FINAL REPORT

QUALITY ASSURANCE PROGRAM

DERMATOPATHOLOGY

2020

NOTES FROM THE COORDINATOR

1. For this 2020 cycle, a total of 8 institutions responded online by the closing date of 30th August 2020
2. IAP-MD QAP provides a platform via the evaluation reports to compare and identify diagnostic insufficiency based on the outcomes of submitted diagnoses and target diagnoses.
3. In the evaluation reports of each cycle, the target diagnosis for each case is provided, followed by a tabulated list of diagnoses submitted by participating laboratories and followed by discussion and possible differential diagnoses on the case.
4. Evaluation of performance of each laboratory is conducted by participating laboratory by comparing own submitted diagnoses with the diagnoses provided in the evaluation reports. Evaluation of performance shall be the responsibility of each participating laboratory.
5. Any queries regarding this final report could be directed to Dr Saleena Awang, email: saleenaawang@gmail.com
6. The coordinator would like to acknowledge the contributions from Dr Lee Bang Rom, Dr Ikhmal Hisyam and Dr Faridah Mohamad Taib

Prepared by,

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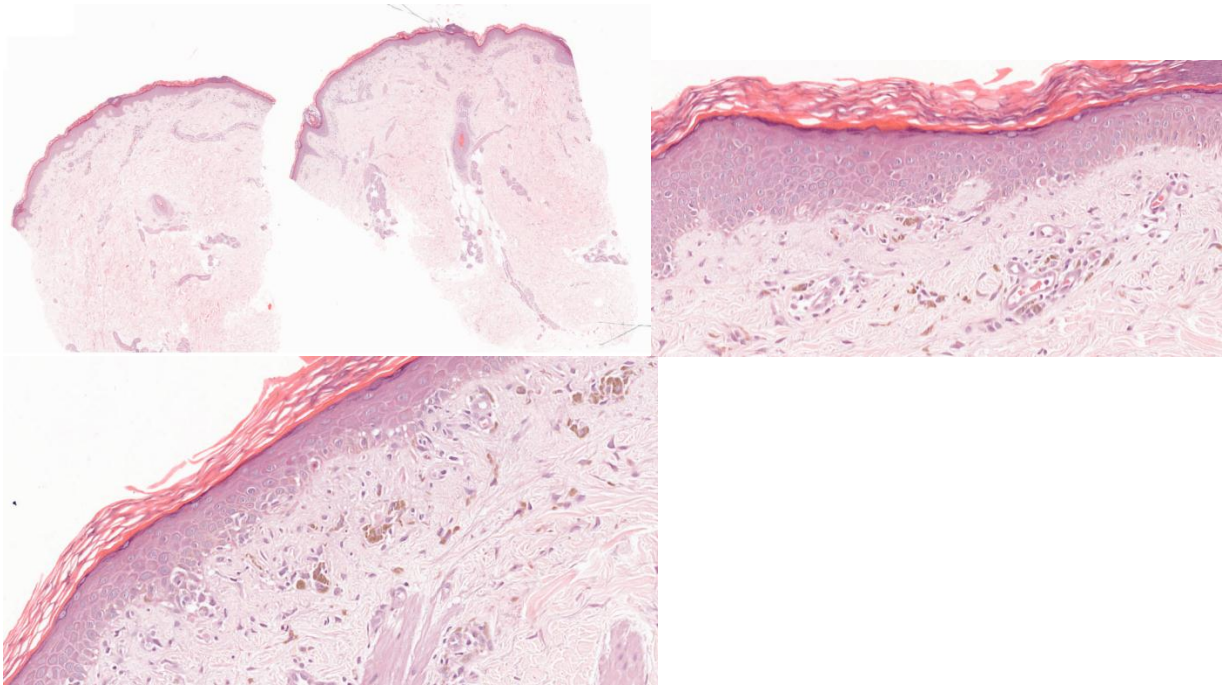
Coordinator for DERMPATH IAP-MD QAP 2020

CASE 1

48 years old, female, hyperpigmented skin over the face and forearm for 1 year with hyper and hypopigmented macules on dorsum of both hands.

Target diagnosis: Erythema dyschromicum perstans (Ashy dermatosis)



Submitted Diagnoses by Participating Institutions	Number	
Erythema dyschromicum perstans (Ashy dermatosis)	3	
interface dermatitis with prominent pigment incontinence, in favour of Ashy dermatosis	1	
Post inflammatory pigmentation	1	
Discoid lupus erythematosus	1	
Lichenoid dermatitis. Comment: Further clinical information and differential diagnosis are needed. If clinical impression is lupus erythematosus, immunoflourescence study, Alcian blue and serology correlation are mandatory	1	
Focal interface dermatitis with melanin incontinence	1	

Target diagnosis: Ashy dermatosis (Erythema dyschromicum perstant)

Minor discordant: Postinflammatory pigment alteration, fixed drug eruption, Lichen planus pigmentosus, Lichenoid drug eruption

Major discordant: Melasma, Discoid lupus erythematosus

EDUCATIONAL NOTES:

1. Section of the skin biopsy show lichenoid tissue reaction with basal vacuolar degeneration, occasional Civatte bodies and apoptotic keratinocytes. There is mild to moderate lymphohistiocytic infiltrate within the superficial and upper part of the deeper dermis. Prominent melanin incontinence seen.
2. It is of unknown etiology, female predilection, and can develop at any age although the majority of patients are in their first three decades. Patients develop oval, irregular or polycyclic, gray macules with erythematous, indurated, inflammatory borders of 1–2 mm. The lesions extend peripherally, show a tendency to coalesce, and often affect large areas of the integument . With progression, the eruption develops a grayblue color and loses the erythematous border, which is sometimes replaced by a hypopigmented periphery. It is usually symmetrical, and particularly affects the trunk, proximal extremities and, to a lesser extent, the face and neck. The palms and soles, scalp, nails, and mucous membranes do not appear to be involved
3. Sections from the inflammatory border show hyperkeratosis and an epidermis of normal thickness or somewhat atrophic, accompanied by basal cell hydropic degeneration and cytoid body formation . Pigmentary incontinence is marked and a mild perivascular or lichenoid inflammatory cell infiltrate is present in the superficial dermis . The pigment usually extends deeper in the dermis than in post inflammatory pigmentation of other causes. Sections from the central gray area show epidermal atrophy, follicular hyperkeratosis, and pigmentary incontinence. The dermal inflammatory infiltrate is composed of both CD4 and CD8 T cells, usually with CD8 forms slightly predominating. Direct immunofluorescence reveals non-specific staining of the cytoid bodies with IgG, IgM, and C3. Fibrinogen may be present at the dermoepidermal junction.
4. The pigmentary incontinence seen in late-stage lesions is quite nonspecific, showing overlap with melasma, third-stage incontinentia pigmenti, and numerous other conditions. Identifying traces of vacuolar alteration of the basilar layer or rare Civatte bodies can sometimes suggest the possibility of erythema dyschromicum perstans in preference to these other conditions, but often, clinical information is needed to secure a correct diagnosis

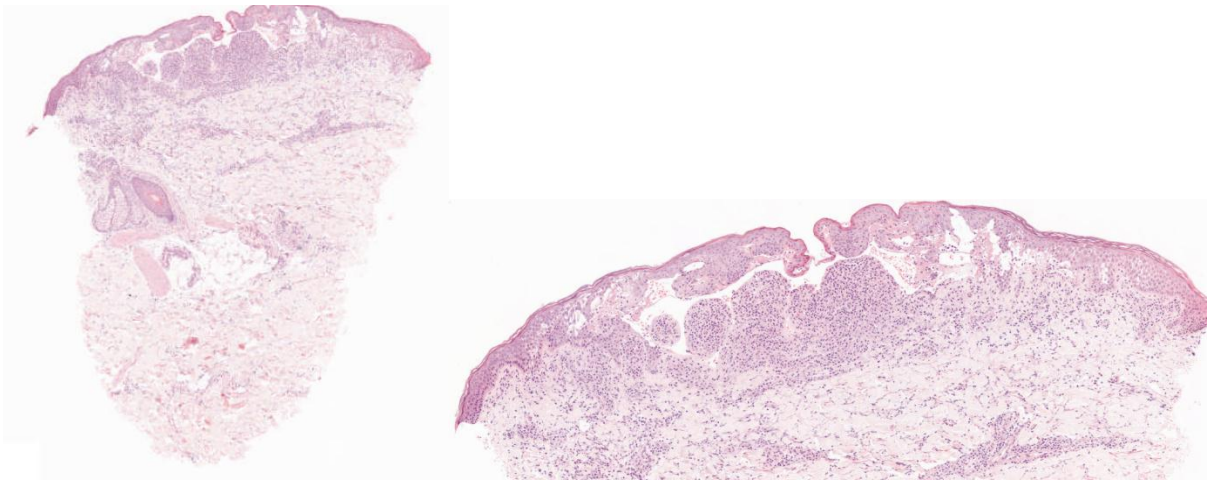
References:

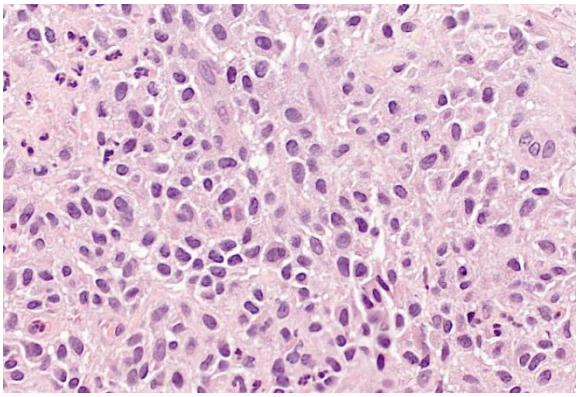
- McKee's Pathology of the Skin, 4th edition 2012, Elsevier Limited
- Weedon's Skin Pathology, Fourth edition
- Lever's Histopathology of the Skin , Eleventh edition

CASE 2

3 months old, male, multiple brownish macules, plaques and vesico-pustular lesions over the whole body

Target diagnosis: Bullous mastocytosis





Submitted Diagnoses by Participating Institutions	Number	
Bullous mastocytosis	2	
Cutaneous mastocytosis	2	
Autoimmune subepidermal bullous dermatitis with mastcytosis	1	
Blistering langerhan cell histiocytosis	1	
Vesicobullous reaction pattern suggestive of epidermolysis bullosa	1	
Epidermolysis bullosa hereditia	1	

Target diagnosis: Bullous mastocytosis

Minor discordant: Mastocytosis

Major discordant: Inflammatory bullous disorder examples BP, Chronic bullous dermatosis of childhood (CBDC) or bullous impetigo

EDUCATIONAL NOTES:

1. Punch skin biopsy demonstrated a large space of separation between the epidermis and dermis (subepidermal blister). The dermis showed moderate to dense monomorphous infiltrate composed of round to oval cells with centrally placed nuclei some of which with fried-egg appearance and cytoplasmic granules. Giemsa and C-Kit stains were strongly positive, confirming the diagnosis of BM.
2. Vesicles and bullae frequently accompany, or precede by a short period, circumscribed lesions of mastocytosis occurring in infancy or early childhood. Bullae, in association with diffuse cutaneous involvement and a varying functional disturbance, in rare examples, continue for many months or even years. Significant systemic involvement, and the ultimate prognosis, may relate to the age of onset of the condition.
3. Histologically, neoplastic mast cells are present in the dermis and have a variable appearance, as they may be round or fusiform; mast cells may display cytoplasmic hypogranularity with uneven distribution of fine granules and have atypical nuclei with monocytoid appearance.

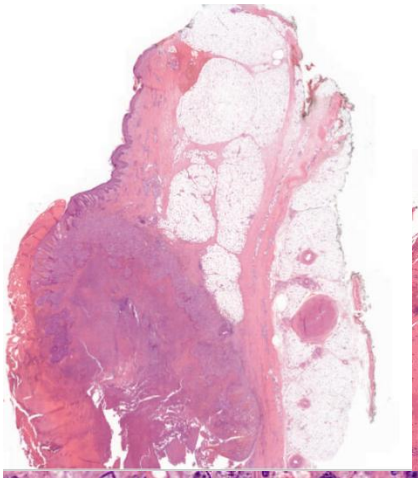
References:

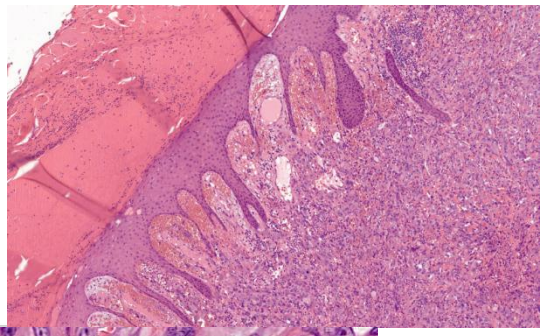
- Orkin M, Good RA, Clawson CC, Fisher I, Windhorst DB. Bullous Mastocytosis. Arch Dermatol. 1970; 101(5):547–564.
- Avshalumov, Kristina, B.A; Pichardo, Rita, MD; Jorizzo, Joseph L, MD; Sangueza, Omar P, MD; Goldenberg, Gary, MD. Bullous Mastocytosis: Report of a Patient and a Brief Review of the Literature. The American Journal of Dermatopathology: 2008; 30(5): 455-457.

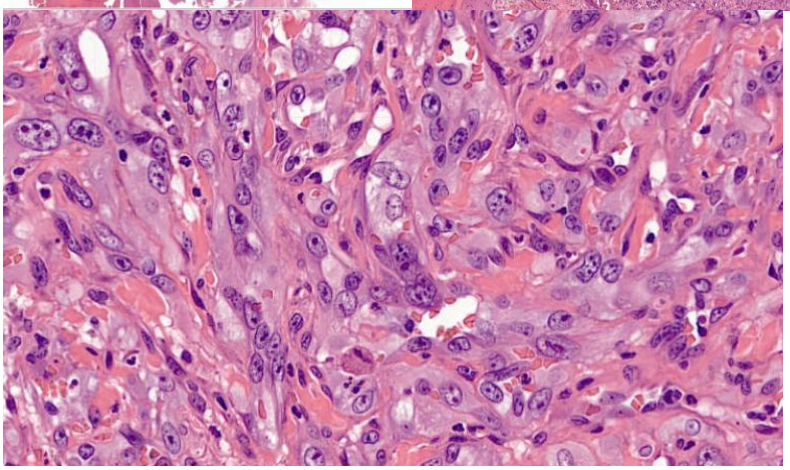
CASE 3

63 years old, male, skin lesion over calf for 6 months, increasing in size associated with pain.

Target diagnosis: Epithelioid angiosarcoma







Submitted Diagnoses by Participating Institutions		
Epithelioid angiosarcoma	1	
Angiosarcoma	2	
Malignant vascular tumour favour angiosarcoma	2	
Kaposiform hemangioendothelioma	2	
High grade sarcoma, possible Epitheliod sarcoma. Need immunostains to confirm	1	

Target diagnosis: Epithelioid angiosarcoma

Concordant responses: Angiosarcoma, Kaposiform haemangioendothelioma

Minor discordance response: Epithelioid sarcoma

EDUCATIONAL NOTES:

1. The tumour is composed of complex anastomosing vessels lined by epithelioid cell infiltrate with multilayering of the tumour cells The tumour cells exhibit large oval or round cells with abundant amphophilic cytoplasm and vesicular nuclei with prominent nucleoli. Mitoses, necrosis and haemorrhage are present
2. Cutaneous angiosarcoma is a highly malignant neoplasm with endothelial differentiation. Primary cutaneous angiosarcoma typically present in sun damaged skin of the head and neck in elderly patient. Radiation induced angiosarcoma commonly seen in the skin of the breast and/or chest wall in the breast cancer patient. Sporadic case in the limbs (unassociated with lymphoedema) may occur at any age. Early stage lesion can be subtle, bruise-like or haemangioma-like area which progress to solitary or multifocal erythematous and violaceous plaques and nodules
3. Cutaneous angiosarcoma has a wide histopathological range. The tumour can show a sieve-like pattern of back-to-back neoplastic vessels, a solid spindle cell pattern, prominent epithelioid morphology with neoplastic vessels lined by epithelioid tumour cells with abundant amphophilic cytoplasm or solid sheets of epithelioid tumour cells. Immunohistochemically the tumour cells are positive for CD31, CD34 and FLI-1 Epithelioid angiosarcoma may be positive for cytokeratin.
   Differential diagnosis: Kaposiform haemangioendothelioma, Metastatic carcinoma, Melanoma, Epithelioid sarcoma

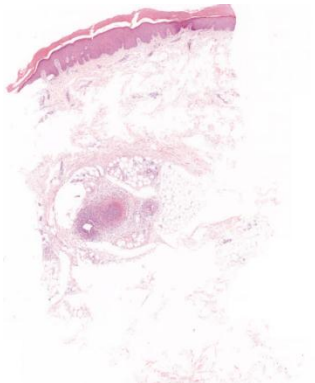
References:

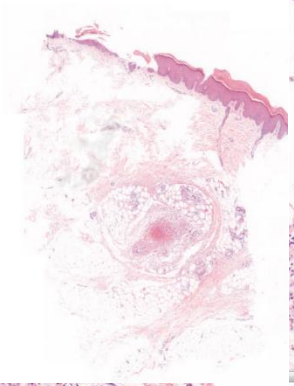
- WHO Classification of Skin tumours. 4th Edition 2018
- McKee's Pathology of the skin. 4th edition. Elsevier Saunders 2012

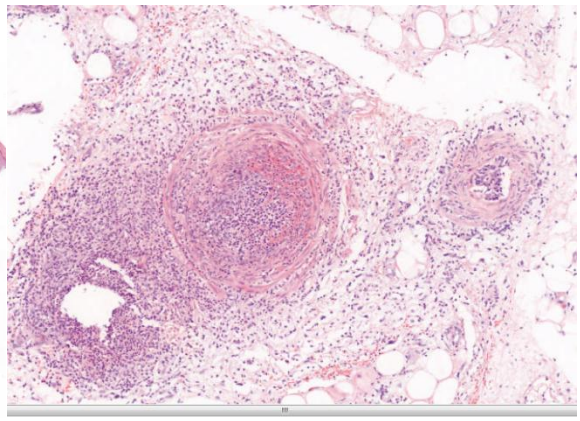
CASE 4

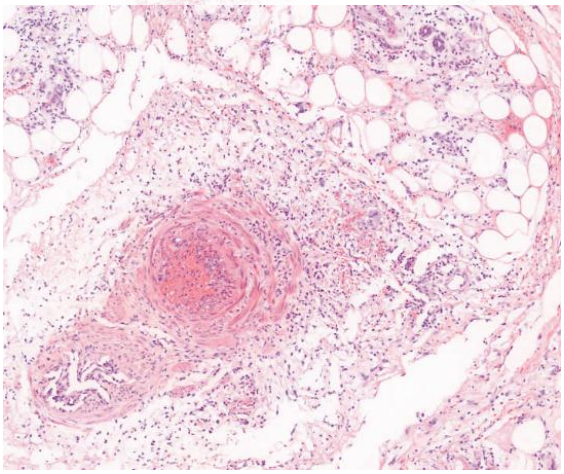
30 years old, female, bilateral calf nodular swelling for 2 weeks.

Target diagnosis: Polyarteritis nodosa









Submitted Diagnoses by Participating Institutions	Number	
Polyarteritis nodosa	5	
Septal panniculitis with granulomatous lesion and vasculitis. Differential diagnosis: 1. Erythema nodosum 2. Erythema induratum. Correlation with clinical and microbiological study is required	1	
Erythema induratum (nodular vasculitis)	1	
Wegener's granulomatosis	1	

Target diagnosis: Polyarteritis nodosa

Concordant responses: Medium vessels vasculitis.

Minor disconcordance response: Leucocytoclastic vasculitis.

EDUCATIONAL NOTES:

1. Microscopy: Epidermis with mild spongiosis. The medial sized muscular arteries at the subcutaneous fat show neutrophils infiltration at the wall. There is fibrinoid necrosis of the vessels and neutrophils karyorrhexis noted. The subcutaneous fat shows septolobular panniculitis, moderate granuloma and multinucleated giant cells.

2. Polyarteritis nodosa is a rare vasculitis affecting small and medium-sized arteries. The systemic form affects many organ systems including kidneys, liver, gastrointestinal tract and nervous system. Skin involvement is seen in approximately 10% of cases. In contrast, the cutaneous form may be accompanied by mild constitutional symptoms but there is otherwise little systemic involvement. It has a more favourable prognosis although runs a chronic relapsing and remitting course. Cutaneous signs include tender papules and plaques, purpura, livedo reticularis, skin necrosis and ulceration.

3. Histology of polyarteritis nodosa: Histological features of systemic and localised cutaneous forms of polyarteritis nodosa are similar. A deep biopsy is preferred as cutaneous polyarteritis nodosa involves medium-sized vessels in the deep dermis and subcutis. Early lesions show fibrinoid necrosis with thickening and infiltration of the vessel wall. Neutrophils, eosinophils and lymphocytes are present. Leucocytoclasis may be present. Thrombi and aneurysmal change may occur and lead to necrosis of the overlying epithelium. In mature lesions vessel occlusion occurs secondary to intimal and mural fibrosis. Lesions at various stages are characteristic and changes are discontinuous with uninvolved skip lesions between affected segments.

4. Special studies for polyarteritis nodosa: Immunofluorescence may be positive for IgM and C3 in the vessel walls. Elastic–van Gieson staining may show disruption of the vessel internal elastic lamina.

5. Differential diagnosis:

    - Microscopic polyangiitis: Involvement of capillaries and venules in addition to the arteriolar involvement seen in polyarteritis nodosa is a major point of distinction between the two disorders.
    - Leucocytoclastic vasculitis: Primarily affects capillaries and venules (and not arterioles). Changes are primarily in the superficial dermis, although severe cases may extend to the subcutis, whereas polyarteritis nodosa affects deep vessels.

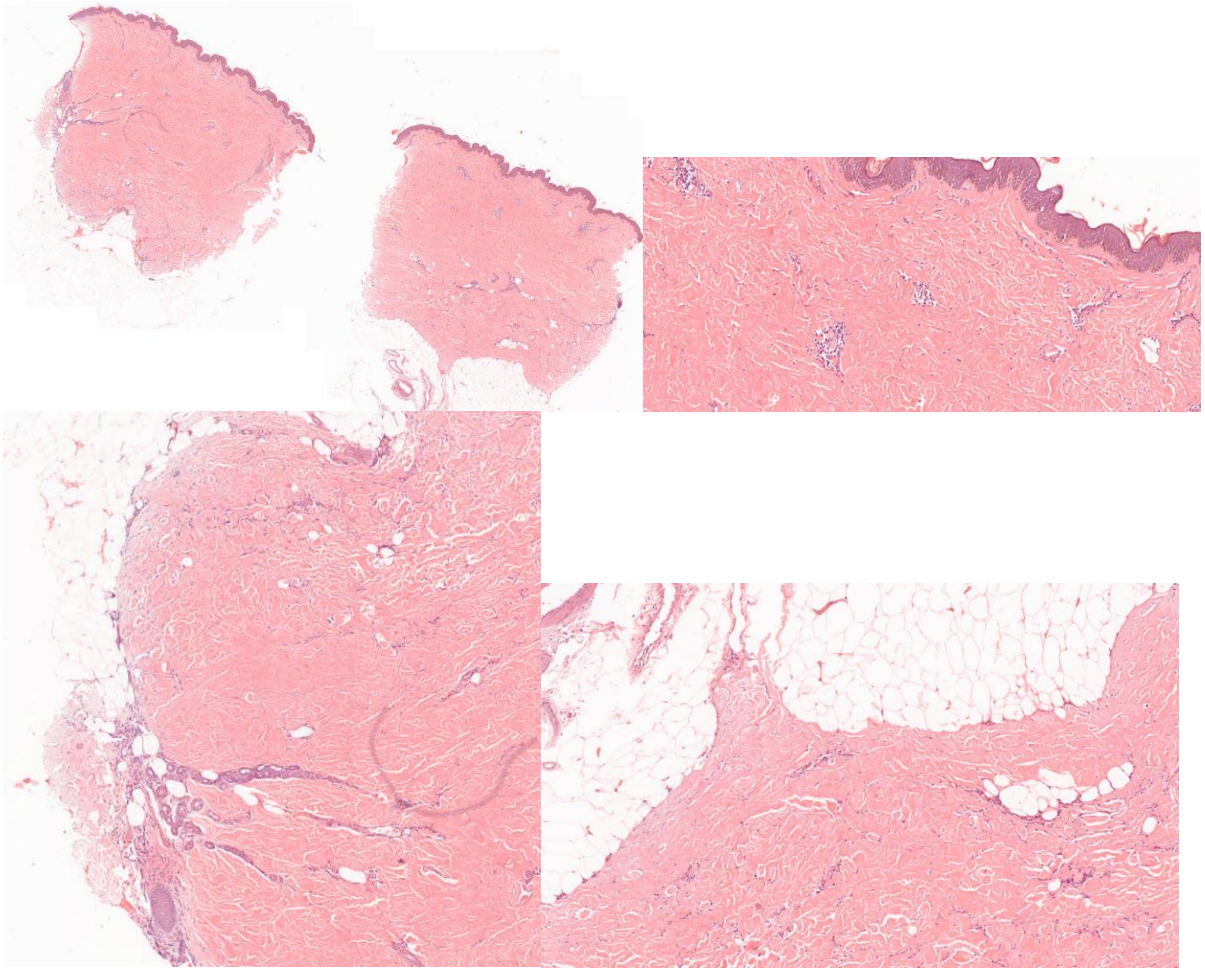
References:

- WHO Classification of Skin tumours. 4th Edition 2018
- McKee's Pathology of the skin. 4th edition. Elsevier Saunders 2012

CASE 5

12 years old, male, non itchy hypopigmented patches over back, spread to hands and legs.

Target diagnosis: Morphea



Submitted Diagnoses by Participating Institutions	Number	
Morphea	5	
Scleroderma	3	

Target diagnosis: Morphea, Localized morphea

Concordant response: Scleroderma

EDUCATIONAL NOTES:

1. Microscopy: Section of the skin shows thickened dermis which is occupied by crowded and swollen collagen fibres. The dermal collagen loses its fenestrations and appears homogenous with squared appearance (square biopsy / cookie-cutter sign"). The abnormal collagen replaces the adipose tissue surrounding the sweat glands which appear atrophic and seen at the level of mid-dermis. There is perivascular infiltrate of lymphocytes, histiocytes, some plasma cells and occasional eosinophils. The epidermis appears atrophic.

2. Morphea (localized scleroderma) is skin limited disease without internal organ involvement. The underlying cause of morphea is unknown. It may be associated with autoimmunity, genetic, triggered by radiation therapy, vascular dysfunction, repeated trauma to the affected area or a recent infection.

3. Clinical features: Plaque-form / circumscribed (most common variant), Guttate lesion, Bullous morphea, Linear morphea, Generalized morphea, Subcutaneous scleroderma (morphea profunda), Disabling pansclerotic morphea of children

   Morphea is usually limited to the skin, but it may extend deeper to involve muscle or bone. Morphea may also involve the inside of the mouth, the genitals and the eyes. It often first occurs in childhood or middle adulthood. It is usually asymptomatic with occasional itch and rarely pain. Morphea usually begins as a red or purple area of skin that then becomes thickened and white. The thick white areas usually thin out over time and turn brown. Systemic scleroderma is associated with diffuse thicknening of the skin along with involvement of internal organs Minor discordance responses.

4. Microscopic variation: Superficial morphea, Deep morphea, Linear morphea, Keloidal morphea, Bullous morphea

5. Differential diagnosis: Acrodermatitis chronica atrophicans, Lichen sclerosus, Figurate erythema, Late porphyria cutanea tarda

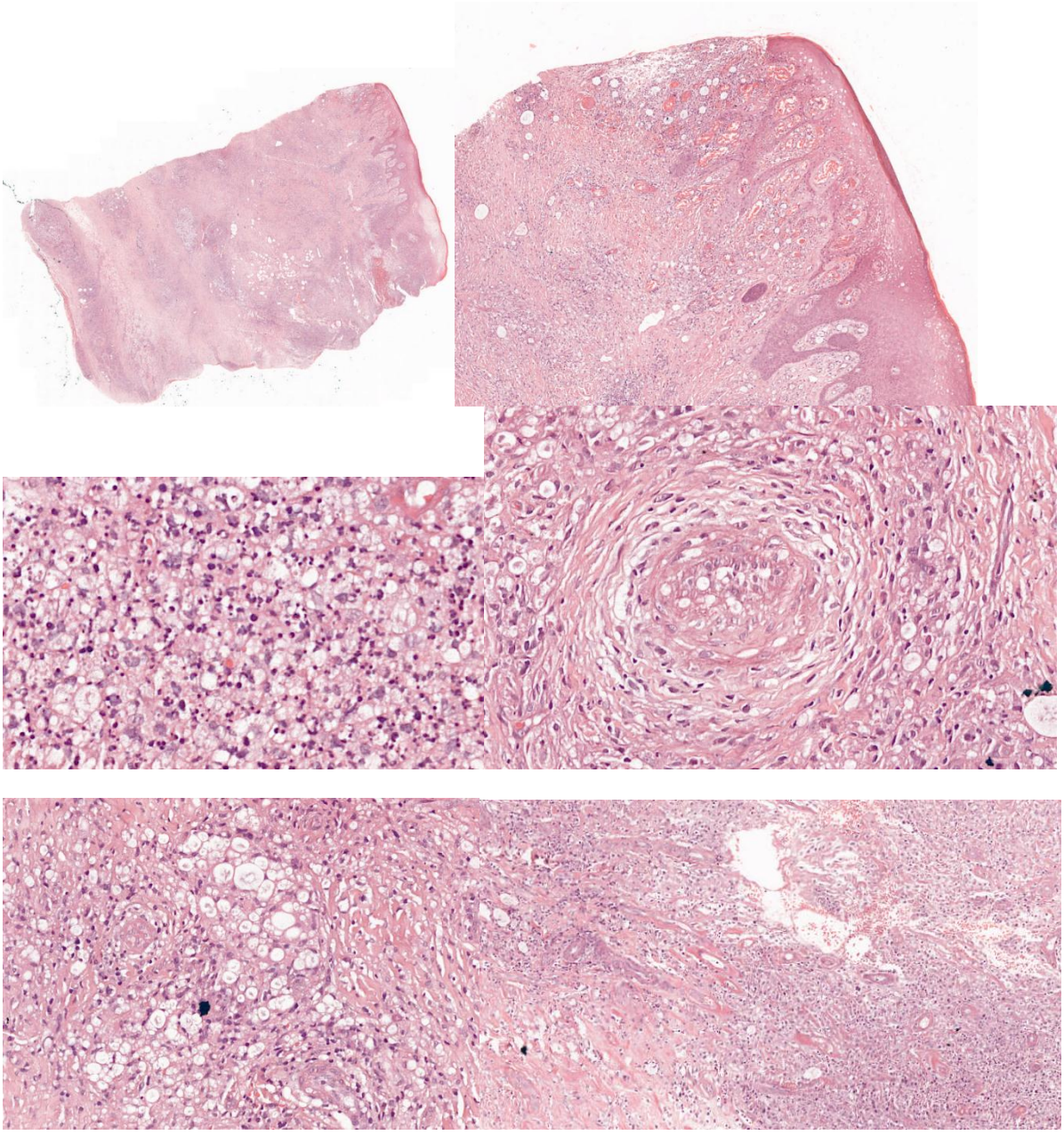
References:

- Asok Biswas. Pearls and pitfalls in Inflammatory Dermatopathology. Cambridge University Press 2017
- McKee's Pathology of the skin. 4th edition. Elsevier Saunders 2012

CASE 6

58 years old, female, passing out maggots from the nostril with multiple vasculitic lesion on the palm and lower limb as well as demarcated punch out painful ulcerated lesion on lower limb. Wade-Fite stain done.

Target diagnosis: Lepromatous leprosy with Lucio phenomenon



Submitted Diagnoses by Participating Institutions	Number	
Lepromatous leprosy with Lucio phenomenon	4	
Lepromatous leprosy	3	
Erythema nodosum leprosum	1	

Target diagnosis: Lepromatous leprosy with lucio phenomenon

Minor discordant: erythema nodosum leprosum, lepromatous leprosy

Major discordant: pyoderma gangrenosum

EDUCATIONAL NOTES:

1. Microscopy: The epidermis is irregularly acanthotic, associated with hyperkeratosis and parakeratosis. The superficial and deep dermis show a dense mixed cells infiltration with numerous scattered foamy cells, laden with acid fast bacilli (Fite stain positive). Suppurative area seen. Dermal blood vessels are increased and congested. On the superficial dermis, some blood vessels show fibrinoid necrosis of their walls. In the deeper dermis, some blood vessels show endothelial cell proliferation leading to luminal obliteration with globi of acid fast bacilli seen within the wall
2. Leprosy is a chronic granulomatous disease principally affecting the skin, nasal mucosa and peripheral nerves. Leprosy is caused by an acid fast bacteria Mycobacterium leprae. Leprosy is most prevalent in tropical countries and the principal mode of transmission is by spread of person to person through nasal secretions or droplets. Leprosy shows a wide spectrum of clinical presentations that correlate with the histopathological changes and the immune status of the patient. These include indeterminate, tuberculoid, lepromatous, borderline-tuberculoid, borderline, and border line-lepromatous leprosy .
3. Lepromatous leprosy (LL) is a systemic disease that occurs in patients with poor cell-mediated immunity to M. leprae, but with higher levels of antibodies. The cutaneous lesions are multiple, symmetrical, and may affect the whole skin, giving a sclerodermatous appearance (diffuse or Lucio-type leprosy). The lesions are typically firm and nodular and are concentrated on the face and backs of hands, facial lesions being associated with hair loss round the eyes . The distribution of the lesions is said to be favored by lower skin temperature. The mucosa of the nose is characteristically involved and becomes hyperemic with frequent epistaxes. The nasal cartilages and bone may be affected, and collapse can result in a picture similar to the saddle nose of congenital syphilis. A variety of macules, papules, and plaques may be present at one time, characteristically sparing the axillae, groins, and perineum. These lesions become anesthetic due to widespread neural involvement with resultant claw hand and foot drop.

4. Lucio's phenomenon was thought to involve an immune complex-mediated mechanism to produce episodes of necrotizing vasculitis in diffuse type of leprosy. Others, however, have since suggested that direct invasion of vascular endothelium by large numbers of bacilli, with subsequent thrombosis of vessels, is the major factor in the evolution of this reaction. Swollen endothelial cells with marked intraendothelial cell bacillary proliferation is characteristic. Hemorrhagic ulcers form as a result of the underlying necrotizing vasculitis or of vascular occlusion due to endothelial swelling and thrombosis.

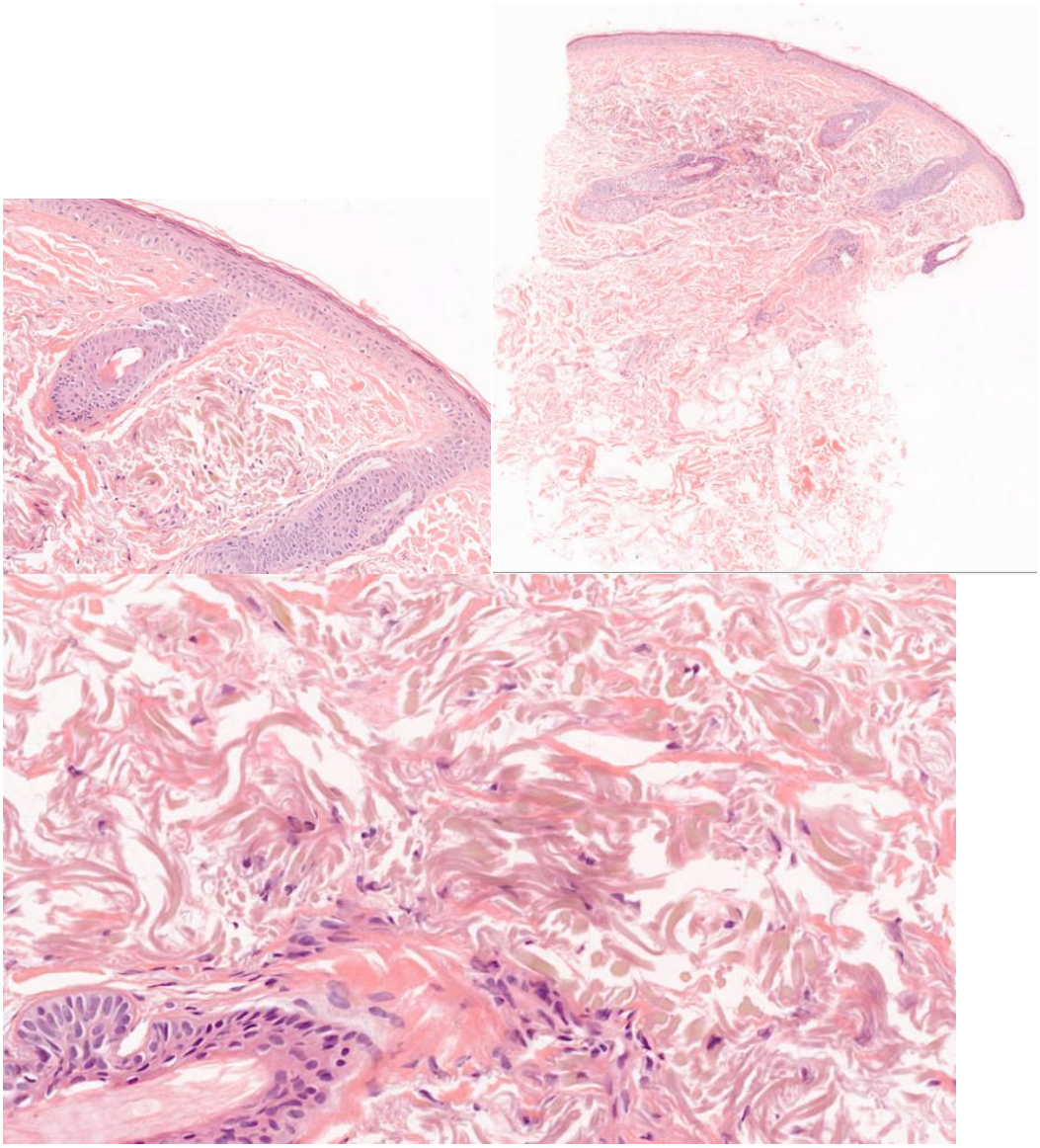
References:

- McKee's Pathology of the skin. 4th edition. Elsevier Saunders 2012
- Weedon's Skin Pathology, Fourth edition

CASE 7

45 years old, female, bluish-gray discolouration over the face after application of skin whitening

Target diagnosis: Ochronosis



Submitted Diagnoses by Participating Institutions	Number	
Ochronosis	5	
Exogenous Ochronosis	3	

Target diagnosis: Ochronosis

Minor discordant: Argyria, keloid, solar elastosis

Major discordant: Nodular amyloidosis, No significant pathology

EDUCATIONAL NOTES:

1. Skin biopsy showed normal epidermis. In the superficial dermis, there are sharply defined yellow-brown "banana" shaped deposits within homogenized elastotic fibers. There are scattered pigment-laden macrophages in the papillary dermis. The deeper dermis and subcutaneous fat are normal.
2. Ochronosis is a cutaneous disorder characterized by blue-black pigmentation resulting as a complication of long-term application of skin-lightening creams containing hydroquinone but may also occur due to topical contact with phenol or resorcinol in dark-skinned individuals.
3. It can also occur following the use of systemic antimalarials such as quinine. EO is clinically and histologically similar to its endogenous counterpart viz., alkaptonuria, which, however, exhibits systemic effects and is an inherited disorder.

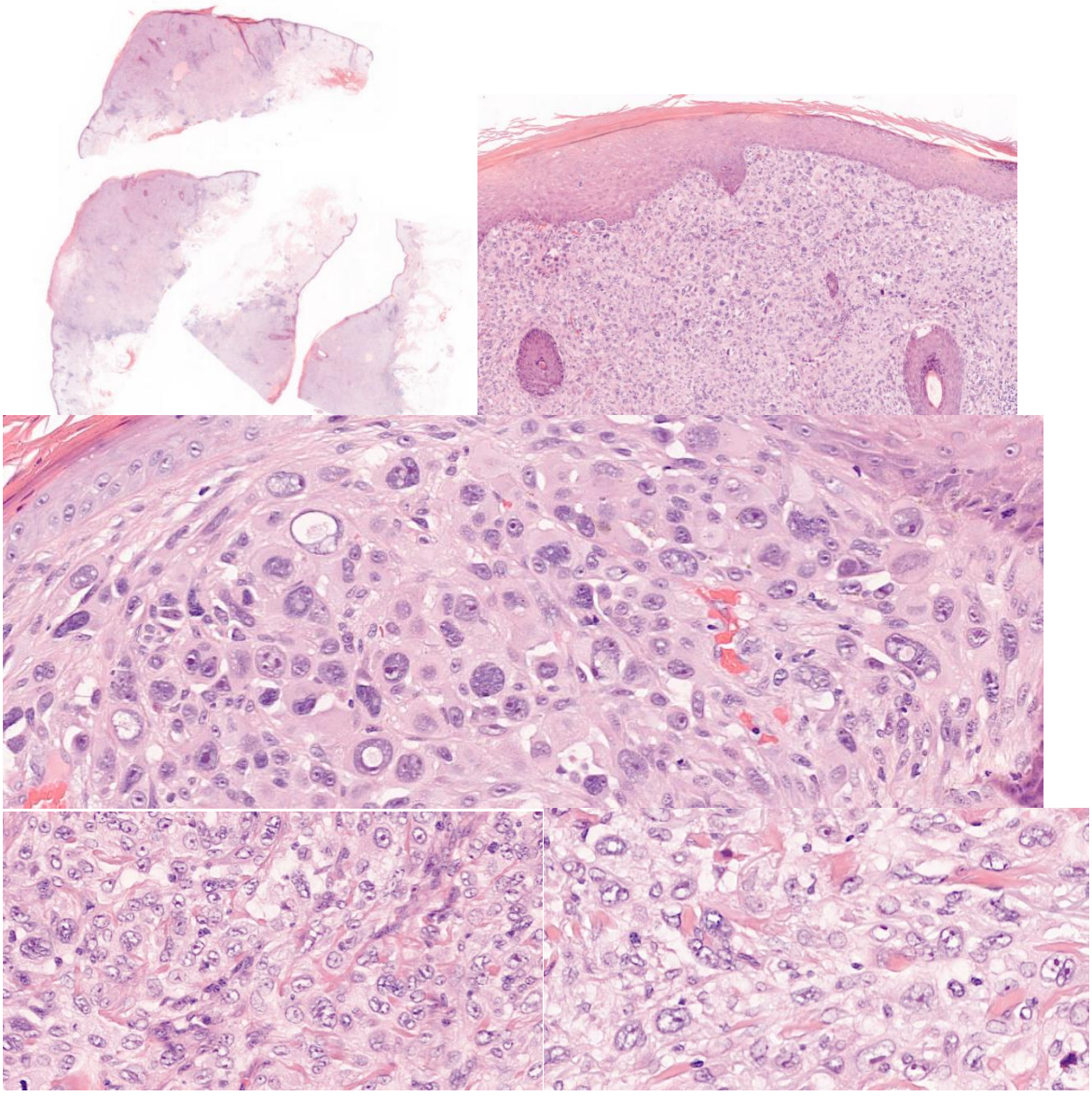
Reference:

- Gandhi V, Verma P, Naik G. Exogenous ochronosis After Prolonged Use of Topical Hydroquinone (2%) in a 50-Year-Old Indian Female. Indian J Dermatol. 2012; 57(5):394-395.

CASE 8

80 years old, male, forearm ulcerated nodule for 2 weeks.

Target diagnosis: Atypical fibroxanthoma



Submitted Diagnoses by Participating Institutions	Number	
Atypical fibroxanthoma	3	
Superficially sampled pleomorphic dermal spindle cell neoplasm. Differential diagnosis: 1. Atypical fibroxanthoma (AFX). 2. Pleomorphic dermal sarcoma (PDS). 3. Melanoma. Comment: 1. Immunohistochemistry study eg: S100 for melanoma. 2. Complete excision is needed to differentiate AFX and PDS	1	
Malignant poorly-differentiated neoplasm; IHC required. Differentials include pleomorphic dermal sarcoma, melanoma, poorly-differentiated carcinoma	1	
Spindle cell squamous cell carcinoma	1	
Melanoma	1	
Malignant Melanoma, need melanoma cocktail to confirm	1	

Target diagnosis: Atypical fibroxanthoma

Minor discordant: Pleomorphic dermal sarcoma (PDS), Angiosarcoma, Spindle cell carcinoma, Spindled or desmoplastic melanoma

EDUCATIONAL NOTES:

1. Microscopy – Epidermis: Unremarkable with presence of grenz zone. Dermis: Circumscribed dermal nodule within skin showing solar elastosis. Tumor often abuts the epidermis but rarely may have a of uninvolved dermis. Spindled to round or epithelioid tumor cells in haphazard or fascicular pattern. Bizarre multinucleated pleomorphic cells present. Frequent mitotic figures; many atypical mitotic figures. No invasion of deeper structures. Histologic variants: angiomatoid, chondroid, clear cell, granular cell, keloidal, myxoid, osteoclastic, osteoid, pigmented.
2. Atypical fibroxanthoma (AFX) is a dermal spindle-cell tumour that typically occurs on the head and neck of sun damaged older people. The tumour-like growth should be considered a type of skin cancer but it may behave in a benign fashion.
3. A rare type of atypical fibroxanthoma occurs in younger patients on parts of the body that are not normally overexposed to the sun. These tumours are usually found on the trunk and extremities and tend to be larger and slower growing.
4. Differential diagnosis:
   The predominant histologic mimics are those atypical spindle cell neoplasms that abut the epidermis, sometimes referred to as the “SLAM” differential for ease of remembrance (spindled squamous cell carcinoma, leiomyosarcoma, AFX, spindled melanoma)

a. Partial biopsy of Pleomorphic dermal sarcoma: superficial aspect of pleomorphic dermal sarcoma (PDS) can appear identical to AFX but on excision a PDS is a much larger and more deeply infiltrative lesion with a worse prognosis
b. Angiosarcoma: spindle cell variant, prominent vascular spaces or blood, vascular markers+
c. Leiomyosarcoma - pleomorphic type: usually more fascicular growth pattern, desmin+
d. Spindled or desmoplastic melanoma: S100+, may have associated atypical intraepidermal melanocytic proliferation (Am J Dermatopathol 2007;29:551)
e. Squamous cell carcinoma - spindle cell type: deep extension, p63+ and high molecular weight cytokeratin positive (J Cutan Pathol 2009;36:543)

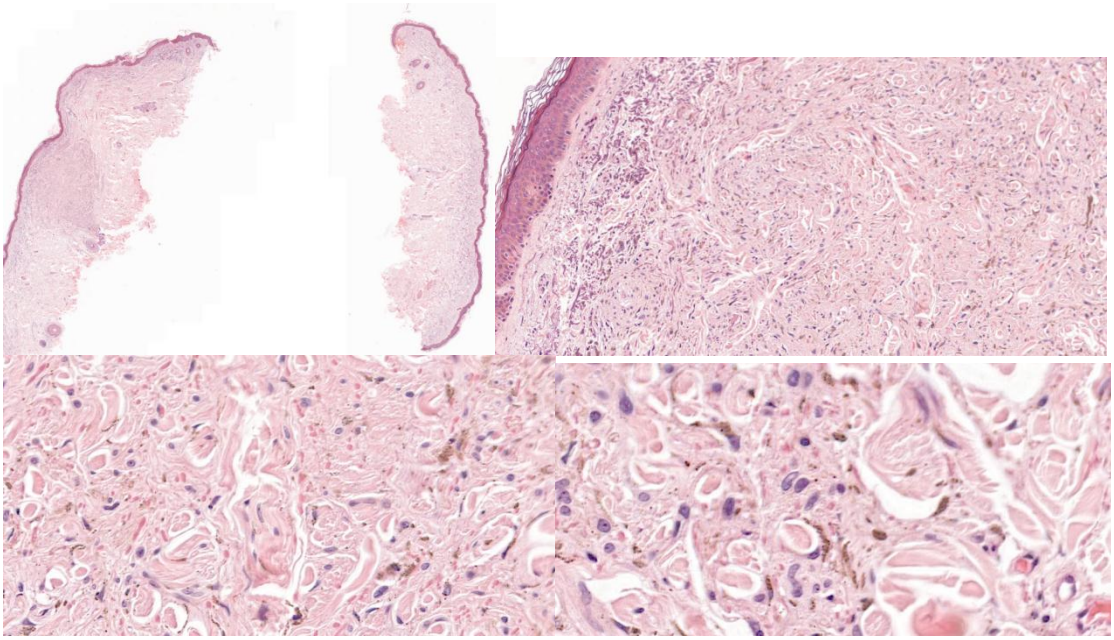
References

- WHO Classification of Skin tumours. 4th Edition 2018
- McKee's Pathology of the skin. 4th edition. Elsevier Saunders 2012

CASE 9

15 years old, female, pigmented nodule over dorsal hand.

Target diagnosis: Common blue naevus



Submitted Diagnoses by Participating Institutions	Number	
Blue naevus	4	
Dendritic blue naevus	1	
Benign intradermal nevus, in favour of desmoplastic Spitz Nevus	1	
Benign spindle cell lesion. Differential diagnosis: 1. Perineuroma. 2. Pigmented neurofibroma	1	
Neurofibroma	1	

Target diagnosis: Common blue naevus

Minor discordant: Dermatofibroma, benign melanocytic lesion

Major discordant: Melanoma, DFSP, Neurofibroma, Perineuroma

EDUCATIONAL NOTES:

1. Section from the skin shows non-ulcerated, symmetrical, intradermal melanocytic lesion composed of proliferation of heavily pigmented spindle shaped dendritic melanocytes. In areas, melanophages are also seen intermingled with the dendritic melanocytes. A moderate dermal fibrosis is also present. Regression is not a feature. No junctional activity

is seen. The lesion appears completely excised in the tissue section examined. There is no feature of malignancy present.

2. Collection of benign type C melanocytes in dermis. Blue colour due to Tyndall effect of selective absorption of parts of the light spectrum by deeply located (dermal) melanin pigment, which is usually abundant.
3. Important histological features are non-circumscribed dermal lesion, dendritic and spindled shaped melanocytes which heavily pigmented (melanophages), sclerotic stroma and no atypia/mitosis.

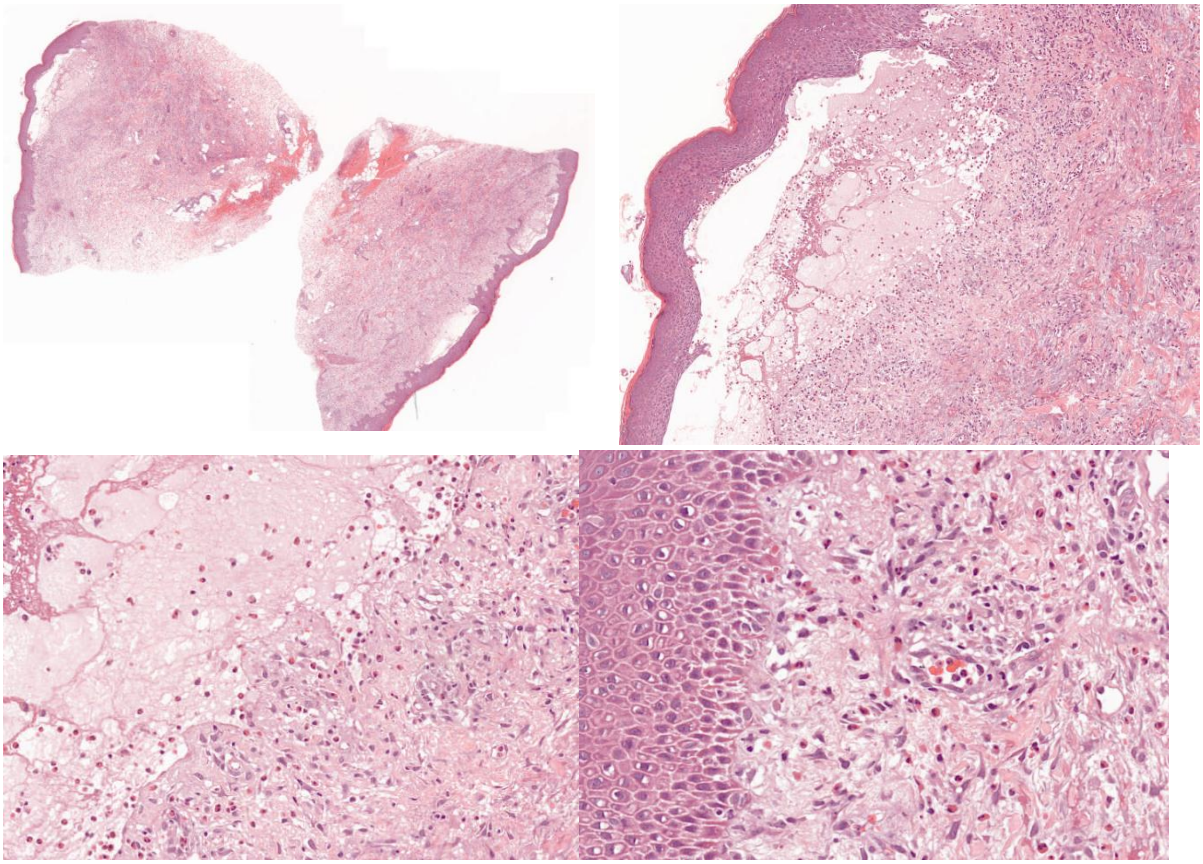
References:

- Elder DE, Massi D, Scolyer RA, Willemze R, eds.
- WHO Classification of Skin Tumours. 4th ed. Lyon. France: IARC; 2018: 126-127.

CASE 10

76 years old, female, generalized bullous lesion for 1 month. IF study: linear dermo-epidermal deposition of IgG and C3.

Target diagnosis: Bullous pemphigoid



Submitted Diagnoses by Participating Institutions	Number	
Bullous pemphigoid	7	
Eosinophils rich sub epidermal bullous dermatitis	1	

Target diagnosis: Bullous pemphigoid

Minor discordant: Inflammatory epidermolysis bullosa acquisita, , bullous systemic lupus erythematosus

Major discordant: Pemphigoid gestationis, linear IgA disease, dermatitis herpertiformis, erythema multiforme, atropod bite, drug reaction

EDUCATIONAL NOTES:

1. Microscopy: Serial sections show subepidermal bullae formation with retention of the dermal papillary outline. The bullae contains fibrin, eosinophils and neutrophils. There is also dermal infiltrates of eosinophils and lymphocytes with upper dermal oedema. IF study shows linear dermoepidermal deposition of IgG and C3c.
2. Bullous pemphigoid is a chronic subepidermal blistering disease that occurs primarily in the elderly. It is the most common subepidermal bullous disease with an annual incidence of 6.6 new cases per one million of the population and accounts for approximately 80% of all subepidermal autoimmune bullous diseases. BP is characterized by the presence of IgG autoantibodies specific for the hemidesmosomal BP antigens BP230 (BPAg1) and BP180 (BPAg2). Autoantibodies of BP target the NC16A domain of BPAg2 The disease is associated with autoantibodies to bullous pemphigoid antigen I (230 kD) and/ or bullous pemphigoid antigen II (180 kD).
3. Bullous pemphigoid is not a single disease entity. Rather, there are many subtypes, which have been classified into primary cutaneous and mucosal variant and into generalized and localized forms .. The characteristic lesions of established disease are tense and often intact blisters arising on normal or erythematous skin . They contain clear or bloodstained fluid. Any area of the body may be affected, but the blisters are most commonly located about the lower abdomen, the inner aspect of the thighs and on the flexural surfaces of the forearms, the axillae, and groin measure up to several centimeters in diameter and are typically dome-shaped . Reported mucosal involvement (frequently as ulcers) is highly variable, ranging from 8% to 58%.
4. A typical finding in bullous pemphigoid is retention of the dermal papillary outline (festooning) which project like sentries into the vesicle cavity. The underlying dermis is inflamed and usually shows widespread severe edema. An infiltrate of eosinophils and mononuclears surrounds the blood vessels and extends between the adjacent collagen bundles. Leukocytoclasis is not seen and features of vasculitis are absent. The adjacent papillary dermis is often edematous and, very occasionally, eosinophil microabscesses are a feature . Exceptionally rarely, neutrophil microabscesses may be seen (, raising diagnostic confusion with dermatitis herpetiformis. Eosinophilic spongiosis is also sometimes evident in the adjacent epidermis
5. The inflammatory cell-rich variant of bullous pemphigoid must be distinguished from other subepidermal blistering dermatoses in which a heavy inflammatory cell component is a typical finding. These include dermatitis herpetiformis, linear IgA disease, inflammatory epidermolysis bullosa acquisita, and bullous systemic lupus erythematosus

6. The cell-poor variant of bullous pemphigoid has a very wide range of differential diagnoses including epidermolysis bullosa (congenital and acquired), porphyria cutanea tarda, bullous amyloidosis, bullosa diabeticorum, and autolysis
7. DIF studies reveal linear deposition of IgG and C3 along the basement membrane. The salt-split skin test shows immunoreactants deposits in the roof of the blister, since this area contains the hemidesmosomes where the BPAg are located (lamina lucida)

References:

- McKee' Pathology of the Skin, Weedon's Skin Pathology
- Dermatopathology expert consult Elsevier 2nd edition
- DSPG-Inflammatory Skin Disorders demosmedical