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The Pervasive Forager-Solitary Reticulohistiocytoma

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Mini Review

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Abstract

Solitary reticulohistiocytoma is an exceptional, benign, non-neoplastic, non-Langerhans histiocytic cell proliferation. The condition appears as a cytokine-induced, localized collection of histiocytic cells emerging as a reaction to an obscure inflammatory stimulus. Reticulohistiocytic lesions are subcategorized into distinct categories as solitary cutaneous reticulohistiocytoma, multiple cutaneous reticulohistiocytoma and multi-centric reticulohistiocytosis. Solitary reticulohistiocytoma appears as an isolated, painless nodule at diverse sites and is devoid of systemic symptoms. A diffuse, dermal infiltration of enlarged, mononuclear or multinuclear histiocytic cells is admixed with lymphocytes and foci of dermal fibrosis.

Keywords: Solitary reticulohistiocytoma; Lymphocytes; Histiocytic cells; Non-Langerhans cell histiocytosis

Abbreviations: WHO: World Health Organization.

Preface

Solitary reticulohistiocytoma is an exceptional, benign, non-neoplastic histiocytic cell proliferation exemplified as a non-Langerhans cell histiocytosis. Solitary reticulohistiocytoma is additionally denominated as solitary epithelioid histiocytoma. Initially scripted by Zak in 1950, solitary reticulohistiocytoma encompasses lesions with diverse clinical manifestations [1]. The lesions can be solitary as discerned in solitary cutaneous reticulohistocytoma or multiple as denominated with multi-centric reticulohistiocytosis [2]. Reticulohistiocytoma is composed of enlarged, mononuclear, histiocytic cells imbued with vacuolated cytoplasm. An admixture of few multinucleated cells is observed. Solitary reticulohistiocytoma can be challenging to discern on account of nonspecific clinical appearance [2].

Disease Characteristics

Of obscure aetiology, lesions of solitary reticulohistiocytoma appear as a consequence to an unexplained inflammatory process which results in localization of cytokine-induced aggregates of histiocytes. Thus, solitary reticulohistiocytoma is a non-neoplastic, cytokine-induced, localized collection of histiocytic cells accumulating as a reaction to an obscure inflammatory stimulus. Few instances with a possible traumatic aetiology such as exposure to laser therapy are documented. Therefore, lesions of solitary reticulohistiocytoma with a dermal histiocytic infiltrate may appear at activated sites such as a preceding burn or thermal injury [3,4].

Goette et al categorized reticulohistiocytic lesions into three distinct categories:

a) Solitary cutaneous reticulohistiocytoma
b) Multiple cutaneous reticulohistiocytoma
c) Multi-centric reticulohistiocytosis.

An additional category of solitary non cutaneous reticulohistiocytoma is denominated wherein lesions of the orbit or ocular adnexa may be discerned [3,4]. World Health Organization (WHO) and Histiocyte Society classifies histiocytic lesions contingent to the cell of origin. Dendritic cell-derived diseases are constituted by Langerhans cell histiocytosis, juvenile xanthogranuloma and solitary

histiocytoma of dendriti cell phenotype [3,4].

Macrophage-derived diseases are denominated by Rosai-Dorfman disease and solitary histiocytoma with a macrophage phenotype. Cogent immunohistochemistry highlights cell of origin of pertinent histiocytic lesions. Macrophages are immune reactive to lysozyme, CD45 and CD14. Langerhans cells are immune reactive to CD45, S100 protein and CD1a. Dendritic cells are immune reactive to CD45 and S100 protein [3,4]. Reticulohistiocytoma exhibits a macrophage histiocytic cell lineage with immune reactive CD68, CD163 and lysozyme [3,4] (Table 1).

Disease	Age/Gender	Clinical Presentation	Morphology	Immunohisto chemistry
Reticulohistiocytoma (solitary epithelioid histiocytoma)	Children, young adults/ male predominance	Solitary skin or soft tissue nodule, orbital, corneal and limbal involvement	Enlarged, mononuclear and multinucleated histiocytes, ground glass cytoplasm, admixed inflammatory cells	CD163+, CD68+, alpha-1 antitrypsin+
Langerhans cell histiocytosis	Children /no gender predilection	Miniature bony or multisystem disease, orbital involvement, lytic defects in the sphenoid	Histiocytes admixed with eosinophils, lymphocytes, plasma cells, neutrophils. Langerhans cells contain Birbeck granules.	S100+, CD1a+
Rosai- Dorfman Disease	Children, young adults/ male predominance	Skin lesions associated with bilateral, massive, painless, cervical lymphadenopathy, low grade fever, weight loss, leukocytosis	Histiocytes with polymorphism, pale, eosinophilic cytoplasm, emperipolesis	S100+, CD68+
Juvenile Xanthogranuloma	Children, young adults / male predominance	Dermal or subcutaneous mass	Touton-type histiocytic cells, numerous eosinophilic granulocytes	CD68+, Factor XIIIa+
Histiocytic Sarcoma	Middle aged/ no gender predisposition	Skin and soft tissue mass	Epithelioid histiocytes with nuclear atypia and mitotic activity	Lysozyme+, KiM8+, S100+,CD21+,CD35+
Erdheim-Chester Disease	Middle aged/ no gender predisposition	Systemic disease with ophthalmic involvement limited to exophthalmos secondary to retrobulbar infiltration and xanthelasma-like lesion on the eyelid.	Dense infiltrates of foamy histiocytes, lymphocytes, monocytes and Touton giant cells	CD68+, S100-, CD1a-

Table 1: Differential Diagnosis of Histiocytic Lesions [4].

Solitary reticulohistiocytoma appears as an isolated, painless, benign nodule appearing at diverse sites and lacks association with systemic symptoms. Cutaneous lesions of solitary reticulohistiocytoma appear at diverse sites such as the head and neck, upper or lower extremities and trunk. Facial lesions are infrequent. Additionally, exceptional lesions are discerned within the penis, orbit and eyelid. Solitary reticulohistiocytoma can occur within the ocular region, eyelid or epi-bulbar area. Solitary reticulohistiocytoma is un-associated with systemic disease or malignant metamorphosis [3,4].

Clinical Elucidation

The non-neoplastic, histiocytic proliferation emerges from macrophages, in contrast to dendritic histiocytic cells. Histiocytic proliferation is confined to cutaneous surfaces or soft tissues [4]. Solitary reticulohistiocytoma configures an isolated lesion appearing in the absence of systemic involvement. The condition predominantly occurs within the adult population and denominates a slight male predominance [4,5]. Common clinical representation is a painless, yellow or reddish-brown, cutaneous papule of

magnitude beneath < one centimetre which may gradually progress. Lesion can be asymptomatic and demonstrate an absence of associated symptoms such as pain, pruritus, ulceration or haemorrhage [4,5].

Histological Elucidation

Upon gross examination, fleshy, fibrotic, globular or nodular, tan coloured tissue of variable magnitude is observed [5]. On microscopy, diffuse infiltration of numerous enlarged, mononuclear or multinuclear histiocytic cells is exemplified, predominantly confined to the dermis. Diffuse histiocytic infiltration is admixed with lymphocytes and dermal fibrosis. Typically, histiocytic cells are incorporated with a dense, pink cytoplasm designated as "oncocytic" or "ground glass" cytoplasm [5,6]. Solitary reticulohistiocytoma is constituted by enlarged, mononuclear and multinucleated histiocytic cells incorporated with abundant, eosinophilic "ground glass" cytoplasm [5,6].

Morphological assessment demonstrates a monomorphic infiltrate of epithelioid histiocytic cells extending throughout the dermis. An infiltrate of lymphocytes is admixed with the histiocytic cells [5,6]. Lesions are constituted of mononuclear and multinucleated histiocytes imbued with abundant, finely granular, amphophilic cytoplasm with a characteristic "ground-glass" appearance [5,6]. Proliferating histiocytes are encompassed by an admixture of diverse inflammatory cells such as granulocytes and T lymphocytes although a population of B lymphocytes is absent [5,6].

Tumour mass is composed of numerous histiocytes incorporated with ground glass cytoplasm. Occasional giant cells are observed. Few histiocytes demonstrate vacuolated cytoplasm. Lymphocytic infiltrate is exceptionally discerned [5,6]. Lesions can depict a folliculo-centric pattern of vertical cellular expansion with an absence of alteration of superimposed stratified squamous epithelium with extension into the subcutaneous adipose tissue. Thus, trauma-induced lesions of solitary reticulohistiocytoma can demonstrate an atypical cellular growth pattern [5,6].

Immune Histochemical Elucidation

Reticulohistiocytoma is immune reactive to CD68, vimentin, alpha-1 antitrypsin and Factor XIIIa. Histiocytic cells are immune non-reactive to CD1a and S100 protein. Lymphocytes are immune reactive to CD3 [7,8].

Differential Diagnosis

Reticulohistiocytoma requires a segregation from diverse histiocytic disorders wherein cellular constituents are devoid of the characteristic "ground glass" cytoplasm. Segregation is mandated from conditions such as Rosai-Dorfman disease, Langerhans cell histiocytosis, juvenile xanthogranuloma, histiocytic sarcoma and Erdheim-Chester disease [7,8].

a) Juvenile xanthogranuloma is an uncommon inflammatory disorder predominantly occurring in children. Classically, lesions denominate Touton-type, histiocytic giant cells admixed with numerous eosinophilic histiocytic cells incorporated with lipid rich cytoplasm. Cells of juvenile xanthogranuloma are immune reactive to CD68 and Factor XIIIa although Birbeck's granules are absent [7,8].
b) Langerhans cell histiocytosis is a histiocytic disorder appearing in children and commonly represents as a lytic defect implicating the orbit or sphenoid bone. Histiocytes constituting Langerhans cell histiocytosis are imbued with Langerhans cell granules or Birbeck's granules which are discernible upon cogent ultrastructural examination. The cells are immune reactive to CD1a and S100 protein [8,9].
c) Rosai- Dorfman disease is additionally denominated as sinus histiocytosis with massive lymphadenopathy. The condition demonstrates multiple cutaneous nodules and generalized lymphadenopathy. Constituent histiocytic cells are non-Langerhans cells and are immune reactive to S100 protein [8,9].
d) Histiocytic sarcoma is an exceptional neoplasm composed of epithelioid histiocytes demonstrating significant cellular and nuclear atypia and mitotic activity. No site of disease emergence is exempt and virtually the entire body viscera and organs may be afflicted [9,10].
e) Erdheim-Chester disease is an exceptional variant of histiocytosis characteristically depicting incrimination of bone, heart, brain, pulmonary, hepatic and renal parenchyma. Occasionally, retro-bulbar infiltration can ensue with consequent proptosis or xanthelasma-like lesions confined to the eyelid [9,10].
f) Exceptional histocytic lesions can be segregated in concordance with clinical symptoms and extensive immunohistochemistry [10,11].

Additionally, clinical segregation from lesions demonstrating a solitary dermal papule such as pyogenic granuloma, haemangioma, dermatofibroma, basal cell carcinoma, amelanotic malignant melanoma, seborrheic keratosis or follicular cyst is necessitated [10,11].

Therapeutic Options

Treatment of lesions of solitary reticulohistiocytoma is usually inessential. Solitary lesions generally undergo spontaneous resolution within a duration of months. Comprehensive surgical resection of the lesions can be undertaken for adequate disease discernment or cosmetic

purposes. Localized lesion reoccurrence may ensue with inadequate excision of the lesion [10,11] (Figures 1-8).

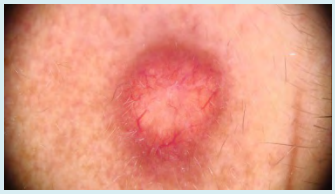

Figure 1: Reticulohistiocytoma delineating a solitary, haemorrhagic, well defined nodule with peripheral arborized vascular articulations [12].

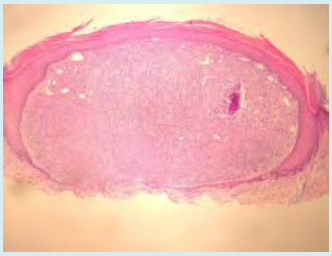

Figure 2: Reticulohistiocytoma depicting a solitary, reddish-brown dermal papule with an unaltered superimposed stratified squamous epithelial layer [13].

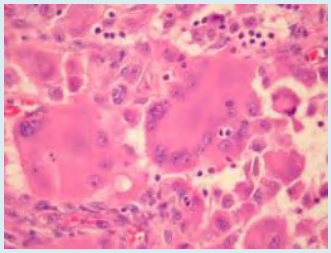

Figure 3: Reticulohistiocytoma demonstrating enlarged histiocytic cells with abundant eosinophilic cytoplasm and vesicular nuclei intermingled with multinucleated giant cells [14].

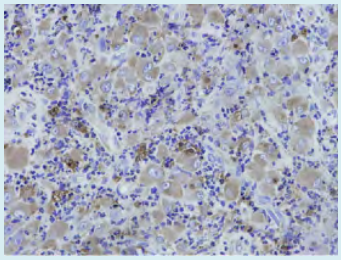

Figure 4: Reticulohistiocytoma exemplifying enlarged histiocytic cells imbued with abundant, eosinophilic cytoplasm and an encompassing fibrotic stroma [15].

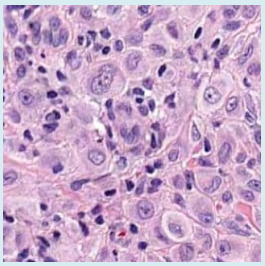

Figure 5: Reticulohistiocytoma delineating scattered histiocytic cells with abundant eosinophilic cytoplasm and vesicular nuclei admixed with patchy lymphocytes [16].

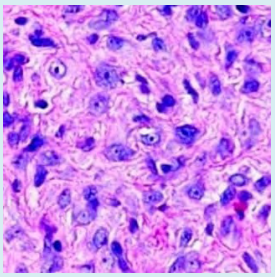

Figure 6: Reticulohistiocytoma depicting disseminated histiocytic cells with abundant cytoplasm, vesicular nuclei and prominent nucleoli intermingled with a scant lymphocytic infiltrate [17].

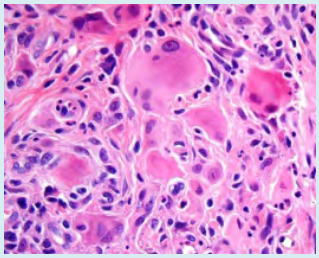

Figure 7: Reticulohistiocytoma composed of enlarged histiocytes with abundant, eosinophilic cytoplasm, uniform nuclei and an admixture of inflammatory cells as lymphocytes [18].

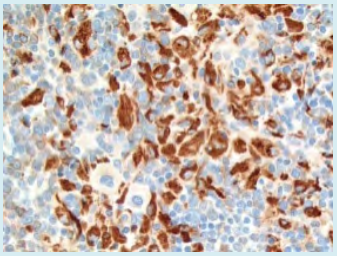

Figure 8: Reticulohistiocytoma immune reactive to CD68 [18].

Conclusion

Solitary reticulohistiocytoma is an exceptional, benign, non-neoplastic, non –Langerhans histiocytic cell proliferation which is immune reactive to CD68, vimentin, alpha-1 antitrypsin and Factor XIIIa. Solitary reticulohistiocytoma requires a segregation from conditions such as Rosai-Dorfman disease, Langerhans cell histiocytosis, juvenile xanthogranuloma, histiocytic sarcoma and Erdheim-Chester disease. Clinical demarcation from appearing as a solitary dermal papule such as pyogenic granuloma, haemangioma, dermatofibroma, basal cell carcinoma, amelanotic malignant melanoma, seborrheic keratosis or follicular cyst is also mandated. Solitary lesions generally undergo spontaneous resolution within a duration of months and surgery may be adopted for cosmetic purposes.

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12. Image 1 Courtesy: JAAD.com

13. Image 2 Courtesy: Dermnet NZ.

14. Image 3 Courtesy: Allied Academies.

15. Image 4 Courtesy: Semantic Scholar.

16. Image 5 Courtesy: You tube.

17. Image 6 Courtesy: Dr Sarma's Path Lab.

18. Image 7 and 8 Courtesy: Pathology Outlines.