ECRONICON OPEN ACCESS

EC CLINICAL AND MEDICAL CASE REPORTS

Editorial

Heaped and Piled-Sarcoidosis

Anubha Bajaj*

Department of Histopathology, Panjab University, A.B. Diagnostics, India

***Corresponding Author**: Anubha Bajaj, Department of Histopathology, Panjab University, A.B. Diagnostics, India.

Received: July 07, 2025; **Published:** July 29, 2025

Sarcoidosis represents as a multi-system disorder associated with granulomatous inflammation. Cutaneous lesions are encountered in up to 35% instances.

Of obscure aetiology, disease occurrence and progression may be concordant to deranged immune response towards extrinsic antigens, especially within genetically susceptible individuals. Clinically, the disorder appears heterogeneous and may simulate diverse dermatological conditions.

Morphological assessment typically depicts discrete, non necrotizing granulomas encompassed within a minimal inflammatory exudate of lymphocytes. The inflammation appears to spill over into subjacent dermis or subcutaneous tissue.

As an inflammatory condition, sarcoidosis may be ascertained as a diagnosis of exclusion.

Disease incidence is variable and disease prevalence is worldwide. Racial preference is absent. No age of disease emergence is exempt. However, female subjects or individuals of Afro-Caribbean descent are commonly implicated. Peak age of disease onset is third decade to fifth decade [1,2].

Nearly 35% instances depict cutaneous lesions and configure as preliminary manifestation of disease.

Majority (~95%) of subjects expound pulmonary lesions which commonly emerge as bilateral hilar lymphadenopathy.

Up to 10% subjects display peripheral lymphadenopathy. Roughly 50% of Caucasians and ~90% of Japanese individuals with sarcoidosis denominate ocular lesions [1,2].

An estimated 27% subjects delineate cardiac lesions which contribute significantly to disease associated mortality and may be appropriately discerned upon autopsy studies. An estimated 15% instances display lesions confined to central nervous system [1,2].

Of obscure aetiology, the lesion may manifest as a chronic immunological response within genetically susceptible individuals which are exposed to an undetermined extrinsic antigen [2,3].

Characteristically, granulomatous inflammation expounds Th1 mediated immune response [2,3].

Inundation of putative agents within antigen presenting cells configures major histocompatibility complex (MHC) peptide complexes which are discerned by CD4+ T cells [2,3].

Cellular immune response ensures secretion of tumour necrosis factor alpha (TNFα), interferon gamma (IFNў), interleukins 1, 2, 6, 12, 15, 18 (IL1, IL2, IL6, IL12, IL15, IL18) and macrophage inflammatory protein 1 [2,3].

Clinically, cutaneous manifestations appear variable and may simulate diverse dermatological conditions. Familial clustering indicates a genetic susceptibility of sarcoidosis in certain instances [2,3].

Clinical countenance and morphology varies from papules, plaques or annular lesions to subcutaneous nodules. No cutaneous site of lesion emergence is exempt [2,3].

Clinical representations emerge as:

- Acute, self limiting variant comprised of Löfgren syndrome demonstrating erythema nodosum, bilateral hilar lymphadenopathy, pyrexia and polyarthralgia.
- Chronic variant with cutaneous lesions encountered within 20% to 40% instances of cutaneous sarcoidosis devoid of systemic involvement.
- Systemic chronic variant demonstrating lesions within multiple organs.
- Lupus pernio emerges as a chronic and disfiguring variant which characteristically expounds indurated lesions confined within the nasal region, cheeks and ears.
- Scar sarcoidosis characteristically delineates lesions arising within surgical scars, tattoos, cutaneous piercings and various sites of trauma.
- Erythema nodosum may emerge in ~40% of subjects inflicted by sarcoidosis [3,4].

Upon microscopy, a nodular, diffuse or angiocentric pattern of granulomatous inflammation emerges within superficial or deep dermis along with or devoid of disease occurrence within the subcutaneous tissue [3,4].

Perineural granuloma may frequently be discerned.

Discrete or confluent, non-necrotizing granulomata constituted of epithelioid histiocytes impregnated with abundant, eosinophilic cytoplasm are pathognomonic. Varying numbers of Langhans or associated giant cells are commingled within the histiocytes.

Few lymphocytic cells configure a cuff which circumscribes granulomata, thereby configuring ‘naked granuloma’.

Miniature foci of fibrinoid necrosis may be discerned. However, geographic or caseous necrosis is exceptionally encountered [3,4].

Characteristically, superimposed epidermal layer appears unaltered. Intracytoplasmic inclusion bodies are non specific or non pathognomonic and emerge as

- Schaumann body comprised of basophilic, calcified, laminated, spherical structures.
- Asteroid body constituted of intracytoplasmic, eosinophilic, ‘star shaped’ structures.
- Foreign material is denominated in ~5% lesions, a feature which may not exclude the occurrence of sarcoidosis [3,4].

Biomarker	Features	Limitations
Angiotensin converting enzyme (ACE)	Indicates granulomatous inflammation-raised	Non specific, raised in tuberculosis and tumours
Soluble interleukin-2 receptor (s IL-2R)	Indicates T cell activation and disease activity	Variable levels, concurrent with various interstitial lung diseases
IL-2, TNFα, pro-inflammatory molecules	Indicates disease activity or progression, elevated	Non specific for sarcoidosis
JAK/STAT signalling	Granuloma formation, STAT1 and STAT3 are biomarkers of JAK/STAT pathway activation	Additional research and validation required
m TOR signalling	Granuloma formation, disease progression, m TORC1 activation predicts response to rapamycin	
Hair cortisol analysis	Non invasive marker of chronic stress and psychological distress	

Table 1: *Biomarkers in sarcoidosis [2].*

IL: Interleukin; TNFα: Tumour Necrosis Factor Alpha.

Radiographic Subtype	Radiographic Characteristics
0	No visible findings
I	Bilateral hilar lymphadenopathy
II	Bilateral hilar lymphadenopathy and parenchymal infiltration
III	Parenchymal infiltration without hilar lymphadenopathy on chest X-Ray
IV	Advanced fibrosis with significant distortion of normal lung architecture primarily affecting middle and upper lobes with conditions as bronchiectasis, hilar retraction, bullae, cysts or 'honeycombing'

Table 2: *Scadding stage of sarcoidosis [4].*

Sarcoid lesions appear immune reactive to CD68.

The lesion may not be high lighted by fungal stains as periodic acid Schiff's (PAS) stain, Gomori methenamine silver (GMS) or acid fast stain as Ziehl Neelsen (ZN) stain [5,6].

Sarcoidosis requires demarcation from foreign body reaction, cutaneous lesions of Crohn's disease, granulomatous cheilitis or Melkersson-Rosenthal syndrome, granulomatous rosacea, tuberculoid leprosy, necrobiosis lipoidica, infective lesions with concomitant neutrophilic infiltrate and discernible bacteria, fungal organisms or mycobacteria, sarcoidal variant of granuloma annulare or granulomata engendered due to exposure to Beryllium and zirconium [5,6].

Sarcoidosis is a diagnosis of exclusion.

A comprehensive clinical history, physical examination and ophthalmic assessment is necessitated in order to evaluate possible occupation with or environmental exposures to chemicals and accompanying systemic signs and symptoms [6,7].

Chest radiographs, pulmonary function tests and cardiac investigations appear appropriate for cogent disease evaluation.

Cutaneous tissue samples may be appropriately examined in order to exclude various infections or inflammatory conditions.

Elevated levels of serum angiotensin converting enzyme (ACE), serum calcium or raised erythrocyte sedimentation rate (ESR) may be enunciated [6,7].

Upon chest radiography, bilateral hilar lymphadenopathy is commonly encountered. Infrequently, pulmonary infiltration, fibrosis, bullae, cysts or emphysema may be encountered. Bone lesions and bone cysts may be occasionally discerned [6,7].

Limited or mild disease may be appropriately managed with topical and intralesional corticosteroids. Additionally, systemic immunomodulators, tetracycline class of antibiotics, antimalarial or diverse agents may be beneficially employed for therapy.

Systemic immunosuppressive and immunomodulatory agents, prednisone, methotrexate, tumour necrosis factor (TNF) inhibitors and diverse biologic therapies appear advantageous [7,8].

Acute variant comprised of Löfgren syndrome demonstrates superior prognostic outcomes.

Chronic cutaneous sarcoidosis, especially facial lesions are associated with unfavourable prognosis and expounds enhanced possibility of pulmonary fibrosis and ocular lesions [7,8].

Lupus pernio exemplifies multisystem disease with lesions within upper respiratory tract, pulmonary parenchyma, ocular lesions and bone cysts and an extended clinical course. Prognostic outcomes are inferior [7,8].

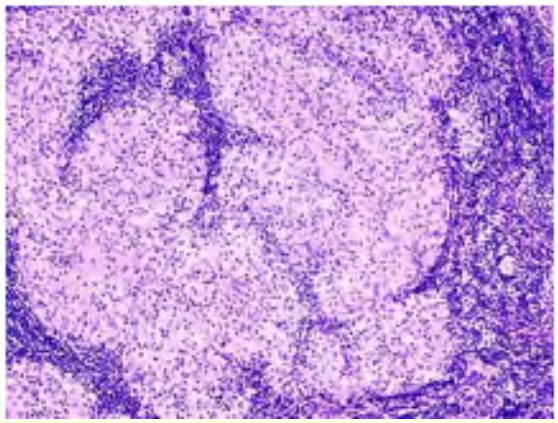

Figure 1: *Sarcoidosis demonstrating aggregates of epithelioid cell granulomas encompassed within a cuff of small lymphocytes. Caseation necrosis is absent [9].*

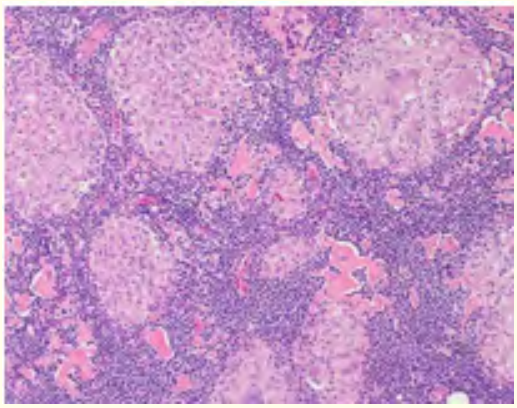

Figure 2: *Sarcoidosis demonstrating epithelioid cell granulomas enmeshed within a cuff of small lymphocytes. Caseation necrosis is absent [10].*

Bibliography

1. Bokhari SRA., *et al*. "Sarcoidosis". Stat Pearls International. Treasure Island, Florida (2025).
2. Waly YM., *et al*. "A review of sarcoidosis etiology, diagnosis and treatment". *Frontiers in Medicine (Lausanne)* 12 (2025): 1558049.
3. Coker RK and Cullen KM. "Sarcoidosis: Key disease aspects and update on management". *Clinical Medicine (London)* 25.3 (2025): 100326.
4. Xu D., *et al*. "Sarcoidosis: molecular mechanisms and therapeutic strategies". *Molecular Biomedicine* 6.1 (2025): 6.
5. Rivera NV. "Big data in sarcoidosis". *Current Opinion in Pulmonary Medicine* 30.5 (2024): 561-569.
6. Belfeki N., *et al*. "Current concepts on pathogenesis, diagnosis and management of hepatic sarcoidosis". *Rheumatology International* 45.5 (2025): 130.
7. Belperio JA., *et al*. "Diagnosis and treatment of pulmonary sarcoidosis: a review". *Journal of the American Medical Association* 327.9 (2022): 856-867.
8. Obi ON., *et al*. "Sarcoidosis: Updates on therapeutic drug trials and novel treatment approaches". *Frontiers in Medicine (Lausanne)* 9 (2022): 991783.
9. Image 1 Courtesy: Pathology outlines.
10. Image 2 Courtesy: Springer link.

Volume 8 Issue 8 August 2025