Sarcoidosis and its Relation to other Immune Mediated Diseases Affecting Different Body Systems Along with Immunohistochemical Study

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Abstract

Background: Sarcoidosis is a systemic disease of indeterminate origin, marked by noncaseating granulomas that can manifest in any organ, with a particular affinity for the lungs. **Aim:** The aim of the study is to investigate the relationship between sarcoidosis and immune-mediated diseases (IMDs). **Method:** This research examines 55 individuals with sarcoidosis and immune-mediated disorders at Al-Azhar hospitals, aged 18 to 65 years. The research employs a retrospective cross-sectional cohort design, incorporating pathological evaluation, immunohistochemical staining, laboratory testing (CBC, Vitamin D, Serum Amyloid A, Anti-CCP, Anti-ANA, Anti-ds-DNA), and radiological assessments. The research employed CD68 monoclonal antibody alongside a combination of laboratory and radiographic assessments to identify anomalies in the lungs, brain, or other organs impacted by sarcoidosis or associated autoimmune disorders. The research received approval from the research ethics committee at Al-Azhar University. The research seeks to offer significant insights into the diagnosis and management of sarcoidosis. **Results:** The research analyses characteristics across six cohorts, comprising five illness cohorts and one control cohort. Results indicate substantial disparities in immunological and inflammatory activity, age, biochemical markers, and granulomas. Correlation coefficients indicate mild to moderate positive associations between sarcoidosis and autoimmune disorders, underscoring the necessity for differential diagnosis. **Conclusion:** The results demonstrated a relationship between rheumatoid arthritis (RA) and sarcoidosis, particularly in patients presenting Anti-CCP antibodies and erosive joint alterations. HLA-DR4 is identified as a significant risk factor, indicating a possible pathogenic link.

Keywords: Sarcoidosis, Autoimmune Diseases, Inflammatory Activity, Rheumatoid Factor, Anti-CCP.

Introduction

Sarcoidosis is a systemic disorder of indeterminate origin, distinguished by the formation of noncaseating granulomas that can affect any organ, predominantly the lungs. Other

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infrequent areas of involvement encompass the skin, eyes, lymph nodes, liver, heart, neurological system, and bones.[1] Granuloma development is believed to be a typical response to currently unidentified triggering factors.[2] Although uncommon in specific areas, sarcoidosis is a prevalent condition in numerous nations. Typically, it impacts young to middle-aged individuals (ages 20 to 50); yet, it can manifest at any age, including childhood.[3] The clinical symptoms of sarcoidosis are diverse, varying from asymptomatic instances identified incidentally to chronic cases characterised by irreversible pulmonary fibrosis or multi-organ involvement. The progression of the disease is very variable. Spontaneous remission may manifest in 30 to 60 percent of cases, but increasing pulmonary and extrapulmonary involvement arises in 10 to 20 percent of patients.[4]

Acute sarcoidosis typically manifests as acute bilateral hilar lymphadenopathy, with or without respiratory symptoms. Chronic sarcoidosis is characterised by pulmonary involvement, while extrapulmonary sarcoidosis pertains to manifestations in sites outside the respiratory system, devoid of pulmonary involvement. In recent decades, bronchoscopy with transbronchial biopsy has emerged as the primary method for acquiring histological confirmation of sarcoidosis. The disease stage can be ascertained using chest X-ray findings, which subsequently inform therapy decisions.[5] Nonetheless, differentiating sarcoidosis from its imitations is arduous. A more significant difficulty is the care of sarcoidosis patients with comorbidities.[6] Establishing a connection between these two entities is exceedingly challenging, and no standard operating procedure exists for such circumstances.

The aim of the study is to investigate the relationship between sarcoidosis and immune-mediated diseases (IMDs).

Material and Method

Study Design

This study employed a retrospective cross-sectional cohort design utilising patient records. The study aims to investigate the temporal relationship and risk of developing sarcoidosis after a diagnosis of various immune-mediated illnesses (IMDs), as well as the risk of acquiring IMDs subsequent to a sarcoidosis diagnosis.

Period of the Study

The study was conducted between April 2024 to November 2024.

Study Settings

The study was conducted at Al-Azhar University hospitals

Study Sample

The trial involved 55 individuals with immune-mediated illnesses, selected based on specified inclusion and exclusion criteria.

Inclusion Criteria

- Patients aged 18 to 65 years.
- Diagnosis of sarcoidosis and immune-mediated disorders confirmed.
- Minimum follow-up duration
- Availability of data concerning the timing of disease diagnosis

Exclusion Criteria

- Patients beyond the specified age range
- Patients lacking a proven diagnosis of immune-mediated illnesses or sarcoidosis.
- Gestation
- Diagnosis primarily attributed to infection or cancer.

Measured Outcomes

Sarcoidosis is a multisystem condition of indeterminate origin. It typically manifests as bilateral hilar lymphadenopathy and reticular opacities in the pulmonary tissue. Additional significant affected locations encompass the skin, eyes, and joints. Nonetheless, it may manifest to varying extents in the musculoskeletal system, reticuloendothelial system, exocrine glands, heart, kidneys, and central nervous system.

Diagnosis of sarcoidosis relies on three criteria.

1. A compatible clinical and radiologic presentation.
2. Pathologic evidence of noncaseating granulomas.
3. Exclusion of other diseases with similar findings, such as infections or malignancy.

Pathological Assessment

Biopsies was obtained and preserved in buffered formaldehyde, systematically processed into paraffin wax blocks, sectioned into 4-µm-thick slices, and stained with haematoxylin and eosin to verify the diagnosis of characteristic noncaseating granulomas containing aggregates of epithelioid histiocytes, giant cells, and mature macrophages.

Immunohistochemical Staining

CD68 (monoclonal antibody) is a 110 kDa integral membrane glycoprotein predominantly expressed on the intracellular lysosomes of monocytes and macrophages and to a lesser extent by dendritic cells and peripheral blood granulocytes. an antibody that was generated by immunizing mouse against the subcellular fraction of human alveolar macrophages.

CD68 (KP1) Mouse monoclonal antibody is used with formalin-fixed and paraffin-embedded sections of collected samples. Pretreatment of deparaffinized tissue with heat-induced epitope retrieval or enzymatic retrieval is recommended. In general, immunohistochemical (IHC) staining techniques allow for the visualization of antigens via the sequential application of a specific antibody to the antigen (primary antibody), a secondary antibody to the primary antibody (link antibody), an enzyme complex, and a chromogenic substrate with interposed washing steps. The enzymatic activation of the chromogen results in a visible reaction product at the antigen site. Results are interpreted using a light microscope. Host: Mouse

Isotype: IgG1 /κ Immunogen: Subcellular fraction of human alveolar macrophages Cellular Localization: Cytoplasmic Concentrate Dilution Range: 1:100-200 Positive control: Tonsil, lymph node, spleen

Lab

The laboratory parameters to be assessed are as follows: A complete blood count (CBC) was conducted utilising an ABX Pentra XL 80 automated cell counter (5-part). Serum Vitamin D concentrations were assessed using an enzyme-linked fluorescence assay (VIDAS). Serum Anti-CCP antibodies were quantified via an electro-chemiluminescence immunoassay analyser (cobas e 411). Serum amyloid A was quantified with a rate-based nephelometric technique (MISPA i3). Serum antinuclear antibodies (ANA) and serum double-stranded DNA (dsDNA) antibodies were evaluated via enzyme-linked immunosorbent assay (ELISA) and subsequently validated through indirect immunofluorescence testing (IF).

Radiology

Radiological examinations, such as chest X-rays, ultrasound (US), computed tomography (CT) scans, and magnetic resonance imaging (MRI) scans, facilitate the identification of abnormalities in the lungs, brain, or other organs impacted by sarcoidosis or related autoimmune disorders.

Ethical Consideration

The study was conducted in accordance with the Declaration of Helsinki, the Islamic Organisation for Medical Sciences, the World Health Organisation, the International Council on Harmonisation, and Good Clinical Practice guidelines. The research ethics committee convened at the Faculty of Medicine, Al-Azhar University, and sanctioned the study under code number: RESEARCH/AZ.ZST./CHT019/5/239/01/2025.

Results

The study sample consisted of 75 individuals according to inclusion and exclusion criteria. The study included 20 healthy individuals, half of whom were female and half male, as the control group, and 55 individuals with sarcoidosis and associated immune diseases. They were divided as follows: Group 1 included 13 individuals with sarcoidosis associated with RA; Group 2 included 13 individuals with sarcoidosis associated with Hashimoto's thyroiditis (HT); Group 3 included 12 individuals with sarcoidosis associated with Sjögren's syndrome (SS); Group 4 included 12 individuals with sarcoidosis associated with systemic lupus erythematosus (SLE); and Group 5 included 5 individuals with sarcoidosis associated with multiple sclerosis (MS).

Table 1: Demographic Characteristics and Laboratory Tests.

Characteristics	Group 1 (13)	Group 2 (13)	Group 3 (12)	Group 4 (12)	Group 5 (5)	Control Group (20)	*P value
Age (years)	41.7 ± 10.6	45.3 ± 10.9	44.2 ± 10.2	44.8 ± 10.32	44.8 ± 10.32	45.2 ± 10.1	0.02
Male(N)	5	4	4	3	3	10	0.0025
Female (N)	8	9	8	9	2	10	0.001
Vit D3(m ± SD)(mg/dl)	46± 3.2	15± 3.4	10± 2.5	9± 2.5	19 ± 3.5	12± 3.2	<0.001
ANA(IU/mL) (m ± SD)	150 ± 6.9	32± 5.6	44± 2.33	38 ± 6.5	2.2 ± 0.6	10± 2.2	<0.001
Anti-CCP(N) (positive number)	12	12	7	11	4	0	<0.001
Serum Amyloid A (m ± SD) (mg/L)	94.3 ± 50.3	88.0 ± 28.9	60.0 ± 11.8	58.8 ± 13.9	12.5 ± 0.8	56.8 ± 12.6	<0.001
HB (g/dL) (m ± SD)	13.95 ± 0.5	13.35 ± 0.5	13.95 ± 0.5	14.6 ± 0.5	14.6 ± 0.5	15.23 ± 0.5	0.02
WBC(×10⁹/L) (m ± SD)	4.2 ± 0.88	5.4 ± 0.92	4.9 ± 0.68	4.02 ± 0.65	5.32 ± 0.65	5.01 ± 0.44	<0.001
(PLT) × 10⁹/L (m ± SD)	225 ± 85	215 ± 90	220 ± 87	218 ± 92	221 ± 40	222 ± 60	<0.001
Granuloma Presence (%)	75% ± 0.4	70% ± 0.24	65% ± 0.6	72% ± 0.33	70% ± 013	0%	<0.001
dsDNA (IU/mL)	120 ± 15	80 ± 10	60 ± 12	45 ± 8	20 ± 6	0%	0.001

Group1: people with sarcoidosis accompanied by rheumatoid arthritis (RA), Group2: people with sarcoidosis accompanied by Hashimoto's Thyroiditis (HT), Group3: people with sarcoidosis accompanied by Sjögren's Syndrome (SS), Group4: people with sarcoidosis accompanied by Systemic Lupus Erythematosus (SLE), Group5: people with sarcoidosis accompanied by multiple sclerosis (MS), Control Group: healthy people, M: Average Value, N: Patient Count, SD: Standard Deviation, P- value: statistically significant.

Table (1) offers a comparison of various traits among six groups of individuals: five disease groups (groups 1, 2, 3, 4 and 5), and a control group. These traits include demographics (sex and age), and vital and laboratory indicators such as vitamin D3, ANA, anti-CCP, serum amyloid A, hemoglobin (Hb), white blood cells (WBC), platelets (PLT), granulomas presence, and anti-dsDNA antibodies. a P value, which is the likelihood that differences between groups occur by chance. By and large, a P value less than 0.05 is statistically significant. The findings indicated notable group disparities in various immune and laboratory metrics, including vitamin D3, ANA, anti-CCP, serum amyloid A, and dsDNA, reflecting heightened immune or inflammatory activity, particularly in the first and second groups. Age exhibited a statistically significant difference (P = 0.02), although its clinical relevance was negligible. The sex ratio was unequal among groups, affecting the interpretation of the remaining data. The disparity between the number of males and females was evident, with P values for both genders being below 0.005, suggesting a possible impact of other variables.

Significant disparities in white blood cell and haemoglobin values were seen between the disease and control groups, with the disease groups exhibiting lower levels. The platelet data were unexpectedly analogous, with a statistically significant P value, prompting enquiries on the interpretation of this outcome.

The existence of granulomas demonstrated distinct group disparities. It was completely missing in the control group, but present at varying rates in the other groups. This necessitates additional clarity regarding the specificity of the diagnosis and the criteria employed. According to immunological indices, group 1 demonstrated the greatest antibody presence frequency, with a mean of 94.3 and a standard deviation of 50.3. Group 4 approximated the control group with a mean of 58.8, in contrast to the control group's 56.8. These findings confirm a strong association between sarcoidosis and other immunological illnesses within the disease cohorts, in contrast to healthy individuals in the control group.

Table2: Correlation Coefficient between Sarcoidosis and the Five Immune Diseases.

Autoimmune Disease	Correlation Coefficient with Sarcoidosis	*p*-value
RA	0.302	0.02
HT	0.302	0.02
SS	0.288	0.018
SLE	0.288	0.018
MS	0.3	0.019

The table presents the correlation coefficients between sarcoidosis and five autoimmune diseases: RA, HT, SS, SLE, and MS, along with their respective p-values. The correlation coefficient for RA is 0.302, indicating a weak to moderate positive connection with sarcoidosis. The p-value is 0.02, which is less than 0.05, indicating that this correlation is statistically significant. The correlation coefficient for HT is 0.302, indicating a comparable direction and strength of relationship with sarcoidosis. A p-value of 0.02 further substantiates the statistical significance of the link. The correlation value for multiple sclerosis is 0.30, indicating a comparable direction and level of relationship with sarcoidosis. The p-value of 0.019 further substantiates the statistical significance of the link.

Table 3: Correlation Coefficient between CD68, Granuloma and the Five Immune Diseases.

Autoimmune Disease	Correlation Coefficient with Granuloma	Correlation Coefficient with CD68	*p*-value
RA	0.88	0.89	0.025
HT	0.85	0.84	0.028
SS	0.85	0.87	0.24
SLE	0.86	0.88	0.025
MS	0.85	0.87	0.03

Table 3 presents the association coefficients among five autoimmune diseases—RA, HT, SS, SLE, and MS—concerning the existence of granulomas and CD68 levels, along with the associated probability values for each condition. The table indicates that individuals with rheumatoid arthritis (RA) have a higher likelihood of granulomas, as evidenced by a correlation coefficient of 0.88 between granulomas and RA. In contrast, the correlation with CD68 is somewhat greater at 0.89, suggesting a more robust association.

In individuals with thyroiditis, the correlation coefficient with granulomas is 85%, and with CD68, it is 84%. This indicates a robust link between thyroiditis and the development of granulomas, as well as CD68, albeit to a lesser degree. Furthermore, for those with SS, the connection with the existence of granulomas is 0.85, and with CD68, it is 0.87. This indicates a significant association between thyroiditis and the development of granulomas, as well as CD68, with the latter being more pronounced.

In patients with systemic lupus erythematosus (SLE), the correlation with granulomas is 0.86, and the correlation with CD68 protein is 0.88, whereas the correlation with CD68 is 0.87. This indicates a significant association between thyroiditis and the development of granulomas, as well as CD68, with the former being more pronounced. The p-value in all instances is below 5%, indicating statistical significance and a robust correlation between the existence of granulomas and CD68 in relation to immunological disorders.

The chart illustrates the association coefficients between CD68 presence and granuloma presence, as well as five autoimmune disorders. The correlation coefficient for CD68 exceeds that of granuloma across all five autoimmune illnesses (RA, Hashimoto's, Sjögren's, systemic lupus erythematosus – SLE, and Multiple Sclerosis – MS). This implies that CD68 may have a stronger correlation with autoimmune disorders than granuloma expression in this context.

Table 4: Radiologically Detected Organs Enlargement.

Disease	Spleen Enlargement (cm)	LN enlargement (cm)	Liver Enlargement (cm)	*p*-value
RA	14.5 ± 1.2	2.8 ± 0.7	16.2 ± 1.1	0.021
HT	13.8 ± 1.5	1.8 ± 0.37	15.7 ± 1.3	0.028
SS	13.2 ± 1.1	0	15.0 ± 1.2	0.024
SLE	15.0 ± 1.6	4.8 ± 0.88	16.5 ± 1.5	0.025
Multiple sclerosis	13.5 ± 1.3	0	15.2 ± 1.4	0.03

Radiological anomalies linked to sarcoidosis suggest potential parallels in organ involvement patterns between autoimmune diseases and sarcoidosis. This highlights the importance of differential diagnosis, considering comorbidities, and further investigation to understand underlying mechanisms and guide treatment. Differential patterns of lymphadenopathy may differentiate autoimmune diseases from traditional sarcoidosis.

A CT study is employed to evaluate lung alterations present in nearly all patients, yet exhibiting varying patterns based on the autoimmune illness associated with sarcoidosis. A wide array of lung alterations is observed, including variably sized pulmonary nodules, ground-glass opacities, air trapping, interstitial thickening, and interstitial pneumonia.

Immunohistochemical Results

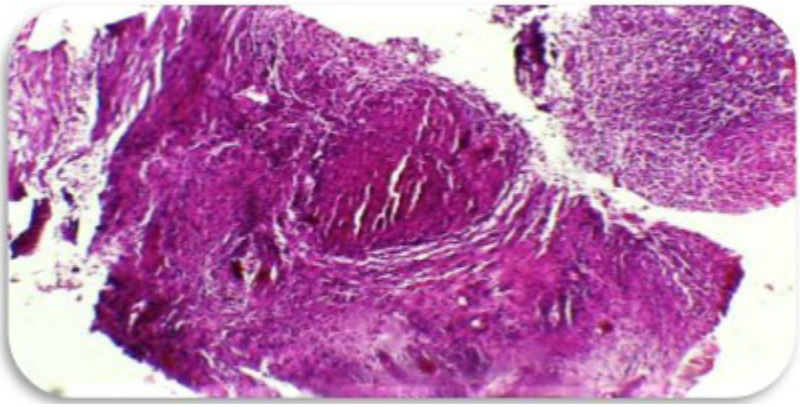

Figure 1: Shows A Biopsy of Non-necrotizing Epithelioid Granuloma with Aggregates of Epithelioid Histocytes.

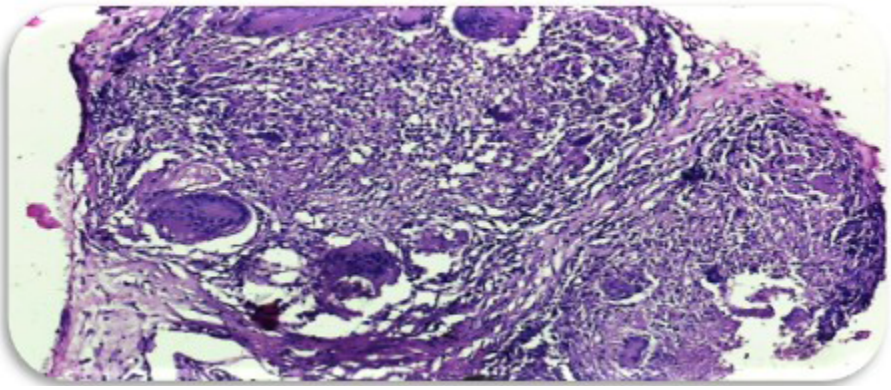

Figure 2: A Biopsy of Sarcoid Granuloma with Multinucleated Giant Cells Formed by Fusion of Epithelioid Histiocytes Typical of Sarcoidosis.

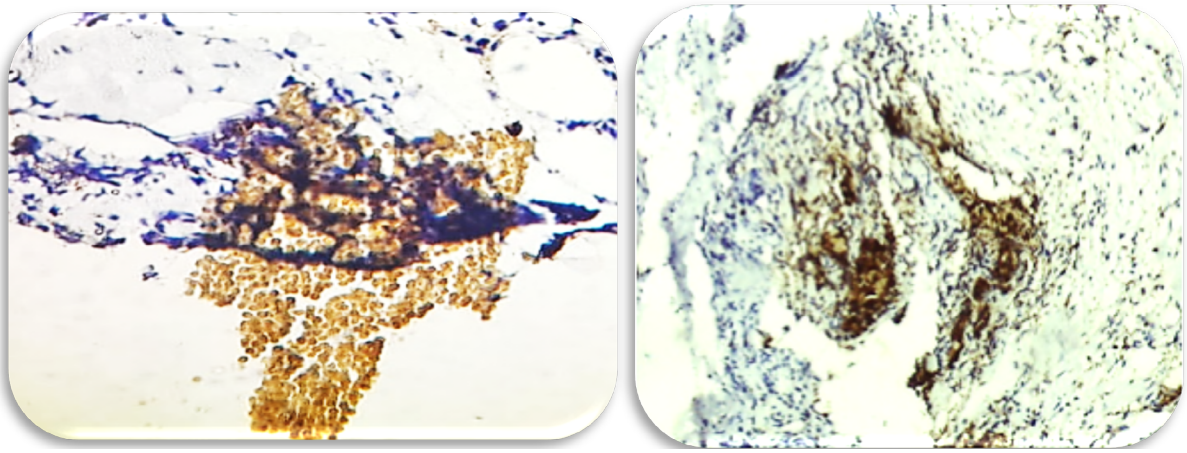

Figure 3: A biopsy of sarcoid granuloma with CD68 positive Immunostaining Labeling the Histocytes.

Case I sarcoidosis with MS

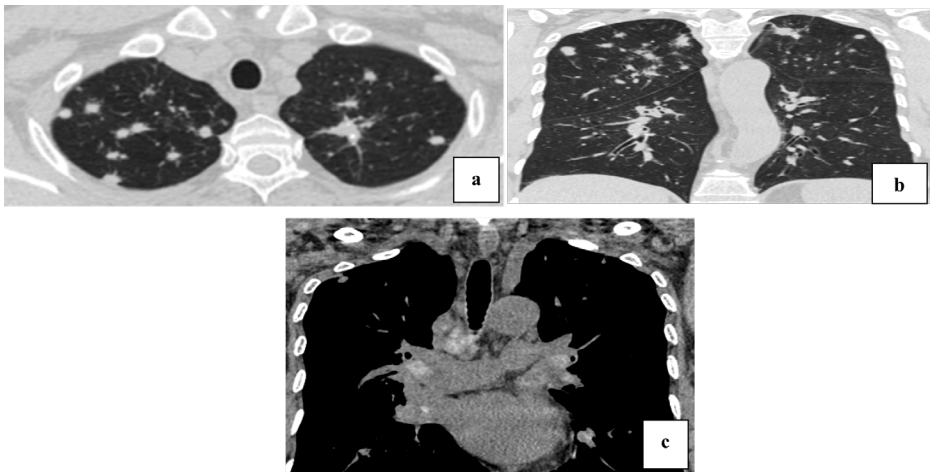

Figure 4: Pulmonary Sarcoidosis in a 35-year-old Male Patient. (a & b) CT Chest, Axial and Coronal Reformats in the Pulmonary Window Reveal Multiple Bilateral ill-defined Small Nodules Predominantly Situated in the Upper Lobes, Exhibiting Lymphatic Distribution: Peri-bronchovascular, Subpleural, And Interlobular Septa. The Mediastinal Window, in Coronal Reformat, Reveals Several Lymphadenopathies Located Retrocaval, Pretracheal, Aortopulmonary, Subcarinal, and Bilaterally Hilar, with Some Exhibiting Calcification.

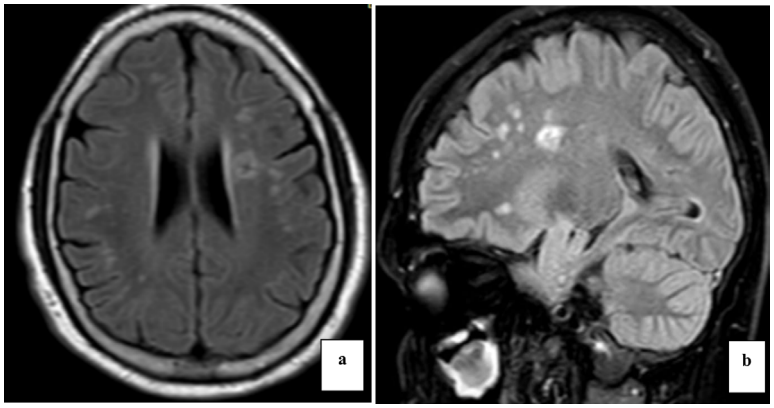

Figure 5: A Diagnosis of Multiple Sclerosis was Established in the Same Patient. MRI Brain (a) Axial and (b) Sagittal FLAIR Images Reveal Several Bilateral Periventricular and Subcortical White Matter Lesions and foci of Elevated Signal, with the Most Prominent Located in the Left Frontal Area, Exhibiting Central Hypointensity.

Case. 2, Sarcoidosis with HT

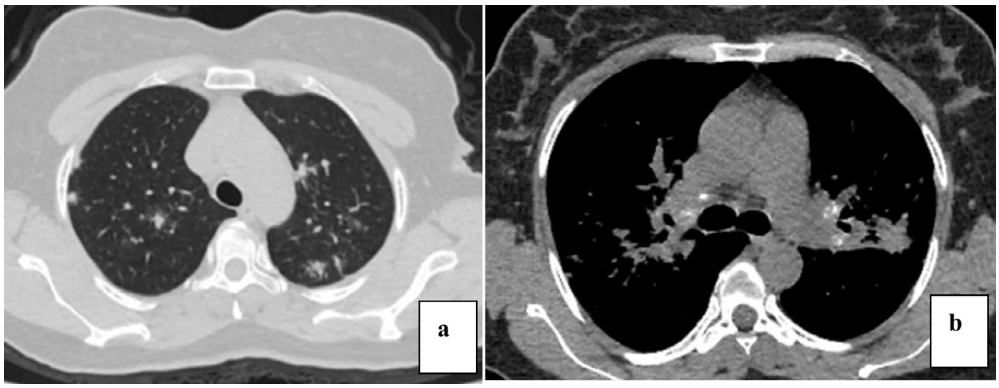

Figure 6: Pulmonary Sarcoidosis in a Middle-aged Female Patient, Ct Chest Axial Reformat, (a) Pulmonary Window Reveals Several Bilateral ill-defined Coalescent Pulmonary Nodules Predominantly Situated in the Upper Lobes, Mimicking the Characteristic Sarcoid Galaxy Sign, with a Lymphatic Distribution of the Nodules. (b) The Mediastinal Window Reveals Numerous Hilar Lymphadenopathies, Some of which are Calcified.

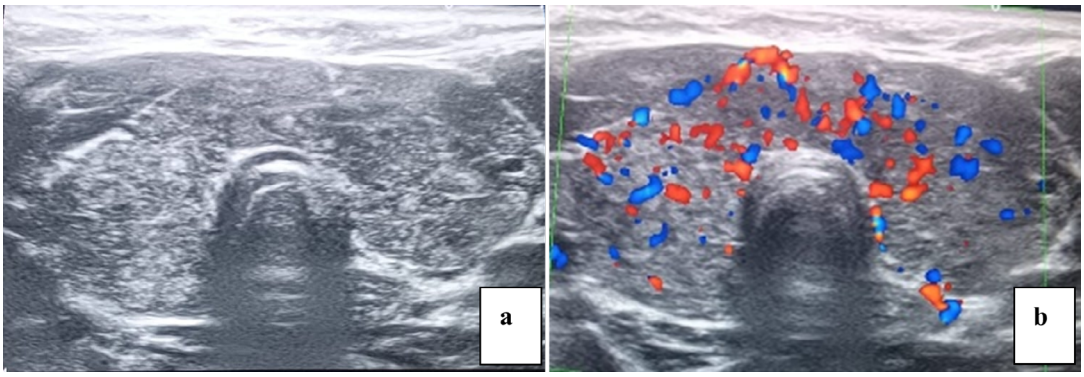

Figure 7: In the Same Patient Diagnosed with HT, Thyroid Ultrasound (a) in B-mode Reveals Extensive Enlargement of the Thyroid Gland with Heterogeneous Echotexture, and (b) Demonstrates Diffuse Enhanced Vascularity on Colour Doppler.

Discussion

The aim of the study is to investigate the relationship between sarcoidosis and immune-mediated diseases (IMDs). Our findings indicated that the immunological landscape of sarcoidosis reveals both consensus and ongoing disputes in research, particularly on disease mechanisms and the efficacy of biomarkers. Although at lower rates than in rheumatoid arthritis (RA), increased antinuclear antibodies (ANA) and rheumatoid factor (RF) are present in certain patient subsets. For example, 28.5% of people with sarcoidosis were found to be ANA-positive.[11,12] Granulomas are distinguished by the prevalence of macrophages and CD4+ T-cells; M2 macrophage polarisation correlates with fibrosis.[13] A CD4/CD8 ratio exceeding 3.5 in bronchoalveolar lavage (BAL) fluid, while nonspecific, serves as a reliable diagnostic indicator.[8] Conversely, some argue that these antibodies demonstrate inadequate diagnostic specificity and may suggest the presence of concomitant autoimmune diseases. The role of B-cells is being examined, as some studies have reported normal serum immunoglobulin levels.[7] The CD103+CD4+/CD4+ ratio in bronchoalveolar lavage fluid is proposed as a diagnostic biomarker, albeit findings are inconsistent.[8] The evidence substantiating sarcoidosis as a bona fide autoimmune disorder is circumstantial, with HLA connections and susceptibility to immunosuppression bolstering this hypothesis. The role of reduced invariant natural killer T (iNKT) cells in the maintenance of granulomas remains disputed.[14] Our research findings indicated a link between sarcoidosis and five autoimmune disorders. Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune condition that affects both sexes, although it is more prevalent in women. HT is the most widespread and well studied organ-specific autoimmune disease in humans, alongside SS, SLE, and MS, which is a chronic, progressive, and complex demyelinating diseases of the central nervous system. The correlation coefficient for RA is 0.302, signifying a modest to moderate positive link. HT exhibits a comparable direction and amplitude, with a p-value of 0.02, whereas MS also demonstrates a similar direction and magnitude, with a p-value of 0.019, so affirming statistical significance. The correlation between sarcoidosis and autoimmune illnesses, including rheumatoid arthritis, Hashimoto's thyroiditis, Sjögren's syndrome, and systemic lupus erythematosus, is supported by some studies but contested by others. Case studies illustrate a correlation between rheumatoid arthritis and sarcoidosis, especially in those exhibiting anti-CCP antibodies and erosive joint changes. HLA-DR4 is proposed as a prevalent risk factor, suggesting a potential pathogenic association, as demonstrated by a 35-year-old woman with both conditions.[8,15]

Sarcoid arthritis, often mimicking rheumatoid arthritis but without erosive changes, complicates differentiation from sarcoidosis; anti-CCP antibodies are rare (4.7%) and indicate potential comorbidity with rheumatoid arthritis, as demonstrated in a study including 42 patients.[16] A case study reveals that 27.4% of sarcoidosis patients present thyroid autoantibodies, indicating a shared aetiology including granulomatous inflammation and autoimmune mechanisms in both disorders.[10] Conversely, the study indicated that thyroid granulomas in sarcoidosis are rare; most thyroid dysfunction in these patients is due to Hashimoto's disease rather than sarcoidosis itself. In the research undertaken by Ramos-Casals *et al.*[17]. Five people demonstrated simultaneous Sjögren's syndrome and sarcoidosis, including granulomas and anti-Ro/La antibodies suggesting shared immunogenetic mechanisms. Studies suggest that sarcoidosis should not be regarded as a disqualifying factor for the diagnosis of SS.Sarcoidosis is a condition characterised by non-necrotizing epithelioid granulomas, typically accompanied by a minimal lymphocytic ring, often found in portal or periportal areas.[18] These granulomas demonstrate a sensitivity of 94% for diagnosis, although exhibit a specificity of just 60%.[18] The granuloma consists of compact aggregates of epithelioid histiocytes and multinucleated giant cells, often incorporating asteroid or Schaumann bodies.[19] The diagnostic criteria include excluding infection and evaluating for elevated serum ACE levels or bilateral hilar lymphadenopathy.[20]

Non-necrotizing granulomas in sarcoidosis may mimic sarcoidosis, as one study revealed that 24% of TB cases displayed this feature.[21] Non-necrotizing granulomas may occur in fungal or mycobacterial infections, autoimmune or inflammatory diseases, and sarcoidosis, although necrotising granulomas are observed in up to 35% of cases.[21]Radio-labelling studies indicate that microglial cells (MGCs) in sarcoidosis originate from the fusion of epithelioid histiocytes rather than from nuclear division. [22] The fusion mechanism is promoted by the expression of adhesion molecules CD44 and CCR-5 in multinucleated giant cells of sarcoidosis, together with E-cadherin, a cell-cell adhesion protein, in mononuclear histiocytes and multinucleated giant cells in cutaneous sarcoidosis. [23] Histopathological features include cohesive epithelioid histiocytes presenting "naked" granulomas, Langhans-type multinucleated giant cells (MGCs) with peripheral nuclei, and foreign-body-type MGCs with dispersed nuclei. [24,25] Non-specific granulomatous features, such as non-necrotizing granulomas containing multinucleated giant cells, are observed in foreign-body responses, tuberculosis, and Crohn's disease.[22] Biopsies of cutaneous sarcoidosis may demonstrate lymphocytic infiltrates, interstitial granulomas, or foreign materials, which can coincide with infectious or inflammatory aetiologies.[26] Atypical necrosis manifests in 16% of patients with cutaneous sarcoidosis. The functional autonomy of MGCs in sarcoidosis remains unclear.[26] CD68 staining in endomyocardial samples identified micro-granulomas in cardiac sarcoidosis cases, exhibiting a 100% association with radiologically confirmed instances. Granulomas displayed extensive CD68/PGM1 positivity, confirming their histiocytic origin. CD68+ histiocytes were situated near CD4+ T-cells.[27-29] The imaging findings indicate bilateral upper-lobe-predominant pulmonary nodules with a lymphatic distribution (peri-bronchovascular, subpleural, interlobular septal) and calcified mediastinal/hilar lymphadenopathy, strongly suggestive of granulomatous diseases, though alternative diagnoses remain feasible.CT chest scans reveal many bilateral pulmonary ill-defined minute nodules in the upper lobes, accompanied by lymphatic dissemination from peri-bronchovascular regions to interlobular septa.[30] Potato nodes are a type of lymphadenopathy, seen in 70% of patients with sarcoidosis. They commonly manifest in the aortopulmonary and right paratracheal regions, usually accompanied by bilateral hilar involvement.[31]

Hashimoto's thyroiditis and sarcoidosis are linked by analogous autoimmune mechanisms, characterised by Th1/Th17-mediated inflammation and elevated thyroid antibodies. Both disorders are associated with aggressive autoimmune thyroiditis, whereas sarcoidosis presents diffuse thyroid hypertrophy, hypoechoic echotexture, and hypervascularity.[32]

The ultrasonography features of Hashimoto's thyroiditis include diffuse thyroid enlargement, heterogeneous hypoechoic echotexture, and hypervascularity. Sarcoidosis can also impact the thyroid, manifesting as hypoechoic nodules resulting from granulomas.[33] Clinical overlap is noted, with thyroid dysfunction often manifesting before or concurrently with the diagnosis of sarcoidosis. HT is the most common autoimmune condition associated with sarcoidosis, with a prevalence of 3-11% across sarcoidosis populations.[34] Immunogenetic correlations suggest interrelated autoimmune processes.[35] Only 3-6% of sarcoidosis patients demonstrate thyroid granulomas during biopsy. Some investigations argue that hypertension and sarcoidosis coexist fortuitously due to polyclonal B-cell activation in sarcoidosis, rather than stemming from a same aetiology.[36]

Conclusion

This study aims to examine the correlation between sarcoidosis and immune-mediated disorders (IMDs). The correlation between sarcoidosis and five autoimmune diseases—rheumatoid arthritis, Hashimoto's thyroiditis, Sjögren's syndrome, systemic lupus erythematosus, and multiple sclerosis is substantiated by certain research and disputed by others.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki, the Islamic Organisation for Medical Science, the World Health Organisation, the International Council on Harmonisation, and Good Clinical Practice guidelines. The research ethics committee convened at the Faculty of Medicine, Al-Azhar University, and sanctioned the study under code number: RESEARCH/AZ.ZST./CHT019/5/239/01/2025.

Conflicts of Interest

Authors declared no conflict of interest.

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