

Testable fibrous and fibrohistiocytic proliferations of the skin: Facts and buzzwords

by Mohammed Shanshal, MD

Angiofibromas	Small, red to skin-colored papules, variants include: ■ Fibrous papule: solitary domed papule; nose/face of adults; mimics BCC ■ Pearly penile papules: multilayered and circumferential manner on the corona of glans penis in up to 30% of young adults. ■ Mutiple Facial angiofibromas: a/w various syndromes→ TS, MEN 1, Birt-Hogg-Dubé syndrome, and NF2 ■ Histology→collagen oriented concentrically around follicles or oriented more perpendicular to the epidermis with few dilated blood vessels
Dermatofibroma (DF, benign fibrous histiocytoma)	■ Firm dermal papules w/ overlying pigmentation and “dimple” sign (moves downward when pinched) ■ F > M; most commonly on lower extremities ■ Eruptive dermatofibromas→SLE, atopic dermatitis, HIV infection. ■ Factor 13a positive, Stromelysin-3 positive, CD34 = positive at the periphery while the center is usually negative (vs DFSP = homogeneously positive) ■ Dermal nodular proliferation of spindled fibroblasts with collagen trapping at the periphery. Can have multinucleated giant cells or Touton giant cells. ■ Testable DF variants: ○ Cellular DF→ most common type to be confused w/ DFSP ○ Hemosiderotic→prominent hemosiderin and small blood vessels ○ Lipidized/xanthomatous→ prominent foam cells ○ Aneurysmal dermatofibroma (sclerosing hemangioma)→dilated B.V, worrisome for melanoma or angiosarcoma ○ DF with “monster” cells→ large, bizarre, and highly pleomorphic cells but still has benign behavior!
Dermatofibrosarcoma protuberans (DFSP)	■ Multinodular, firm plaque on the trunk (50–60%), proximal extremities (20–30%) ■ t(17;22) → COL1A1-PDGFB fusion protein ■ CD34 strongly positive, factor XIIIa-negative ■ Storiform spindle cells with characteristic multilayered or “honeycomb” infiltration of fat ■ Can see accelerated growth during pregnancy and multiple DFSPs in children with adenosine deaminase-deficient SCID. ■ Mohs micrographic surgery→ the standard treatment ■ Imatinib (targets the PDGF receptor)→ FDA-approved for unresectable, recurrent, and/or metastatic DFSP ■ Subtypes of DFSP: ■ Bednar tumor ○ The pigmented variant of DFSP, Less than 5% of DFSPs ■ Giant cell fibroblastoma ○ Pediatric variant of DFSP according to the WHO classification ○ Boys >> girls; favors head/ neck ○ Histologically resembles DFSP, but has distinctive multinucleated giant cells lining vascular-like spaces
Fibrosarcomatous changes of DFSP	■ Compared to the classical DFSP, it is associated with: ○ ↑ recurrence rate ○ ↑ metastasis to the lung ○ ↓ CD34 staining (weak or lost) ○ ↑ cellularity ○ ↑ mitoses ○ ↑ atypia intersecting fascicles in herringbone pattern



Mohammed Shanshal, MD, is a specialist dermatologist at Baghdad Teaching Hospital, department of dermatology and venereology.

Testable fibrous and fibrohistiocytic proliferations of the skin: Facts and buzzwords

by Mohammed Shanshal, MD

Dermatomyofibroma	■ Young adults; F > M; solitary, well-circumscribed oval plaque resembling plaque type DFSP or DF; most commonly on upper trunk/neck ■ SMA+ (tram-track); CD34 negative (vs DFSP), factor 13a negative (vs DF), and desmin negative (vs pilar leiomyoma) ■ Histology→well-defined, long fascicles of spindle cells with east-west orientation (parallel to the skin surface), corkscrew (wavy) appearance of some myofibroblast nuclei. The adnexal structures are spared.
Atypical fibroxanthoma (AFX is considered superficial variant of undifferentiated pleomorphic sarcoma)	■ Rapidly growing/ ulcerated red nodule occurs in elderly (70–80 years old) ■ Chronically sun-damaged skin —head and neck #1 ■ Non-specific immunohistochemistry→stain positive for vimentin, CD68, CD99, procollagen-1 and strongly positive for CD10 ■ Histology→composed of both atypical spindle-shaped cells and overtly malignant large atypical cells with abundant pale- staining vacuolated cytoplasm, AFX never extensively infiltrates SQ fat (vs UPS) ■ Treatment: Mohs > WLE ○ Patients should be followed as local recurrence rate of 25– 30% and a metastatic rate of 10%
Undifferentiated pleomorphic sarcoma (UPS)	■ The most common soft tissue sarcoma of middle and late adulthood, thigh or buttock are #1 site ■ The pathologic features are similar to AFX but have deep subcutaneous invasion, necrosis, and/or lymphovascular or perineural invasion, pleomorphic cellular elements and bizarre mitotic figures are characteristic ■ The prognosis is related to the site; deeper and more proximally located tumors have a poorer prognosis
Fibromatosis	■ Superficial fascial fibromatosis: ○ Dupuytren disease=palmar fibromatosis→ flexion contractures especially of the fourth and fifth fingers ○ Ledderhose disease= plantar fibromatosis→ associated with trisomies 8 and 14 ○ Peyronie disease= penile fibromatosis→ penile bending deformity associated with pain and erectile dysfunction ○ knuckle pads (holoderma)→ extensor surfaces of the IP + MCP joints, Bart-Pumphrey syndrome (knuckle pads+ PPK+ hearing loss+ leukonychia) ○ Pachydermodactyly→ soft tissue swelling of the lateral aspects of the PIP joints of 2nd-4th fingers ■ Deep musculoaponeurotic fibromatosis: ○ Desmoid tumor → deep /aggressive fibromatosis seen in abdominal wall, may be associated with Gardner's syndrome, have β-catenin mutations, and stain β-catenin+ ■ Histology→all forms demonstrate corkscrew-shaped myofibroblasts and collagen. Ledderhose disease tends to form large whorled nodules.
Sclerotic fibroma	■ Very collagenous variant of fibroma→firm/pearly papule or nodule ■ May be a marker for Cowden's syndrome and also reported in MEN2A ■ Histology→sclerotic collagen bundles arranged as intersecting stacks ("plywood" pattern, whorl-like or Starry night pattern), very few CD34+ and factor XIIIa+ fibroblasts (hypocellular)
Infantile Myofibromatosis	■ Most common form of fibromatosis in children ■ Multiple skin-colored to purple, dermal or subcutaneous nodules in the head and neck or trunk ■ Can involve the skeletal muscle and/or internal organs. Visceral involvement associated w/ high mortality ■ Histology→Biphasic proliferation: ○ Hypocellular areas w/ fascicles of bland corkscrew myofibroblasts ○ Hypercellular areas and ectatic staghorn ("hemangiopericytoma-like") vessels ■ Stains confirm myofibroblastic derivation (SMA+, Vimentin +, actin +, and desmin negative) ■ If limited to soft tissue and bone involvement→ self-resolves; good prognosis

Testable fibrous and fibrohistiocytic proliferations of the skin: Facts and buzzwords

by Mohammed Shanshal, MD

Infantile digital fibroma (Inclusion body fibromatosis)	■ Multiple firm papules on dorsolateral fingers and toes (spares thumb/first toe); ■ Histology→ criss-cross fascicles of spindle cells; on high power can see the pathognomonic pink-red inclusion bodies (same size as an RBC) ■ The inclusions stain with PTAH and Masson's trichrome. They are actin positive, PAS negative. ■ Spontaneous regression within 2–3 years is the usual, surgery may indicated (50% recurrence rate)
Nodular fasciitis (pseudosarcomatous fasciitis)	■ Benign transient tumor ("transient neoplasia") in young to middle aged adults ■ Rapidly growing nodules on upper extremities (#1 site overall) and head/neck (#1 site in children) ■ Histology→ pseudo sarcoma = Proliferation of spindle shaped and plump fibroblasts arranged in a haphazard array with focally myxoid stroma (tissue culture-like appearance) ■ MYH9-USP6 is the most common fusion product, FISH for USP6 can aid in diagnosis.
Acral fibrokeratoma (Acquired digital/periungual fibrokeratoma)	■ Pink exophytic papule arising from the dorsal surface of the finger, collarette at the base of the lesion is characteristic ■ Histology→digitated fibrovascular core with vertically arranged collagen bundles lined by epidermal hyperplasia ■ Important DDx: ○ supernumerary digit (has abundant nerve fascicles) ○ periungual fibroma (more vascular)
Skin tags (Acrochordons)	■ Very common, 50% have at least one skin tag ■ Birt-Hogg-Dubé syndrome and Cowden syndrome→ can have numerous skin tags ■ Histology→polypoid with loose to dense collagenous stroma and thinwalled blood vessels.
Pleomorphic fibroma	■ F > M, clinically resemble skin tags, neurofibromas, or intradermal melanocytic nevi. ■ Histology similar to acrochordon, but has scattered hyperchromatic, bizarre, multinucleated, or stellate cells; lacks mitoses
Fibrous hamartoma of infancy	■ Solitary subcutaneous nodule favors the axilla, shoulder and upper arm ■ Occasionally a/w hyperhidrosis and hypertrichosis ■ Histology→ composed of triphasic proliferation: ○ Plump of spindle cells in fascicles associated with collagenous stroma ○ Small aggregates of immature mesenchymal cells ○ Mature fat ○ Organoid (compartmentalized) appearance and surrounding skin has "kid" skin appearance (delicate collagen bundles that stain deeply red with small lipocytes and adnexal structures)
Giant cell tumor of tendon sheath (Tenosynovial giant cell tumor)	■ Most common tumor of the hand, F > M ■ Subcutaneous nodule; most common on fingers ■ Histology→nodular proliferation of round polygonal cells and numerous ○ Osteoclast-like giant cells that have eosinophilic cytoplasm and from a few to 50 nuclei
Multinucleate cell angiohistiocytoma	■ Grouped red to violaceous papules on dorsal hands or legs, resembling Kaposi sarcoma, granuloma annulare, or sarcoidosis clinically ■ Histology→ resemble richly vascularized dermatofibroma with proliferation of dilated blood vessels, stellate and angulated giant cells ■ Stains like DF (factor 13a+ and S100 negative)

Testable fibrous and fibrohistiocytic proliferations of the skin: Facts and buzzwords

by Mohammed Shanshal, MD

Connective tissue nevus (collagenoma and elastoma)	■ Syndromes a/w connective tissue nevi: ○ Shagreen patch→ tuberous sclerosis = pebbly plaque with a “pigskin” appearance on the lower back ○ Pedunculated collagenomas→MEN-1 ○ Dermatofibrosis lenticularis disseminate→ Buschke– Ollendorf syndrome ○ Cerebriform plantar connective tissue nevi→ Proteus syndrome ■ Histology→ Collagenoma: haphazard, thickened collagen bundles, Elastoma → elastic fibers; histologic changes may be very subtle → need VVG stain
Fibrosarcoma	■ Slowly growing, large and deep subcutaneous nodules on the lower extremities (#1 site, followed by upper extremities) ■ Classification of fibrosarcomas→ ○ Adult-type (classic, sclerosing, myxoid, fibromyxoid fibrosarcoma) ○ Congenital or infantile fibrosarcoma ■ Histology→densely hypercellular proliferation of atypical spindle-shaped in herringbone or fir tree pattern, variable mitotic rate and the nuclei may be large and hyperchromatic
Epithelioid sarcoma	■ Two clinicopathologic subtypes: ○ The classic (“distal”) form→ occurs on the extremities and has a pseudo-granulomatous, biphasic (transition between epithelioid and spindle cells) growth pattern. ○ The proximal-type (“large-cell”)→ usually arises on the trunk or proximal extremities and is composed of nests and sheets of large epithelioid cells ■ CD68 -, co-expression of keratins and vimentin with loss of INI1 expression

List of abbreviations:

a/w = associated with

TS = tuberous sclerosis

MEN = multiple endocrine neoplasia

NF = neurofibromatosis

B.V = blood vessels

T = translocation

COL1A1-PDGFB = collagen type I alpha 1 gene with the platelet-derived growth factor beta chain

SCID = Severe combined immunodeficiency

WLE = wide local excision

PTAH = Phosphotungstic acid haematoxylin

VVG = Verhoeff–Van Gieson

References:

1. James WD, Elston D, Treat JR, Rosenbach MA, Neuhaus I. Andrews' Diseases of the Skin E-Book: Clinical Dermatology. Elsevier Health Sciences; 2019 Jan 18.
2. Elston D, Ferringer T, Ko CJ, Peckham S, High WA, DiCaudo DJ. Dermatopathology E-Book: Expert Consult-Online and Print. Elsevier Health Sciences; 2013 Oct 16.
3. Rapini RP. Practical dermatopathology. Elsevier Health Sciences; 2012 Aug 23.
4. Bologna J, Jorizzo J, Schaffer I. Dermatology. Philadelphia: Elsevier; 2017.
5. Alikhan A, Hocker TL. Review of Dermatology E-Book. Elsevier Health Sciences; 2016 Oct 22.