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Editorial

Connate and Cognate-Sarcoid-Like Reaction (Sarcoid-Like Granuloma)

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Non infectious epithelioid cell granulomas associated with lymphadenitis appear secondary to conditions such as berylliosis, Hodgkin's lymphoma, non-Hodgkin's lymphoma, lymph nodes draining cancer, Crohn's disease, sarcoidosis and sarcoid-like reaction. Centric necrosis and abscess concurring within aforesaid granulomatous reaction is exceptional.

Non necrotising or 'naked granulomas' may display features such as focal aggregates of epithelioid histiocytic cells, giant cells and miniscule, marginal exudate of chronic inflammatory cells, akin to sarcoid granulomas.

Of obscure pathogenesis, an immunological response to tumour antigens is posited to contribute to occurrence of sarcoid-like reaction. Activation of immune cells and subsequent configuration of epithelioid cell granuloma may occur on account of secretion of various cytokines and chemokines within the tumour microenvironment which transmits to and impregnates distant sites and organs [1,2].

Sarcoid-like reaction is frequently encountered following immunotherapy. Sarcoid-like reaction appears to configure as an indicator of superior prognosis within certain malignancies and is associated with augmented immune response against the tumour [1,2].

Sarcoid-like reaction elucidates epithelioid cell granulomas recapitulating sarcoid nodules, confined to regional lymph nodes. The reaction is associated with concomitant disease processes. Nevertheless, sarcoid-like granuloma may not indicate occurrence of systemic sarcoidosis. Concurrent inflammatory disease or sarcoidosis manifesting or worsening with malignant disorders may be absent [2,3].

Sarcoid-like reaction occurring within diverse carcinomas in the absence of therapy appears essential for precise staging and appropriate therapy [2,3].

Sarcoid-like reaction is encountered in up to 14% of subjects with carcinomas. The reaction is engendered by T cell mediated hypersensitivity reaction configuring epithelioid cell granulomas.

Sarcoid-like reaction may concur with infection, various therapies or foreign bodies. Additionally, the reaction may occur with precision targeted and immune checkpoint inhibitor therapy as BRAF and MEK inhibitors [3,4].

Disorders concurrent with sarcoid-like granuloma emerge as carcinoma, toxoplasmosis, fungal infection, tuberculosis, atypical mycobacterial disease, pneumoconiosis, immunocompromised individuals as encountered in Crohn's disease, primary biliary cirrhosis or Sjogren's syndrome, extrinsic allergic inflammatory alveolitis (farmer's lung), anticancer chemotherapy, exposure to chemicals as beryllium, zirconium, silicon, starch granules or pine pollen [3,4].

Sarcoid-like reaction may concur with various malignancies as breast, pulmonary or renal parenchyma. Visceral carcinoma of uterus, breast, pulmonary parenchyma and stomach may induce sarcoid-like reaction.

The exceptional extra-thoracic sarcoid-like reaction represents with obscure proportions. However, sarcoid-like reaction within the cutis, hepatic parenchyma, spleen, central nervous system, pancreas, bone or ocular tissue may be encountered [3,4].

Bacterial Infection	*Bartonella henselae*, *Brucella* spp, *Actinomyces* spp, *Chlamydia trachomatis* (L1,L2L3 serovars), *Coxiella burnetii*, *Francisella tularensis*, *Listeria monocytogenes*, *Malakoplakia* (various bacteria), *Mycobacterium tuberculosis*, Non tuberculous *Mycobacteria*, *Yersinia granulomatosis*
Fungal infection	*Aspergillus* spp, *Blastomyces dermatitidis*, *Coccidioides* spp, *Cryptococcus* spp, *Histoplasma capsulatum*, *Mucorales*, *Sporothrix schenckii*
Viral and parasitic infection	Cytomegalovirus, Epstein Barr virus, *Leishmania* spp, *Toxoplasma gondii*
Auto-immune origin	Churg Strauss disease, Granulomatosis with polyangiitis, Sarcoid
Malignant origin (neoplasm)	Dendritic cell sarcoma, Erdheim Chester disease, Haemophagocytic lymphohistiocytosis, Histiocytic sarcoma, Hodgkin's lymphoma, Interdigitating cell sarcoma, Langerhans cell histiocytosis, Langerhans cell sarcoma, Metastasis, Rosai Dorfman disease
Other	Foreign body reaction

Table 1: *Aetiological allocation of lymph node granulomas [5,6].*

Features	**Sarcoid like**	**Infective granuloma (tuberculosis like)**
Association with metastasis	May or may not be associated with metastasis	Independent of the metastatic status
Granuloma	Simulating the sarcoid granuloma, small or large, may be confluent	Discrete granuloma like tuberculosis, with or without necrosis
Giant cells (Foreign body / Langhans)	+/-	+/-
Necrosis	Fibrinoid necrosis+/-	Caseation Necrosis +/-
Calcification	May be present	Generally absent
Asteroid bodies	May be present	Generally absent
AFB staining	Negative	+/-

Table 2: *Distinction of sarcoid like and infective granuloma [5,6].*

Progression of carcinoma in combination with sarcoid-like reaction is associated with favourable prognostic outcomes [7,8].

An extensive, biological defence mechanism engendered by continually stimulated lymph nodes may initiate sarcoid like reaction in order to combat metabolites and malignant disintegration [7,8].

Concordant disease processes may initiate non specific constitutional symptoms. Enlargement of pulmonary hilar lymph nodes may occur which appears non discernible upon imaging. Tuberculin test and Kveim test appear non reactive [7,8].

Upon microscopy, miniature, poorly defined epithelioid cell granulomas with minimal epithelioid cells and miniature component of small, mature lymphocyte may be disseminated within the lymph node parenchyma. Granulomas are configured of T lymphocytes, dendritic reticulum cells and macrophages. CD4+/CD8+ lymphocyte percentage of 0.8 to 2.25 may emerge within confluence of granulomas [8,9].

Cogent clinical picture and biochemical assay may assist distinction between sarcoidosis and sarcoid-like reaction [9,10].

Diverse malignancies as carcinoma prostate may demonstrate fluoro-deoxy glucose (FDG)-avid enlargement of mediastinal and hilar lymph nodes, thereby indicating a sarcoid-like reaction. The manifestation is uncommon in the absence of tumour dissemination into localized visceral structures wherein sarcoid-like reaction appears fluoro-deoxy glucose (FDG)-avid [9,10].

Absence of cogent clinical features or disease emergence following commencement of therapy may aid in identifying sarcoid like reaction, although distinction from sarcoidosis may necessitate precise tissue sampling [11,12].

Surgical tissue sampling of hilar lymph nodes is necessitated in order to exclude metastatic disease [11,12].

Classically, the condition recapitulates sarcoidosis and involves mediastinal and hilar lymph nodes which appear as enlarged with augmented fluoro-deoxy glucose (FDG) uptake upon FDG positron emission computerized tomography (PET/CT). Concomitant pulmonary nodules or pulmonary infiltrates may or may not be present [13,14].

Administration of corticosteroids emerges as a predominant therapeutic option. Besides, discontinuation of immunotherapy may be beneficial and mandated in severe instances [13,14].

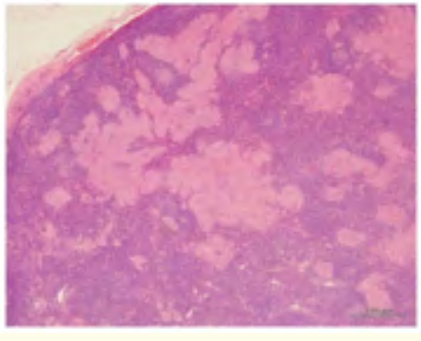

Figure 1: *Sarcoid-like reaction depicting epithelioid cell granulomas disseminated within lymphoid parenchyma. Caseation necrosis is absent [15].*

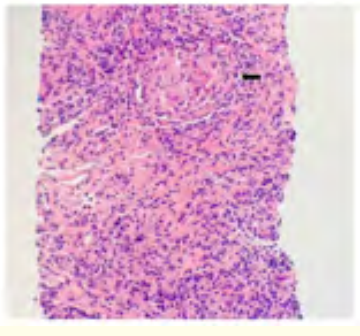

Figure 2: *Sarcoid-like reaction delineating epithelioid cell granulomas disseminated within lymphoid parenchyma. Caseation necrosis is absent [16].*

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15. Image 1 Courtesy: Science direct.

16. Image 2 Courtesy: The Rheumatologist.

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