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The Enclosed Leviathan- Pleomorphic Fibroma

Dr Anubha Bajaj*

Consultant Histopathologist, A. B. Diagnostics, A-1, Ring Road, Rajouri Garden, New Delhi, India.

***Corresponding Author**: Dr Anubha Bajaj, Consultant Histopathologist, A. B. Diagnostics, A-1, Ring Road, Rajouri Garden, New Delhi, India.

Preface

Cutaneous pleomorphic fibroma was initially described by Kamino et al in 1989 as a dermal, pauci-cellular neoplasm with an abundant fibrous tissue stroma, atypical fibro-histiocytic cells and disseminated multinucleated giant cells(1). Pleomorphic fibroma is an exceptional, benign, polypoid ordome shaped, sparsely cellular, cutaneous fibroblastic neoplasm characteristically delineating aberrant, pleomorphic, hyperchromatic and giant multinucleated cells embedded in a collagenous stroma (2). Pleomorphic fibroma is contemplated to originate from dendrocytes, in contrast to myofibroblasts. The exceptional neoplasm can simulate adjunctive fibro-histiocytic, melanocytic or lipomatous neoplasia. Despite cellular and nuclear atypia accompanying pleomorphic, bizarre cells, the neoplasm is contemplated as architecturally and biologically benign, on account of exceptional or absent mitosis(2). Pleomorphic fibroma may be interlinked with sclerotic fibroma. Martin-Lopez defined the terminology "pleomorphic sclerotic fibroma" which posits pleomorphic fibroma, sclerotic fibroma and pleomorphic sclerotic fibroma as neoplasia representing a morphologic continuum (3).

Disease Characteristics

As an exceptional, fibro-histiocytic neoplasm, pleomorphic fibroma commonly arises upon the trunk and proximal extremities. Infrequently, the tumefaction can arise upon sites such as head and neck, scalp, tendon sheath, subungual space, forehead, retro-auricular area, eyelid or nose. Typically, pleomorphic fibroma occurs in middle aged to older adults with a peak emergence within the fifth decade of life. A specific gender predilection is absent (2,4).

Pleomorphic fibroma is associated with benign biological behaviour in spite of extensive cellular pleomorphism (2).

Of obscure pathogenesis, pleomorphic fibroma is contemplated as a neoplasm of fibroblastic or myofibroblastic origin on account of immune reactivity to vimentin and actin along with abundance of collagenous stroma. Certain instances are immune reactive to Factor XIIIa and CD34 due to the presence of reactive dermal dendrocytes, a theory favouring a dermal dendritic cell origin. Immune non reactivity to S100 protein eliminates the possibility of melanocytic or neural tumour genesis (4).

Distinct variants are described, contingent to denomination of predominant intervening stroma, as sclerotic and myxoid pleomorphic fibroma (4).

Cutaneous pleomorphic fibroma is a variant of sclerotic fibroma, thus can be designated as pleomorphic sclerotic fibroma.

Myxofibrosarcoma can arise from myxoid pleomorphic fibroma. The metamorphoses can be a true malignant metamorphoses or an incidental alteration although the fact remains undecided (4,5).

Clinical Elucidation

Pleomorphic fibroma is predominantly situated within the dermis and the polypoid, sparsely cellular neoplasm is configured with coarse bundles of collagen. Marked cellular atypia and pleomorphism in the absence of mitosis is a characteristic feature of the neoplasm.

Concurrent absence of necrosis and mitosis demarcates the tumour from malignant neoplasia (4,5).

The tumefaction represents as a superficial, painless, gradually evolving, enlarged, pedunculated, polypoid, indurated, flesh coloured soft tissue lesion. The neoplasm can manifest as a dome shaped papule, nodule or an asymptomatic neoplasm of variable magnitude, commonly between 4 millimetres to 40 millimetres. The neoplasm can clinically simulate a nevus or neural tumour or skin tag or acrochordon with cytological atypia(4,5).

Histological Elucidation

Grossly, a well circumscribed, solid, dome shaped nodule with greyish/ white, fibrotic cut surface is denominated. The tumefaction is variably cellular, resembles a fibro-epithelial polyp and denominates spindle- shaped cells with striking nuclear pleomorphism and atypia. The sparsely cellular neoplasm is configured of pleomorphic cells admixed with dense, haphazardly scattered collagen bundles. Pleomorphic tumour cells are fusiform with enlarged, hyperchromatic, bizarre and smudged nuclei. Few multinucleated tumour giant cells are observed (5,6).

On fine needle aspiration cytology, cellular aggregates are intermixed with metachromatic stromal fragments comprised of collagen bundles. Pleomorphic tumours cells are singly dispersed or configure clusters and incorporate enlarged nuclei (monster cells) with scanty cytoplasm or tumour cells may be stripped of cytoplasm. Few nuclei display a singular nucleolus. Nuclear membrane is undulating and frequently depicts notches, creases and folds. Pleomorphic tumour cells are admixed with spindle-shaped cells and multinucleated giant cells. Foci of necrosis or mitosis are absent or scarce (5,6).

A dermal, pauci-cellular neoplasm with an abundant, fibrous tissue stroma is observed which is composed of atypical, fibro-histiocytic cells and few disseminated multinucleated giant cells. Occasional, aberrant mitosis, attributed to degenerative alterations, can be discerned. Mononuclear cells with atypical nuclear features can concur with multinucleated tumour giant cells. Cellular degeneration, ischemia or paracrine influence of entangled mast cells can generate the cytological atypia characteristic of pleomorphic fibroma (5,6).

A well circumscribed, pedunculated neoplasm with superimposed stratified squamous epithelial layer can be delineated. Papillary and reticular dermis display a hypo-cellular tumefaction with haphazardly dispersed, thick collagen bundles intermixed with partially detached stroma and dilated vascular articulations. Tumour cells are spindle-shaped or irregular with scanty cytoplasm and indistinct cytoplasmic outline. Floret- like, giant multinucleated cells are intermingled with the cellular component. Cellular nuclei are significantly atypical, enlarged, pleomorphic and hyperchromatic. Foci of tumour sclerosis or myxoid foci may be discerned (5,6).

Discernible nuclear atypia simulates degenerative alterations demonstrated in several benign mesenchymal neoplasms. Variants of pleomorphic fibroma with a myxoidstroma can be delineated (6).

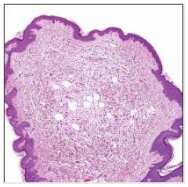

Figure1. Pleomorphic fibroma enunciating accumulation of plump, atypical fibroblasts with hyperchromatic nuclei and a superimposed stratified squamous epithelium (10).

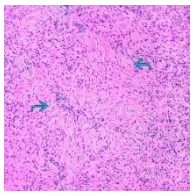

Figure2. Pleomorphic fibroma exhibiting aggregates of plump, atypical fibroblasts enveloped in a fibrotic stroma and an absence of mitosis (11).

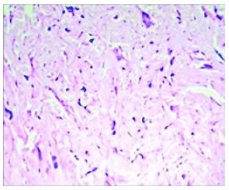

Figure3. Pleomorphic fibroma with dispersed plump fibroblasts displaying nuclear atypia, hyperchromasia and pleomorphism with a lack of mitosis, embedded in a collagenous stroma (12).

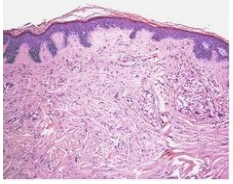

Figure4. Pleomorphic fibroma depicting dispersed plump fibroblastic cells with nuclear atypia and pleomorphism, encompassing fibrous tissue stroma and a superficial lining of stratified squamous epithelium(13).

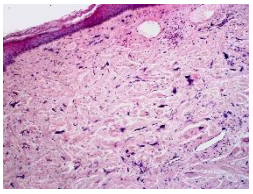

Figure5. Pleomorphic fibroma delineating aggregates of plump, pleomorphic, fibroblastic cells with nuclear atypia and lack of mitosis, a circumscription of fibrotic stroma and a superimposed layer of stratified squamous epithelium(14).

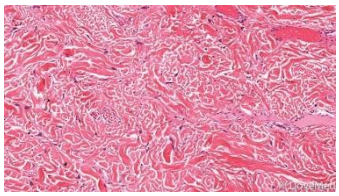

Figure6. Pleomorphic fibroma demonstrating atypical, pleomorphic fibroblastic cells intermixed within a collagenous stroma and absent mitosis(15).

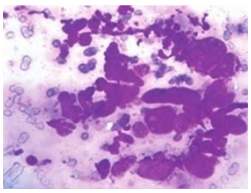

Figure7. Pleomorphic fibroma on fine needle aspiration cytology depicting clusters of enlarged, pleomorphic cells entangled with fibro-connective tissue stroma(16).

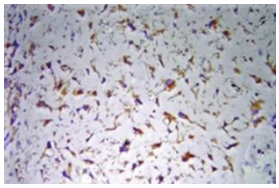

Figure8. Pleomorphic fibroma immune reactive tovimentin (16).

Immune Histochemical Elucidation

Tumour cells are diffusely immune reactive to vimentin, CD34, smooth muscle actin (SMA) and CD68. Occasional immune reactivity to muscle specific actin (MSA) is discerned. Cells are immune non reactive to desmin, S100 protein, cytokeratin, CD10, CD31, α1- anti-chymotrypsin, α1-antitrypsin and Factor XIIIa. Proliferation index Ki-67 is usually beneath <5%. Immune reactivity to CD68 and Factor XIIIa can be absent, moderate or patchy (2,4).

Differential Diagnosis

Pleomorphic fibroma necessitates a demarcation from diverse fibro-histiocytic and melanocytic neoplasms demonstrating cellular pleomorphism and significant cellular atypia such as dermatofibroma with monster cells (DFMC) and atypical fibroxanthoma (AFX) (6).

Atypical fibroxanthoma (AFX) and pleomorphic dermal sarcoma are neoplasms which generally exhibit enhanced cellularity and pleomorphism with frequent mitosis and often demonstrate xanthomatous cells. Atypical fibroxanthoma is a cellular neoplasm with an excess of mitotic figures. Atypical fibroxanthoma manifests as a rapidly progressive lesion of enhanced cellularity. The neoplasm is composed of pleomorphic or spindle- shaped cells along with numerous mitotic figures, a few of which may be atypical (6, 7).

Anomalous variations of dermatofibroma such as dermatofibroma with atypical or monster cells (DFMC) characteristically demonstrate epithelial hyperplasia, a hyper-cellular stroma along with foam cells and hemosiderin- laden macrophages. Aforesaid macrophages are occasionally immune reactive to CD68 although the neoplasm is immune non reactive to CD34, in contrast to pleomorphic fibroma (6,7).

Cytological distinction of cutaneous pleomorphic fibroma is necessitated from atypicalfibroxanthoma, dermatofibroma with monster cells, giant cell fibroblastoma, desmoplastic Spitz nevus and desmoplastic melanoma. Pleomorphic fibroma can be misinterpreted as a malignant soft tissue neoplasm upon fine needle aspiration cytology on account of constituent bizarre, pleomorphic cells with significant atypia (7,8).

The cellular atypical fibrous histiocytoma or dermatofibroma with atypical or monster cells (DFMC) is a cellular neoplasm with a storiform tumour configuration and displays typical histological foci of dermatofibromaalong with foam cells and hemosiderin- laden macrophages and are immune non reactive to CD34. In contrast, pleomorphic fibroma delineates bundles of collagen and is immune reactive to CD34, thus eliminating atypical fibroxanthoma and dermatofibroma with atypical or monster cells (7,8).

Giant cell fibroblastoma is a paediatric neoplasm typically associated with localized tumour infiltration and manifests sinusoidal articulations. Characteristically, pseudo-vascular spaces layered by aberrant multinucleated cells, immune reactive to CD34, are discerned whereas adult lesions are devoid of invasive tumour growth and sinusoidal configurations (8,9).

Spitz nevus, desmoplastic melanoma and atypical variants of neural tumours demonstrate milder cellular pleomorphism and are immune reactive to S100 protein (8).

Desmoplastic Spitz nevus and desmoplastic melanoma exhibit focal areas of melanocytic differentiation wherein tumour cells are immune reactive to S100 protein(8). Benign nerve sheath tumours with atypical features such as neurofibroma with atypical features or schwannoma with ancient change necessitate a demarcation. Benign nerve sheath tumours are immune reactive to S100 protein. Atypical cellular modifications can be degenerative and probably arise secondary to ischemia (8,9).

Angiofibroma is a predominantly vascular neoplasm which demonstrates pleomorphic cells identical to pleomorphic fibroma (8,9).

Atypical cutaneouslipomatous neoplasm mandates a segregation on account of prominent adipose tissue component or in instances where pleomorphic fibroma exhibits entrapped adipose tissue cells. Cogent immune reactivity and fluorescent in situ hybridization (FISH) assay to discern enhanced expression of mouse double minute 2homolog (MDM2) within atypical lipomatous tumours can be adopted. The neoplasm incorporates chromosomal rearrangement 12q 15(8,9).

Nevertheless, fluorescent in situ hybridization (FISH) is contemplated as a specific, pertinent diagnostic modality (9). Associated adipose tissue neoplasms, immune reactive to S100 protein require segregation. Sclerotic lipoma, a variant of lipoma demonstrates adipocytes interspersed within a whorled, fibrotic stroma. Dermal pleomorphic liposarcoma is an exceptional, high grade variant of liposarcoma which typically enunciates pleomorphic lipoblasts(8,9).

Pleomorphic lipoma is a benign entity which simulates pleomorphic fibroma with an immune non reactive and absent expression of retinoblastoma1 (Rb1) molecule upon fluorescent in situ hybridization (FISH). Thus, pleomorphic fibroma may be posited as a variant of pleomorphic lipoma(8,9).

Pleomorphic fibroma mandates a demarcation from soft fibroma, intradermal nevus, neurofibroma and cutaneous appendageal tumours. In contrast to aforementioned neoplasms, pleomorphic fibroma demonstrates cellularity with atypical cells, pleomorphic, hyperchromatic nuclei and exceptional mitotic figures (8,9).

Cogent evaluation of clinical representation, histological features and immune reactivity of pleomorphic fibroma is necessitated in order to circumvent potential misinterpretation as a benign soft fibroma or skin appendageal tumour or a neoplasm with atypical cellular articulations such as dermatofibroma with monster cells (DFMC) or atypical fibroxanthoma (AFX), conditions which can be therapeutically alleviated with a comprehensive surgical extermination(8,9).

Therapeutic Options

Comprehensive surgical extermination of the neoplasm is recommended and usually curative. Although uncommon, shave biopsy and electrodessication can be accompanied by localized tumour reoccurrence, a feature which usually follows incomplete surgical extermination of the neoplasm. Extended monitoring is necessitated (8,9).

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[10] Image 2 Courtesy: Basic Medical Key

[11] Image 3 Courtesy: Research Gate

[12] Image 4 Courtesy: Plastic Surgery Key

[13] Image 5 Courtesy: Wikipedia

[14] Image 6 Courtesy:Dovemed.com

[15] Image 7 and 8Courtesy:J Cytol.com

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