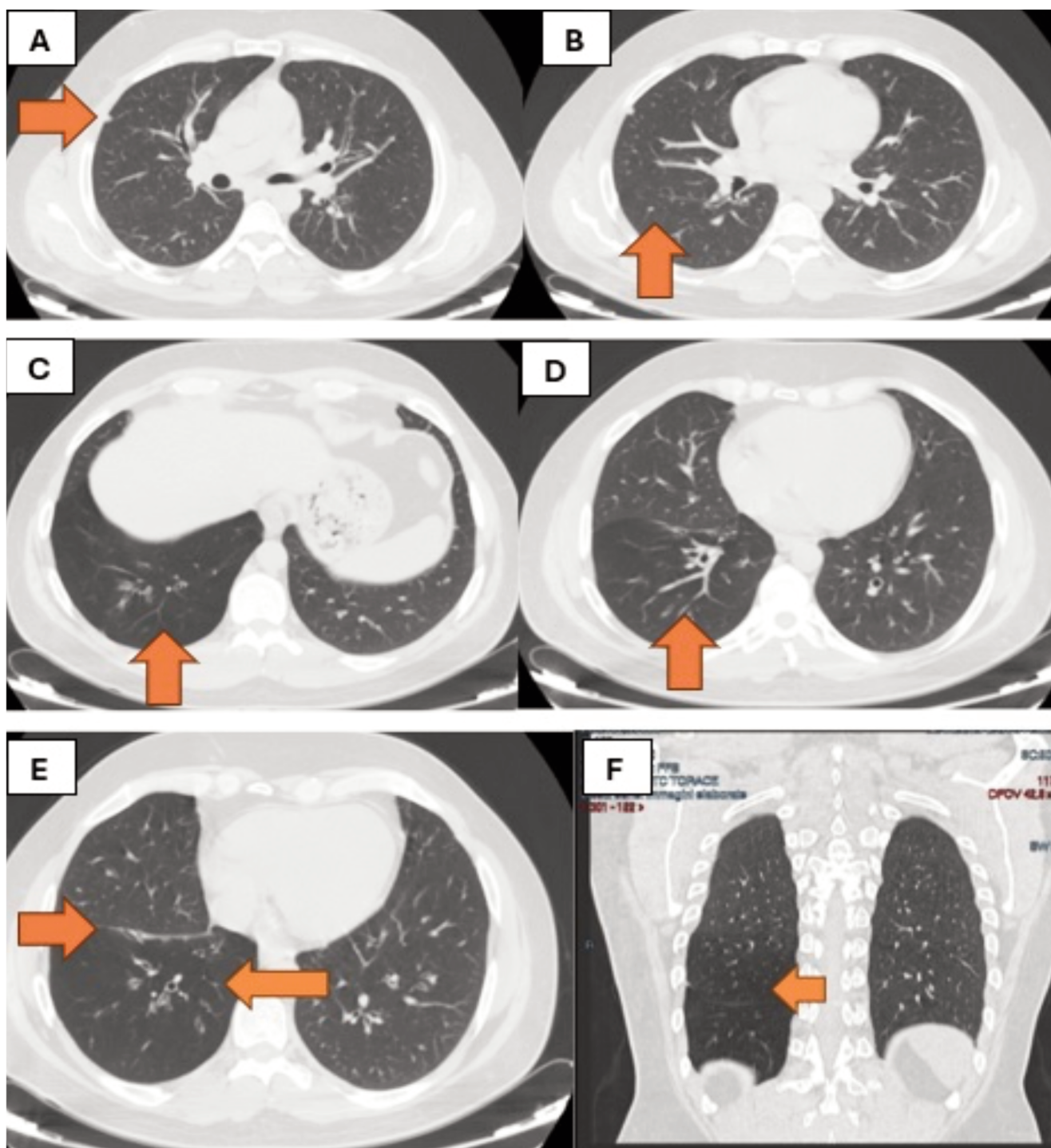


Figure 1. In the images, a fine thickening of the bronchiolar walls is visible. In the anterior segment of the right upper lobe, there is a subpleural pseudonodular element (A) with a maximum diameter of approximately 5 mm; a similar lesion measuring about 3 mm is observed caudally at the same level (B). Lymph nodes (A) approximately 15 mm in size are noted in the right paratracheal region, Baret's lodge, aorto-pulmonary window, and along the aortic arch. A mosaic perfusion pattern is present (E,F). Additionally, nodules with perilymphatic and scissural distribution are seen in the images (B,E).

Conclusions

Early and accurate diagnosis of sarcoidosis, especially in patients with neurological symptoms suggestive of MS, can alter the therapeutic approach. In this case report, the early detection of sarcoidosis through chest CT imaging, which revealed highly suggestive features, led to a reconsideration of the initial MS diagnosis. This guided neurologists towards appropriate sarcoidosis treatment protocols, potentially involving corticosteroids or other immunosuppressive therapies, rather than MS-specific treatments. This case highlights the importance of considering sarcoidosis in the differential diagnosis for borderline clinical presentations. The highly suggestive chest CT findings redirected the diagnostic process towards sarcoidosis, demonstrating the value of comprehensive imaging studies. By acknowledging the overlap in clinical and radiological features of sarcoidosis and MS, clinicians (a multidisciplinary team with neurologists, pulmonologists, and radiologists) can avoid diagnostic pitfalls and ensure timely and accurate diagnoses, ultimately improving patient management and prognosis. Early diagnosis of sarcoidosis, particularly through detailed imaging, can significantly influence therapeutic decisions and improve outcomes for patients with overlapping symptoms of sarcoidosis and MS.

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