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The Benignant Lymphatic-Acquired Progressive Lymphangioma

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Mini Review

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Abstract

Benign lymphangioendothelioma is an extremely exceptional lymphatic, vascular proliferation which morphologically recapitulates adjunctive malignant, vascular neoplasms. The complex, vascular hamartoma is comprised of three distinctive components denominated as lymphatic vessels, blood vessels and smooth muscle. Essentially a vascular lesion of lymphatic origin, the condition demonstrates focal, benign proliferation of lymphatic vessels accompanied by localized soft tissue infiltration. The disorder was initially scripted by Wilson Jones in 1964 and is additionally designated as "acquired progressive lymphangioma" or benign lymphoendothelioma. The uncommon, benign, vascular proliferation layered with endothelial cells immune reactive to D2-40 can simulate well differentiated angiosarcoma or patch stage Kaposi's sarcoma. Appropriate characterization of the neoplasm is challenging and the condition can be misinterpreted as cutaneous low grade angiosarcoma.

Keywords: Neoplasm; Lymphangioma; Benign lymphangioendothelioma

Mini Review

Disease Characteristics

Disease Characteristics of obscure aetiology and pathogenesis, the condition may be associated with predisposing factors such as trauma, surgery, radiation therapy, femoral arteriography, tick bites or hormonal stimulation. Alternatively, a preceding history of trauma or drug ingestion may be absent. Chronic lymphedema following mastectomy is exceptionally associated with or contemplated as a predisposing factor for occurrence of benign lymphangioendothelioma [1,2]. Benign lymphangioendothelioma may be contemplated as a lymphatic vascular malformation instead of a true neoplasm on account of absence of Wilm's tumour 1(WT-1) immune reactivity. The neoplasm commonly appears within middle aged or elderly individuals between 17 years to 90 years with an average age of disease emergence at 43 years. Children are rarely implicated. Lesions gradually progress over a duration of several years. Lesions are unrelated to associated vascular anomalies or infection with immune deficiency virus (HIV).

A specific gender predilection is absent [2,3]. Commonly, the lower extremity, head and neck, wrist, shoulder, upper extremity, trunk, mucosal surface, breast, arm, face, scalp or thigh is incriminated although no site of disease emergence is exempt. Prognostic outcomes are excellent. Localized tumour reoccurrence is exceptional [2,3].

Clinical Elucidation

Benignlymphangioendotheliomaisusuallyasymptomatic although the lesion can manifest pain, pruritus or a stinging sensation. Typically, a solitary, well circumscribed, reddish, bruise- like macule, nodule or a gradually progressive, brownish, erythematous patch or plaque is denominated. The lesion is manifested within a median duration of 5.5 years. Lesions of benign lymphangioendothelioma may simulate actinic keratosis [3,4].

Occasionally, the condition can represent as multiple nodular and/or papular lesions. Synchronous and metachronous lesions can appear. The disorder can emerge as an elevated, symptomatic, bluish, gradually enhancing,

cutaneous lesion or a spot situated upon disease specific sites. An overt history of extraneous haemorrhage or oozing is absent [4]. The lesion can manifest as a poorly- defined, non tender, soft, bluish, elliptical plaque of varying magnitude situated within diverse sites of disease representation. Few dark blue or reddish papules can emerge. Pertinent lesions are associated with focal, superficial or extraneous crusting. Adjacent cutaneous surfaces, hair, nail or mucosae are devoid of associated lesions [3,4].

Histological Elucidation

Lesions range from 0.3 centimetres to 10 centimetres in magnitude with a median diameter of 1.5 centimetres. The neoplasm is comprised of proliferation of dilated vascular channels situated within the dermis or subcutaneous tissue. Superficial vascular spaces are widely distended whereas deep-seated vascular channels are elongated and tapered. Papillary projections layered with endothelial cells are accompanied by mild fibrosis. Endothelial cells may be mildly hyperchromatic although significant atypia is absent [4,5]. Characteristically, lesions display irregular, tortuous, anastomosing lymphatic channels layered with endothelium depicting "hobnail" morphology. Vascular channels intersect between collagen bundles of the dermis as deep-seated dermis is permeated, recapitulating infiltrative features of malignant neoplasms [4,5].

Benign lymphangioendothelioma classically demonstrates thin walled, interconnected lymphatic channels along with distended lymphatic spaces confined to the upper dermis and miniature, irregular lymphatic articulations discerned within the lower dermis. Endothelium coated lymphatic configurations are interspersed between strands of collagen-rich matrix [4,5].

Dermal aggregates of vascular channels demonstrating an invasive growth pattern wherein vascular channels are devoid of red blood cells are indicative of benign lymphangioendothelioma [5]. The normo-cellular neoplasm is devoid of poorly differentiated areas although endothelial cells layering the lymphatic channels depict mild cellular atypia along with absence of significant nuclear pleomorphism or mitotic activity [4,5]. The lesion is associated with compact hyperkeratosis and irregular acanthosis. Distended, thin- walled, lymphatic spaces are intermittently layered with flattened endothelial cells and recapitulate lymphatic channels denominated within upper and mid dermis. Additional slit- like vascular channels are situated within the deeper dermis along with distended vascular articulations impacted with red blood cells [4,5].

Lymphatic channels coated with delicate, thin walled endothelium are accumulated within the superficial dermis. Intravascular papillary projections of stromal tissue are discerned which resemble papillary endothelial hyperplasia. Deep-seated lymphatic channels appear collapsed and dissect fascicles of collagenous stroma, akin to patch stage Kaposi's sarcoma [4,5]. Pre-existing vascular channels and cutaneous adnexal structures within the dermis appear intersected by nascent lymphatic channels. Focal dissemination of smooth muscle fibres surrounding vascular spaces is observed. Endothelial cells depict a "hobnail" appearance with configuration of a "morula" akin to giant cells. Endothelial cells appear crowded and aggregated. However, endothelial cell atypia is absent. Lympho-vascular spaces are devoid of erythrocytes and hemosiderin pigment deposits. Cellular or nuclear atypia and mitotic figures are absent [4,5]. Lesions can also manifest endothelium- layered continuous lymphatic spaces, impacted with hemosiderin, abutting eosinophilic aggregates which are confined to the upper dermis. An accompanying inflammatory infiltrate is absent. Hemosiderin pigment is disseminated within disorganized, dermal collagen fibres [4,5].

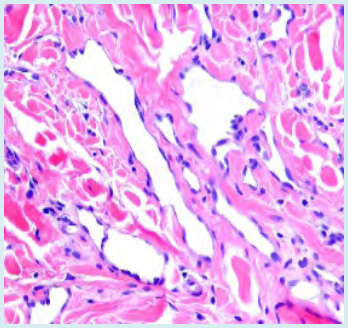

Figure 1: Benign lymphangioendothelioma demonstrating irregular, dilated lymphatic channels layered with "hobnail" endothelium and a circumscribing collagenous stroma [9].

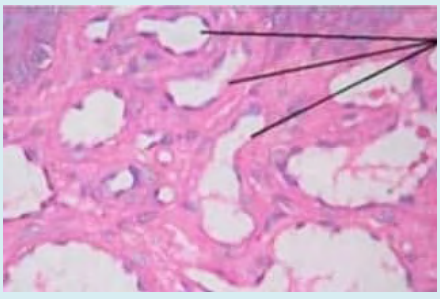

Figure 2: Benign lymphangioendothelioma delineating irregular lymphatic channels layered with plump endothelial cells surrounded by a collagenous stroma [10].

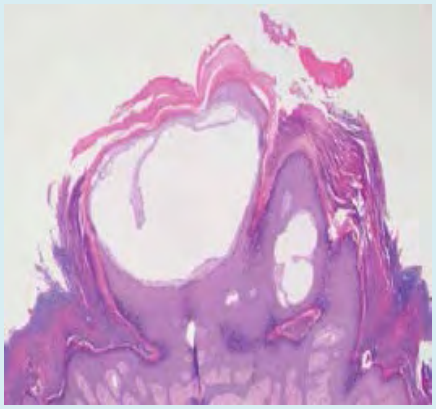

Figure 3: Benign lymphangioendothelioma exhibiting irregular lymphatic channels lined with plump endothelium, enveloping collagenous stroma and a superimposed hyperkeratotic, acanthotic stratified squamous epithelium [11].

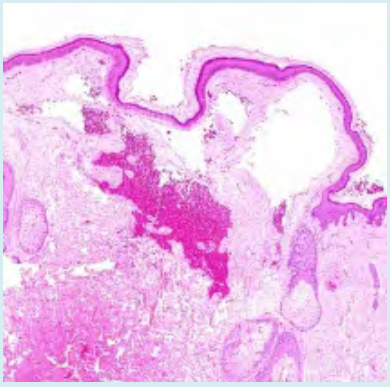

Figure 4: Benign lymphangioendothelioma depicting irregular lymphatic channels accumulated within dermal tissue with a coating of "hobnail" endothelium and a superimposed hyperkeratotic epidermis [12].

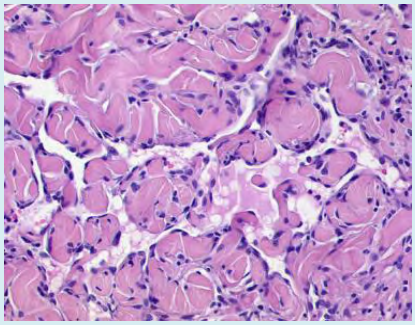

Figure 5: Benign lymphangioendothelioma enunciating irregular lymphatic spaces layered with "hobnail" endothelium and an encompassing fibro-collagenous stroma [13].

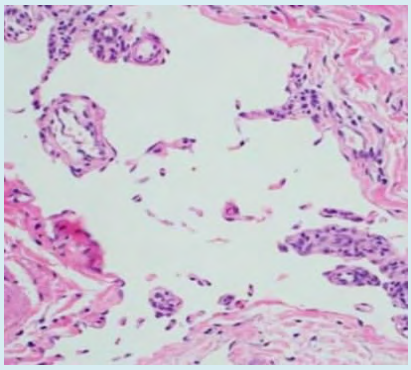

Figure 6: Benign lymphangioendothelioma exemplifying enlarged, irregular lymphatic spaces layered with plump endothelium enmeshed within a collagen-rich stroma [14].

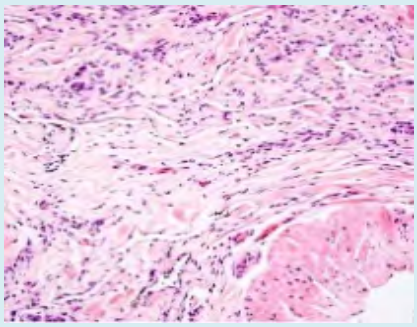

Figure 7: Benign lymphangioendothelioma exhibiting irregular lymphatic spaces coated with plump endothelial cells and a circumscribing collagenous stroma [15].

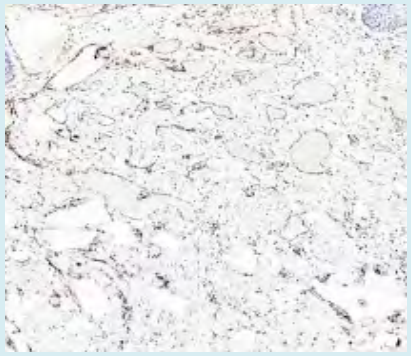

Figure 8: Benign lymphangioendothelioma demonstrating immune reactive CD31 [15].

Immune Histochemical Elucidation

Benign lymphangioendothelioma is intensely immune reactive to pertinent lymphatic marker denominated as lymphatic vessel endothelial receptor 1 (LYVE-1) which permits segregation from adjunctive malignant, vascular tumours [2,3]. Endothelial cells are immune reactive to

specific markers of lymphatic vessels such as podoplanin (D2-40), smooth muscle actin (SMA) or lymphatic vessel endothelial receptor 1 (LYVE-1) and variably immune reactive to Factor VIII, Ulex europaeus -I lectin, CD31 and CD34. Lesions are immune non-reactive to human herpes virus 8 (HHV8) [5,6].

Differential Diagnosis

Benign lymphangioendothelioma necessitates a demarcation from low grade angiosarcoma as the neoplasms demonstrate an extensive dissection of collagen bundles. Low grade angiosarcoma can appear following mastectomy and is associated with chronic lymphedema, designated as Stewart- Treves syndrome. Tumefaction appears as reddish-blue, firm, nodule, plaque, haemorrhagic blister or ulcer and is commonly associated with lymphedema, usually following in excess of a period of ten years [5,6]. Average duration of progression to angiosarcoma subsequent to radical mastectomy is around 12.5 years [3]. Well differentiated, low grade angiosarcoma is observed in elderly subjects as reddish- blue plaques or nodules. Endothelial atypia is significant along with multi-layering and configuration of micro-papillary tufts. Epithelioid or spindle-shaped endothelial cells can be exemplified. Inflammatory infiltrate is frequently intermingled within the lesions [5,6].

Localized tumour infiltration or distant metastasis is absent following surgical resection, immunotherapy or adjuvant chemo-radiotherapy. Besides the discernment of innumerable mitotic figures, significant cellular and nuclear atypia, extensive infiltration of inflammatory cells and red cell extravasation along with immune staining for MIB-1 labelling index is an advantageous adjunctive tool to segregate benign lymphangioendothelioma from low-grade angiosarcoma [5,6]. Benign lymphangioendothelioma requires a clinical or histological segregation from diverse vascular proliferations such as patch-stage Kaposi's sarcoma, retiform haemagioendothelioma, lymphangioma circumscriptum, cutaneous lymphangiomatous papule or targetoid haemosiderotic haemagioma [5,6].

Kaposi's sarcoma is observed in subjects infected with human immune deficiency virus (HIV). Kaposi's sarcoma demonstrates cellular and nuclear atypia, prominent mitotic activity, extensive infiltration of inflammatory cells and red cell extravasation. The neoplasm is immune reactive to human herpes virus 8 (HHV-8) [5,6]. Patch stage of Kaposi's sarcoma is accompanied by multiple, disseminated lesions usually discerned in individuals infected with human immune deficiency virus (HIV) or as extensive lesions emerging within lower extremities in elderly Jewish or Mediterranean subjects [6]. Commonly, a lymphoplasmacytic infiltrate is discerned along with accumulation of inflammatory cells surrounding vascular articulations. Red cell extravasation is frequent. Associated categories of Kaposi's sarcoma are observed [5,6]. retiform haemangioendothelioma and Kaposi's sarcoma are conditions with concomitant lymphoplasmacytic or lymphocytic infiltrate disseminated within the dermal interstitial tissue [5,6]. lymphangioma circumscriptum or lymphangiomatous papules are disorders with benign proliferation of lymphatic vessels which are minimally associated with features of "hobnail" endothelial morphology and/or anastomosing or papillary articulations [5,6]. lymphangioma is predominantly composed of numerous distended and uniform lymphatic vessels [6]. targetoid haemosiderotic haemangioma manifests as a centric, violaceous papule with circumscribing foci of pallor and ecchymosis. The lesion exhibits vascular channels layered by plump or hobnail endothelial cells admixed with a variable inflammatory infiltrate along with red cell extravasation and deposition of hemosiderin pigment circumscribing vascular articulations. Ancient lesions demonstrate anastomosing, collapsed, thin- walled vascular channels with focal deposition of hemosiderin pigment [7,8]. atypical or benign vascular proliferations of breast tissue are usually accompanied by history of radiation therapy [7,8].

Investigative Assay

Evaluation of miniature tissue samples can result in misinterpretation of the lesion as a malignant, angiosarcoma-like tumefaction. A cogent histological evaluation is crucial in obtaining precise discernment of disease [7].

Therapeutic Options

The vascular malformation can be subjected to comprehensive or localized surgical excision. Comprehensive surgical extermination of the lesion is an optimal treatment strategy. The benign condition is accompanied by occasional localized reoccurrence [7,8].

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9. Image 1 Courtesy: Dermamin.com

10. Image 2 Courtesy: Europe PMC

11. Image 3 Courtesy: SciELO.com

12. Image 4 Courtesy: Basic medical key

13. Image 5 Courtesy: Medscape

14. Image 6 Courtesy: Wiley online library

15. Image 7 and 8 Courtesy: Pathology outlines