International Academy of Pathology
Malaysian Division

FINAL REPORT

QUALITY ASSURANCE PROGRAM
DERMATOPATHOLOGY
2022

NOTES FROM THE COORDINATOR

1. For this 2022 cycle, a total of 10 institutions responded online by the closing date of 15th January 2023.
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 Awla Mohd Azraai, email: awla3399@uitm.edu.my.
6. The coordinator would like to acknowledge the contributions from Dr Saleena Awang, Dr Lee Bang Rom, Dr Faridah Mohamad Taib, Dr Sandhya Raj and Dr Zuliatul Faizah Baharom.

Prepared by,
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Coordinator for DERMPATH IAPMD QAP 2022

Awla Mohd Azraai, MBBS, MPath

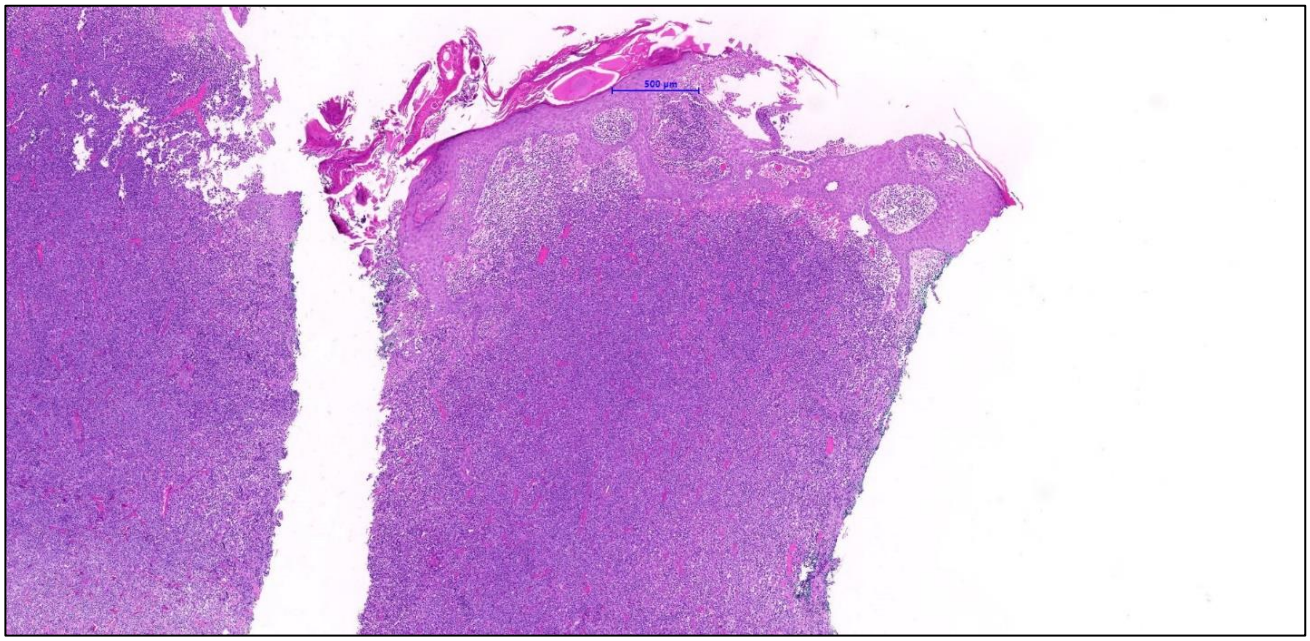
CASE 1

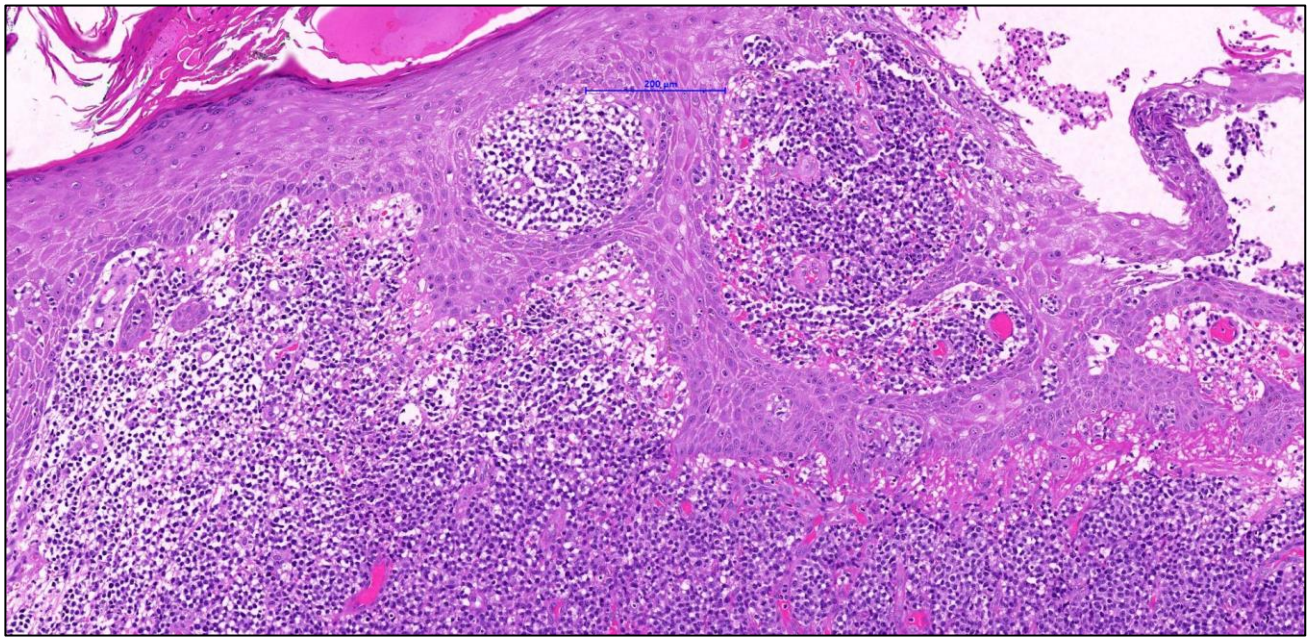
HISTORY: 68/Male/Presented with patches and plaques at trunk, UL, LL with tumour-like lesion at thigh

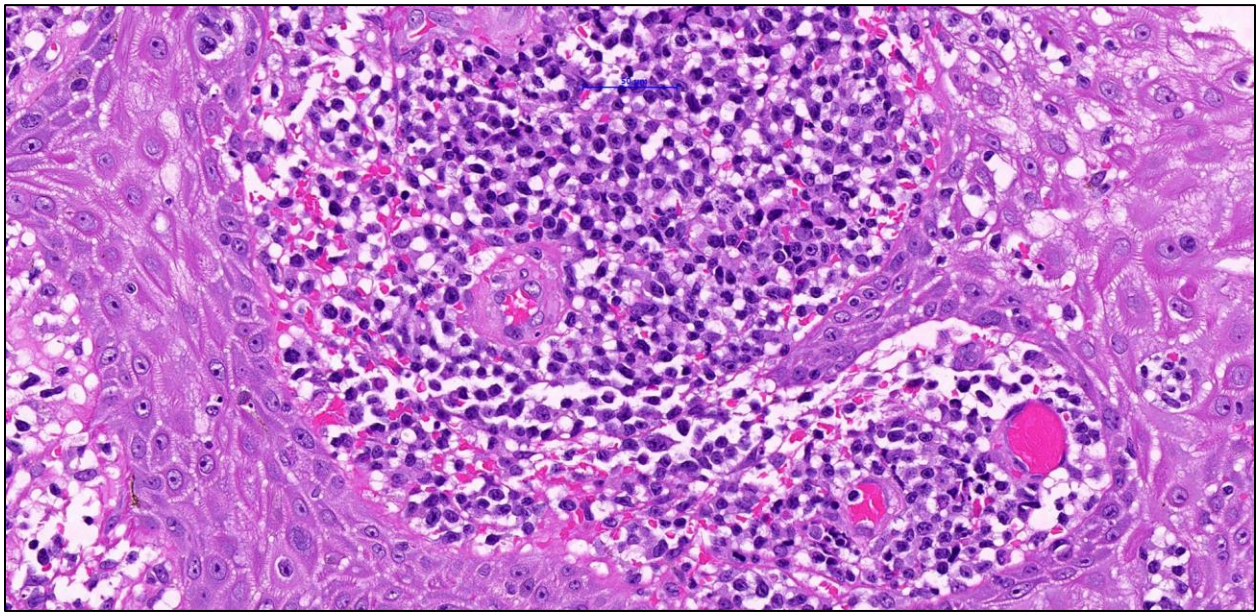
TARGET DIAGNOSIS: Mycosis fungoides with large cell transformation

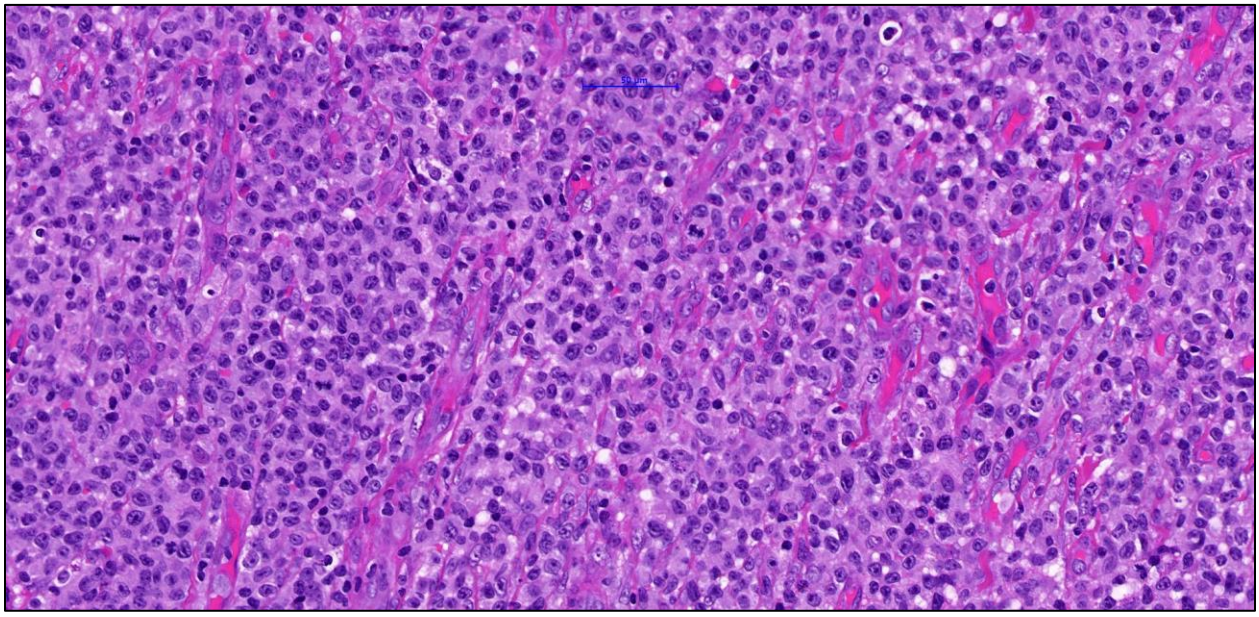
MINOR DISCORDANT: Mycosis fungoides, Metastatic nodal ALCL, other high-grade CTCL

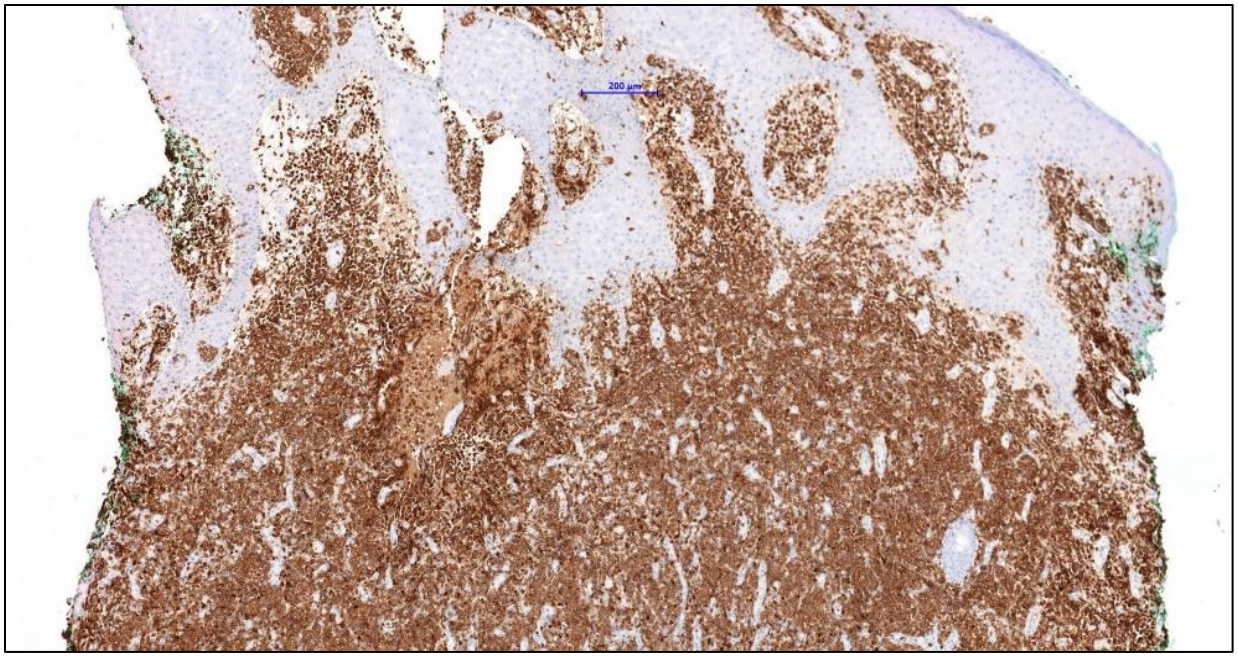
MAJOR DISCORDANT: Primary cutaneous ALCL, Lymphomatoid papulosis



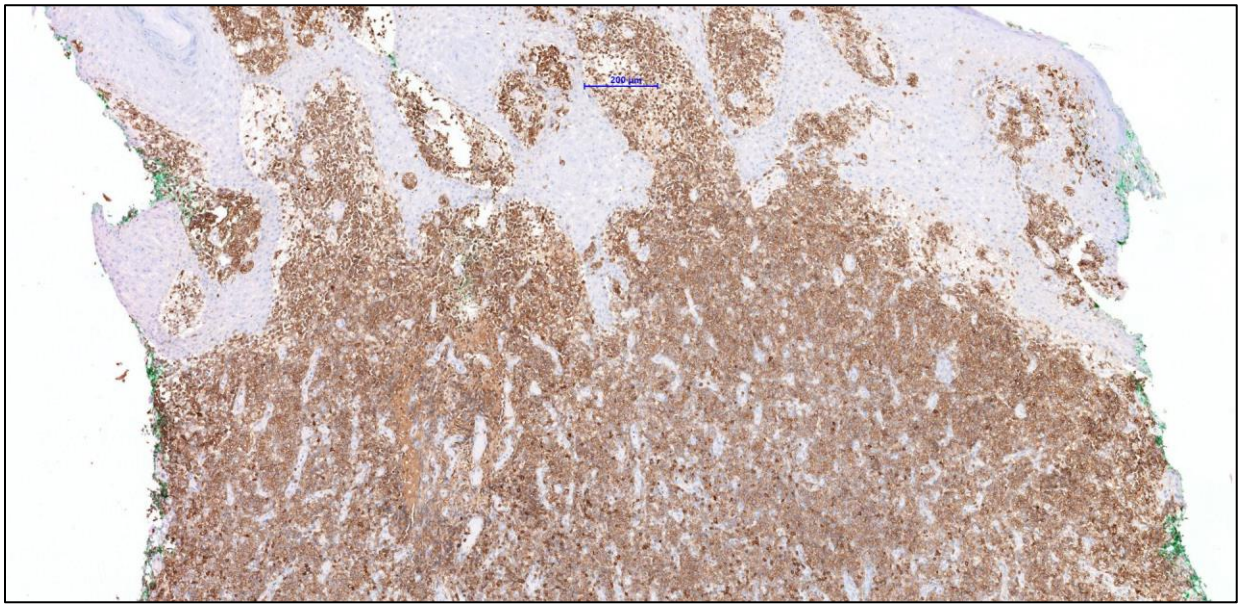




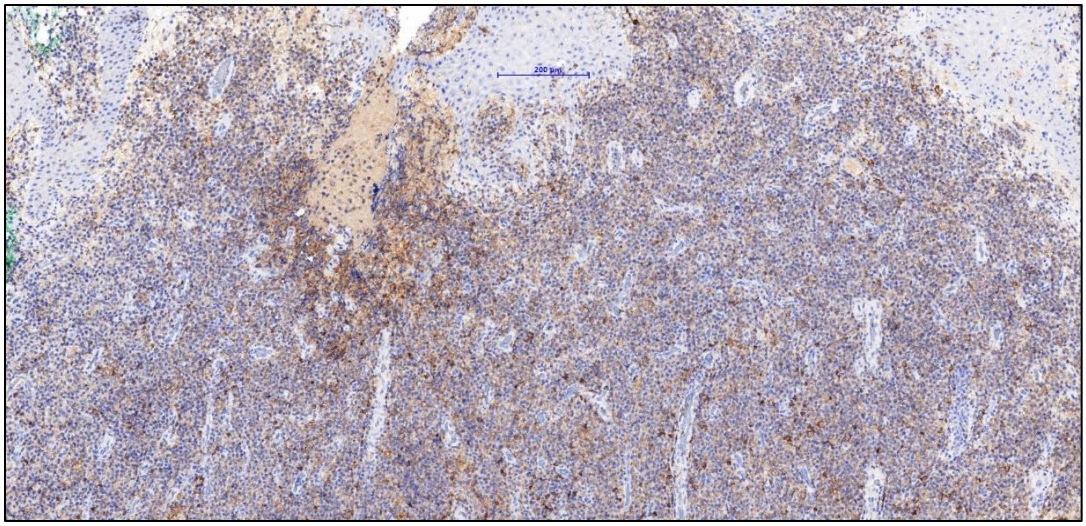




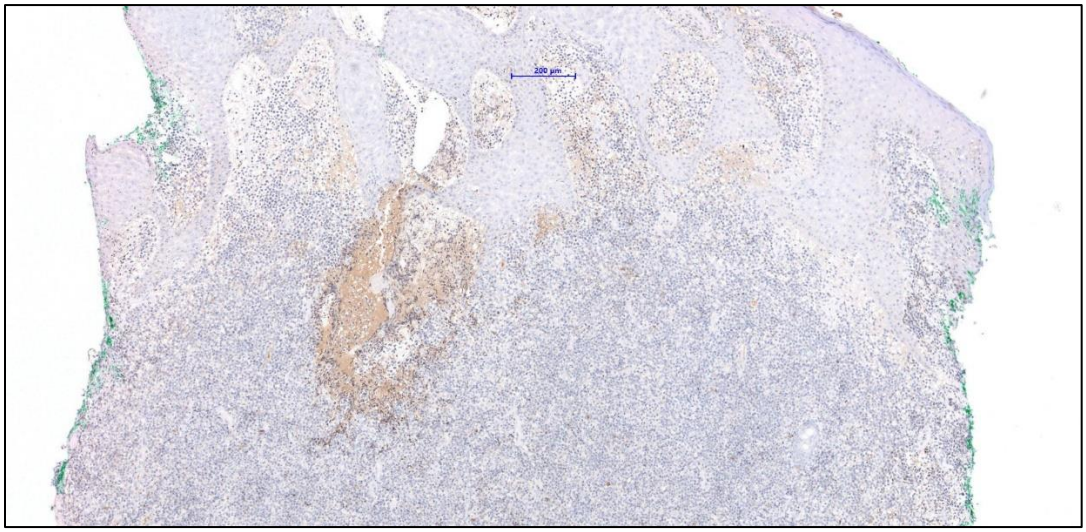
CD3



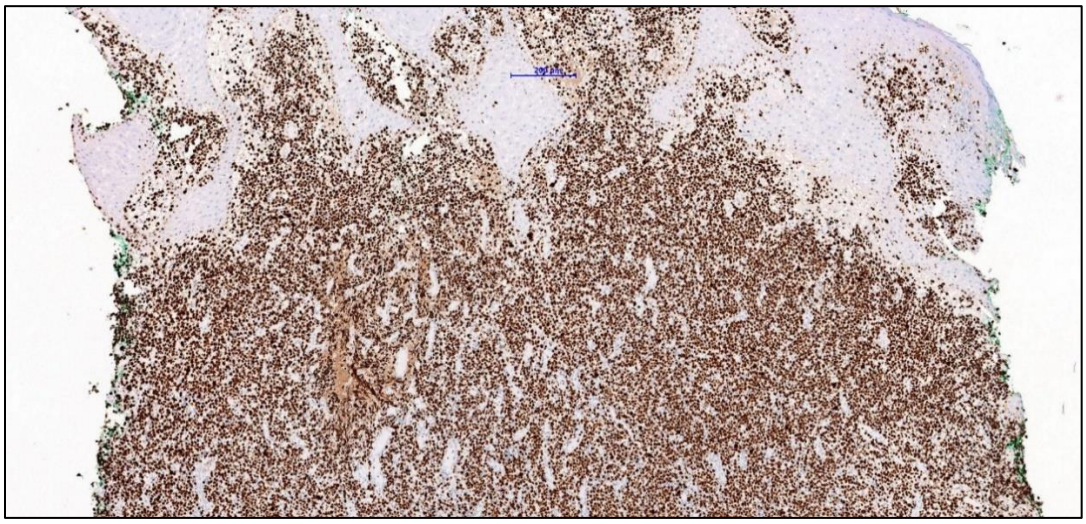
CD5



CD4



CD30



Ki67

Submitted Diagnoses by Participating Institutions	Number	Assessment
Mycosis fungoides with large cell transformation	1	Concordant
Mycoses fungoides	4	
Mycosis fungoides, tumour stage	2	
Cutaneous T cell lymphoma	2	
T cell lymphoma suggestive of Mycoses Fungoides. Comment: Need to obtain clinical history and further immunohistochemical stain to exclude secondary cutaneous involvement by lymphoma.	1	

EDUCATIONAL NOTES:

1) Section from the left thigh punch biopsy shows diffuse dermal infiltration by large neoplastic lymphoid cells arranged in solid sheets. The cells display moderate to markedly pleomorphic vesicular nuclei with prominent multiple nucleoli. The cytoplasm is eosinophilic and ample in amount. Mitotic figures are frequently seen.
   Occasional histiocytes and small reactive lymphocytes are appreciated in the background.
   The overlying epidermis shows marked acanthosis and parakeratosis with prominent lymphocyte epidermotropism and Pautrier microabscesses. No angio-invasion or angio-destruction is seen.
2) Immunohistochemistry study shows the neoplastic lymphoid cells are immunoreactive (+) for CD2, CD3 and CD5, with aberrant loss in CD7 and CD8. CD4 is positive (+) in a significant number of cells. CD30, ALK-1 and CD20 are negative (-). The proliferative index as estimated by Ki67 is high (>90%).
3) The evolution of patches and plaques followed by tumoral stage further supports the diagnosis of large cell transformation Mycosis fungoides (MF).
   Transformation MF is defined by: -
   1. Presence of 25% blastic cells (large cells, 4x reactive lymphocytes).
   2. Discrete tumour cell nodule.
   CD30 positive cells are only seen in ~ 30-50% of cases and is not required in making the diagnosis.
4) MF is defined as epidermotropic PCTCL of small to medium-sized T lymphocytes with cerebriform nuclei. The term should only be used for classical cases (i.e evolution of patches, plaques, and tumours + variants with a similar clinical course).
5) MF is the most common subtype of CTCL, accounting for approximately half of all cutaneous lymphomas. Patients with MF most often experience a protracted clinical course in which disease patches, plaques, and tumors develop over several years or even decades.
6) Some patients, however, undergo a process of large-cell transformation (LCT) which may be characterized by a more aggressive disease course and shortened survival. Early recognition of the clinical clues associated with LCT allows the dermatologist to diagnose this entity earlier and offer patients more aggressive treatment regimens.
7) The prognosis of LCT is reportedly worse than classic MF, and the median survival from diagnosis of LCT has been cited as 37 months for patients with LCT compared with 163 months

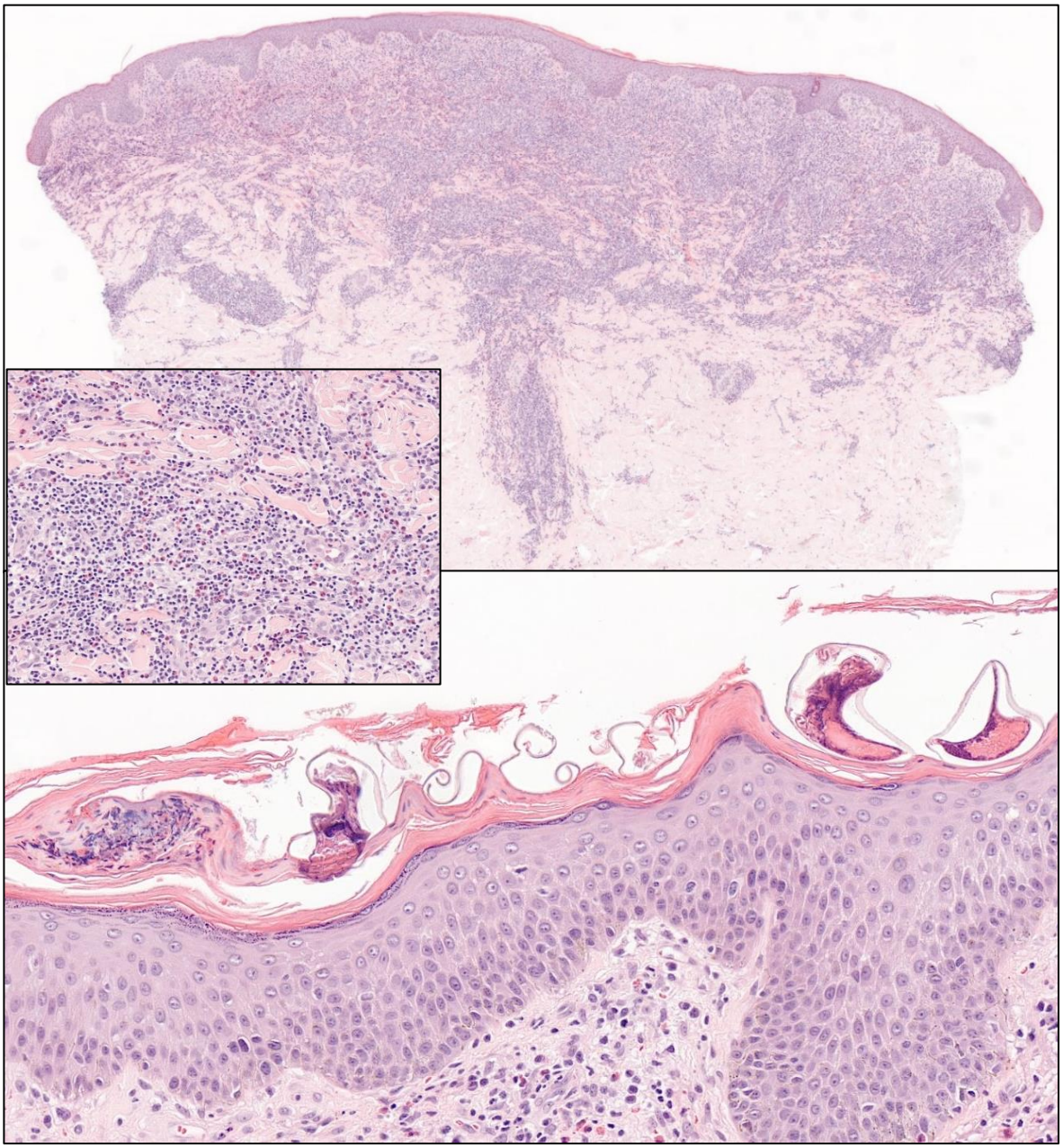
for those with more classic MF without LCT. Other studies have reported median survivals as low as 1 month.

REFERENCES:

- Mc Kee's Pathology of The Skin
- E. Olsen et al. Revisions to the staging and classification of mycosis fungoides and Sézary syndrome: a proposal of the International Society for Cutaneous Lymphomas (ISCL) and the cutaneous lymphoma task force of the European Organization of Research and Treatment of Cancer (EORTC). Blood (2007)
- B. Vergier et al. Transformation of mycosis fungoides: clinicopathological and prognostic features of 45 cases. French Study Group of Cutaneous Lymphomas. Blood (2000)
- WHO Classification of Skin Tumours. WHO Classification of Tumours, 4th Edition, Volume 11. Edited by Elder DE, Massi D, Scolyer RA, Willemze R

CASE 2

HISTORY: 17/Female/Vesicles over fingers
TARGET DIAGNOSIS: Scabies
MINOR DISCORDANT: Bullous pemphigoid, allergic contact dermatitis, fibreglass dermatitis
MAJOR DISCORDANT: -



Submitted Diagnoses by Participating Institutions	Number	Assessment
Scabies	5	Concordant
Eosinophilic dermatitis secondary to scabies.	3	Concordant
Dermal eosinophilia due to arthropod bite (scabies)	1	Concordant
Parasitic infection- Demodex	1	

EDUCATIONAL NOTES:

1) Scanning power view of scabies shows a pattern of an epidermal and wedge shaped dermal inflammatory process. The epidermis may show significant scale crust comprised of serous exudate, neutrophils, and eosinophils. There may be focal ulceration or erosion secondary to excoriation. The inflammatory infiltrate may show a wedge shaped or diffuse superficial and deep perivascular and interstitial pattern. Lymphocytes with numerous eosinophils are the rule with scattered superficial neutrophils seen in excoriated or impetiginized cases. Deep interstitial eosinophils are an important clue to an arthropod bite reaction.
2) The presence of scabies parts evident as solid pink eosinophilic fragments is diagnostic, representing the chitinous exoskeleton of the Sarcoptes scabiei mite. Pink pigtails can also be seen occasionally within the stratum corneum and are thought to represent remnants of the eggshell.
3) Differential diagnoses of scabies include the following conditions:
   - Bullous pemphigoid

   The urticarial phase of bullous pemphigoid can show similar features to scabies, though typically the infiltrate is superficial with lining up of the eosinophils along the basal layer of the epidermis and mild vacuolar change evident. It is important to remember that positive linear basement membrane staining on direct immunofluorescence testing has been reported in scabies infestation.
   - Allergic contact dermatitis

   The presence of spongiosis with vesiculation, while favouring allergic contact dermatitis, is also seen in scabies, and so cannot be relied upon as a differentiating factor. A superficial infiltrate with numerous eosinophils within the epidermis may serve as a clue.
   - Fibreglass dermatitis

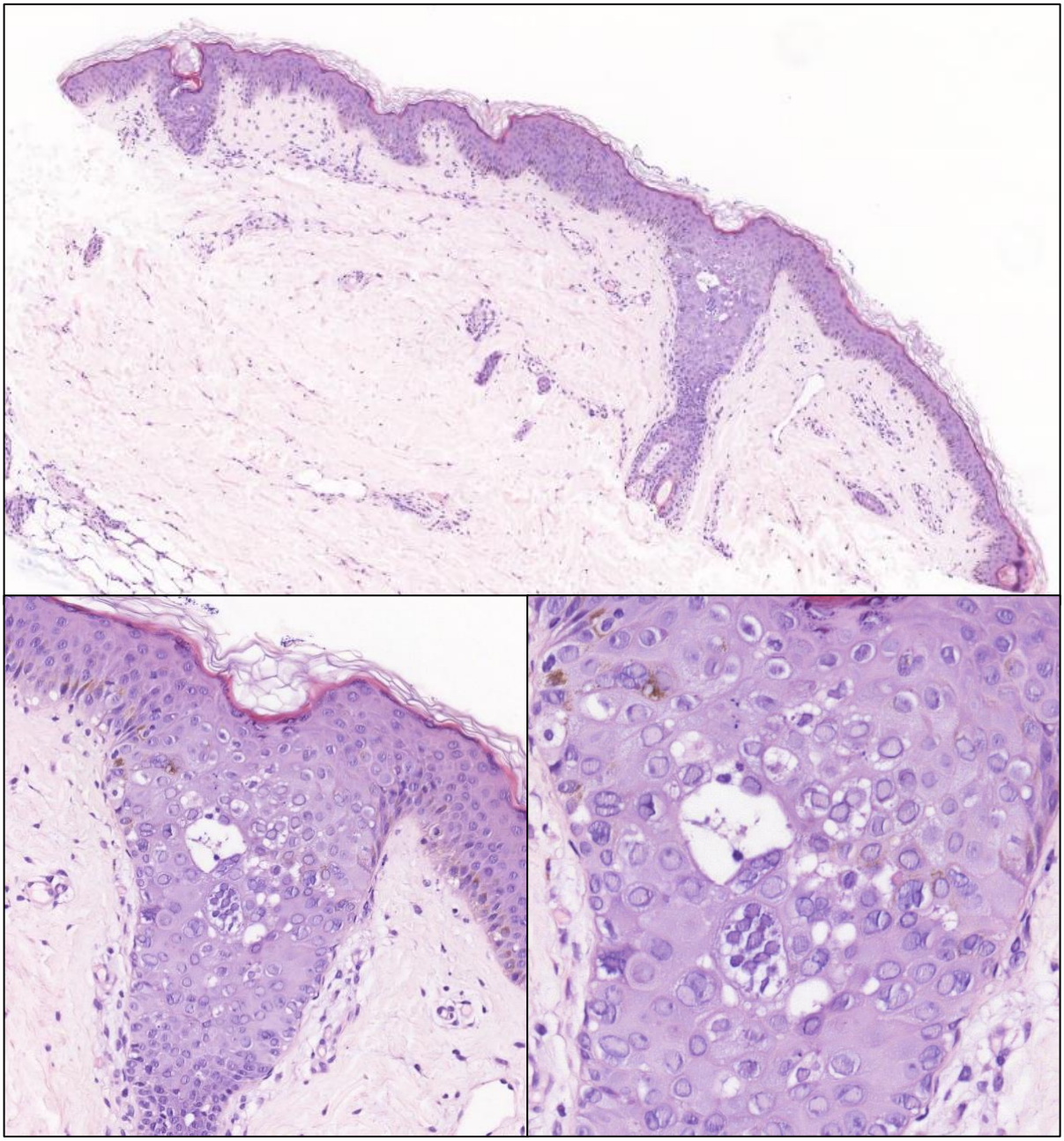
   Fibreglass can be identified within the stratum corneum. It largely causes irritant dermatitis with eosinophils, a less dominant feature in fibreglass dermatitis.

REFERENCES:

- Mc Kee's Pathology of The Skin

CASE 3

HISTORY: 25/Female / Small blisters over trunk.
TARGET DIAGNOSIS: Eczema herperticum
MINOR DISCORDANT: -
MAJOR DISCORDANT: Impetigo, hand-foot-and-mouth disease, eczema coxsackium, primary varicella infection, disseminated herpes zoster, disseminated molluscum contagiosum, acute generalized exanthematous pustulosis, dermatitis herpetiformis, cellulitis, and erysipelas



Submitted Diagnoses by Participating Institutions	Number	Assessment
Herpes simplex infection, possibility of eczema herpeticum needs to be excluded. Clinical correlation is advised.	1	Concordant
Herpes virus dermatitis	2	Concordant
Herpes simplex infection	2	Concordant
Herpes folliculitis	1	Concordant
Herpes infection	1	Concordant
Cutaneous Herpes simplex infection.	1	Concordant
Herpes virus infection	1	Concordant
Viral cytopathic effect consistent with Herpes simplex virus infection.	1	Concordant

EDUCATIONAL NOTES:

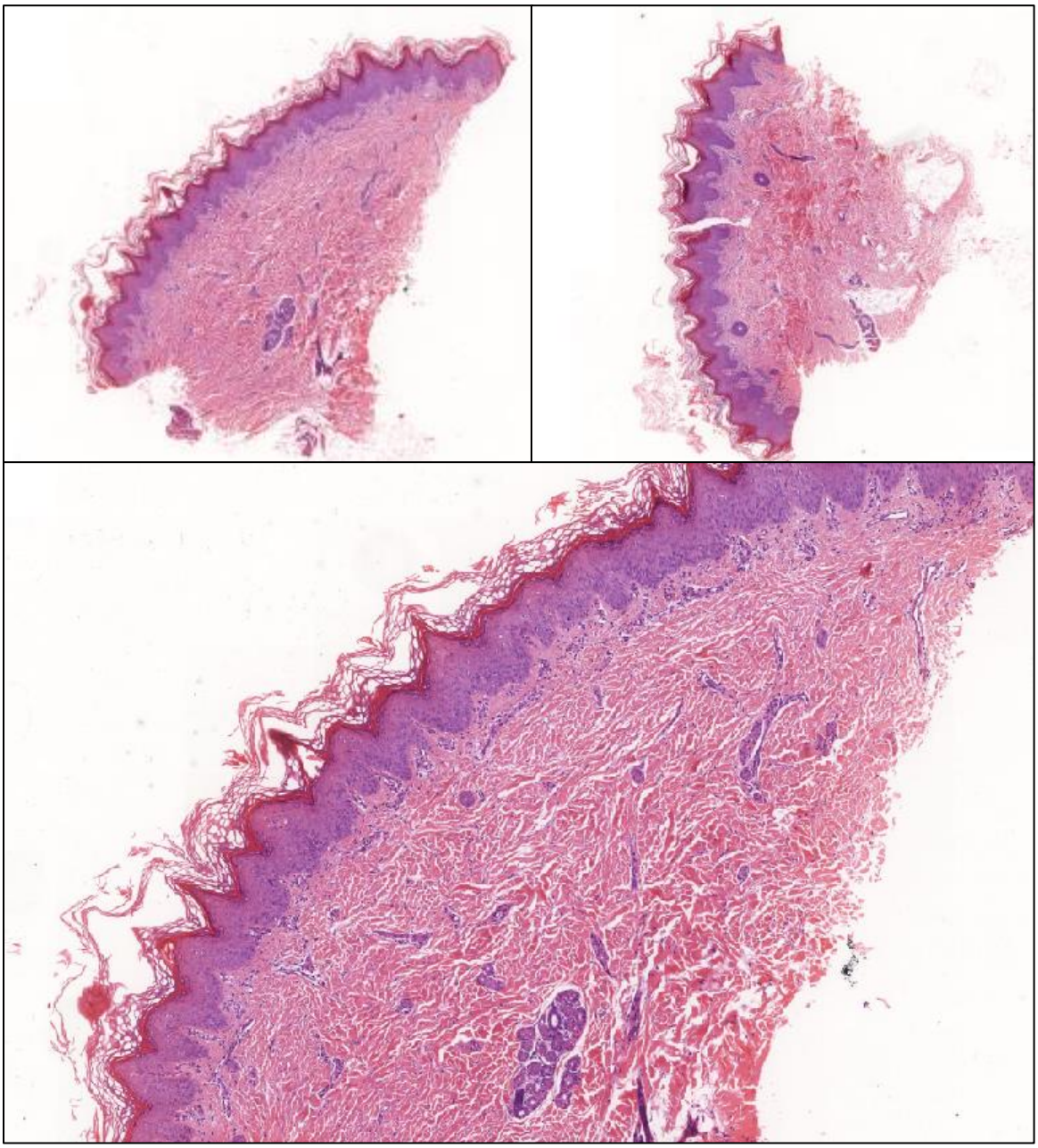
1) Eczema herpeticum is a disseminated viral infection characterized by fever and clusters of itchy blisters or punched-out erosions. It is most often seen as a complication of atopic dermatitis/eczema. Most cases of eczema herpeticum are due to Herpes simplex type 1 or 2.
2) Microscopic findings include multinucleated giant cells with ground glass nuclei due to intranuclear virus, more common at interface between ulcerated and nonulcerated areas. Intraepithelial vesicles containing rounded acantholytic keratinocytes are seen. The keratinocytes show viral cytopathic changes of ground glass nuclei, nuclear molding, and multinucleated giant epithelial cells. Well defined acidophilic inclusions can also be seen.
3) The differential diagnoses for eczema herpeticum include impetigo, hand-foot-and-mouth disease, eczema coxsackium, primary varicella infection, disseminated herpes zoster, disseminated molluscum contagiosum, acute generalized exanthematous pustulosis, dermatitis herpetiformis, cellulitis, and erysipelas.
4) Misdiagnosis of EH can lead to delayed initiation of antiviral treatment and subsequent complications. Diagnostic clues that favor EH are painful lesions, monomorphic size of the lesions, and characteristic "punched-out" erosions in areas of pre-existing atopic dermatitis. Unlike herpes zoster, EH does not respect dermatomal boundaries.

REFERENCES:

- Mc Kee’s Pathology of The Skin
- Weedon’s Skin Pathology, 4th edition
- PathologyOutlines.com

CASE 4

History: 5-year-old male with hyperpigmented plaque at the lower limbs since 1 month old. Family history of rashes.
TARGET DIAGNOSIS: Acrokeratosis verruciformis
MINOR DISCORDANT: Linear epidermal nevi
MAJOR DISCORDANT: Verrucae vulgaris, Stuccokeratosis



Submitted Diagnoses by Participating Institutions	Number	Assessment
Acrokeratosis verruciformis	3	Concordant
Benign papillomatous lesion. Differential Diagnoses: 1. Acrokeratosis verruciformis 2. epidermal nevus.	1	Concordant
Hyperkeratosis, acanthosis, papillomatosis with church spire epidermal elevation consistent with Acrokeratosis verruciformis.	1	Concordant
Epidermal nevus	3	Concordant
Intradermal nevus	1	Discordant
Keratosis pilaris	1	Discordant

EDUCATIONAL NOTES:

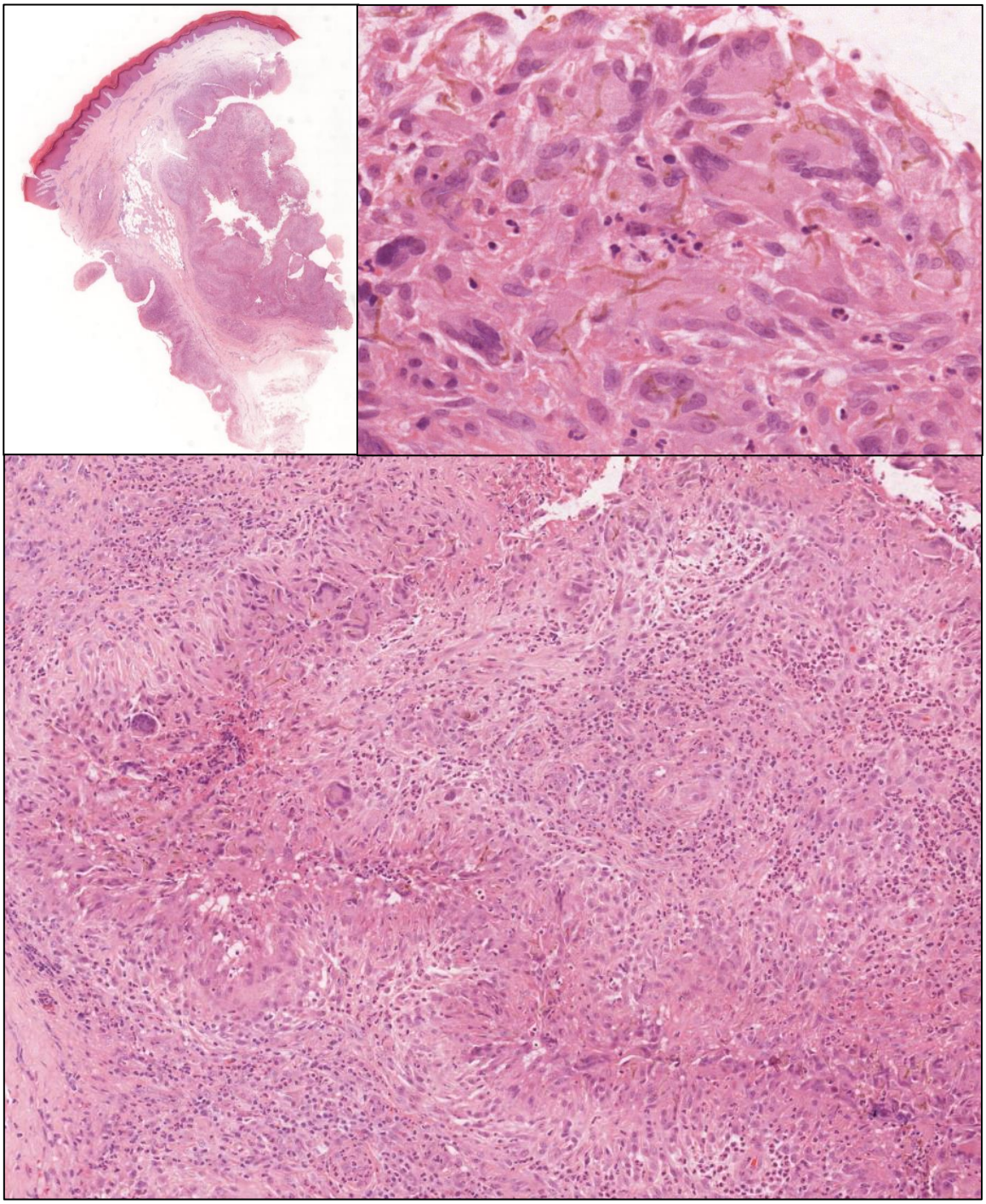
1) Section from the skin biopsy shows regular epidermal acanthosis, low papillomatosis and hyperkeratosis. No parakeratosis or epidermal vacuolation seen. The granular layer is prominent.
2) Acrokeratosis verruciformis is a rare dermatosis with an autosomal dominant mode of inheritance. The disease presents in infancy or early childhood as dry, rough, brownish or skin coloured verrucoid, keratotic papules, located particularly on the back of the hands and feet, and on the knees and elbows. Keratotic punctate pits are found on the palm and soles.
3) The lesions are acanthotic with prominent granular cell layer, typically showing a 'church spire' appearance. There is usually moderate to marked hyperkeratosis. Parakeratosis is not a feature.
4) Lesions identical to those of Acrokeratosis verruciformis develop in a significant number of patients with Darier's Disease. Steps section sometimes reveal acantholytic dyskeratosis in those cases associated with Darier's Disease

REFERENCES:

- Mc Kee's Pathology of The Skin
- Weedon's Skin Pathology, 4th edition

CASE 5

History: 47-year-old Indonesian man with crusted nodule on the right leg.
TARGET DIAGNOSIS: Chromoblastomycosis
MINOR DISCORDANT:
MAJOR DISCORDANT:



Submitted Diagnoses by Participating Institutions	Number	Assessment
Chromoblastomycosis	2	Concordant
Chronic granulomatous inflammation secondary to chromoblastomycosis	1	Concordant
Chronic granulomatous inflammation secondary to dematiaceous fungi. Differential diagnoses: 1. Phaeohyphomycosis 2. Chromoblastomycosis. To correlate with fungal culture.	1	Concordant
Granulomatous inflammation consistent with Chromoblastomycosis	1	Concordant
Granulomatous inflammation associated with fungal infection suggestive of chromoblastomycosis	1	Concordant
Subcutaneous mycosis, consistent with chromoblastomycosis	1	Concordant
Chronic granulomatous inflammation secondary to pigmented fungal infection.	1	
Phaeohyphomycosis	2	

EDUCATIONAL NOTES:

1) Section from the punch skin biopsy shows overlying skin with pseudoepitheliomatous hyperplasia and dermis infiltrated by epithelioid histiocytes and multinucleated giant cells forming granuloma. Lymphocytes and plasma cells accompany chronic inflammatory cells. Within the cytoplasm of the multinucleated giant cells one can appreciate pigmented fungal sclerotic bodies or also known as Medlar bodies or copper bodies. The fungal bodies can be highlighted by PAS and GMS stains. Ziehl-Neelsen and Wade-Fite stains can also be used to demonstrate the sclerotic bodies.
2) Clinical suspicion is important to alert pathologists to check for sclerotic bodies, which may be rare. Fungi appear in clusters that reproduce by equatorial septation rather than budding.
3) Chromoblastomycosis, a disease of the tropics caused by saprophytic, pigmented fungi, presents as chronic cutaneous and subcutaneous lesions, developing at the site of a previous transcutaneous trauma. The lesion starts as a scaly papule which slowly expands into a verrucous nodule or plaque. Rare presentations include ulcer, generalised skin lesions, lymphangitic nodules or hematogenous lesions. Secondary bacterial infection often causes foul smelling discharge, ulceration, and lymphadenitis. In long duration untreated lesions, squamous cell carcinoma and melanoma may develop.

REFERENCES:

- McKee's Pathology of the Skin, 4th edition 2012, Elsevier Limited
- Weedon’s Skin Pathology, Fourth edition
- Pathology Outlines.
- Chromoblastomycosis: an overview of clinical manifestations, diagnosis and treatment, Flavio Queiroz-Telles et al. Medical Mycology February 2009, 47 (Special Issue), 3- 15

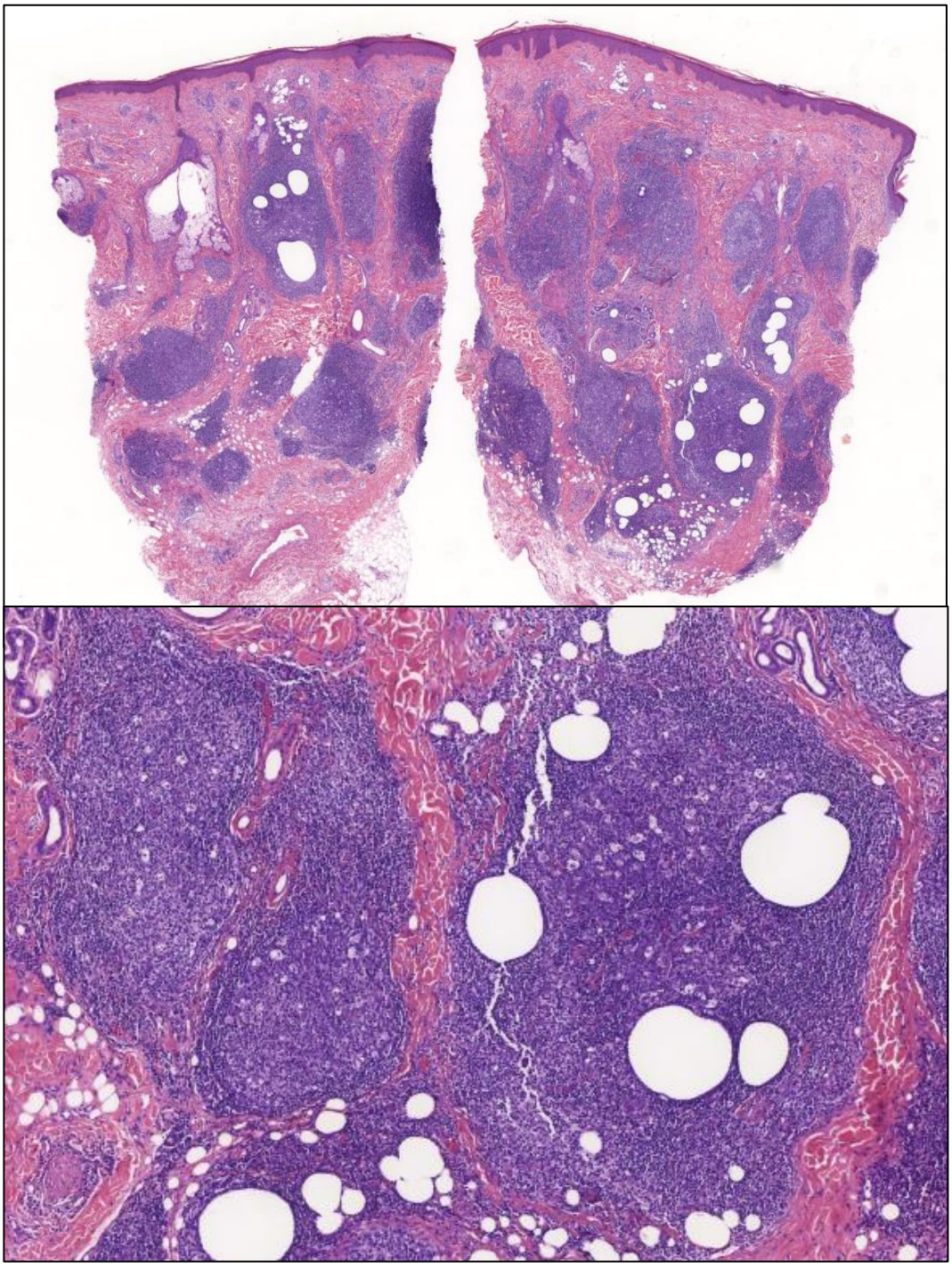
CASE 6

History: 60-year-old male with 1 year duration of itchy erythematous nodules and plaques over neck and scalp.

TARGET DIAGNOSIS: Lymphocytoma cutis (Synonyms: B-cell pseudolymphoma, B-cell cutaneous lymphoid hyperplasia, lymphadenosis benigna cutis and cutaneous lymphoplasia)

MINOR DISCORDANT: Lymphoid hyperplasia, Angiolymphoid hyperplasia with eosinophilia

MAJOR DISCORDANT:



Submitted Diagnoses by Participating Institutions	Number	Assessment
Lymphocytoma cutis	1	Concordant
Cutaneous lymphoid hyperplasia.	3	Concordant
Cutaneous lymphoid hyperplasia (pseudolymphoma)	1	Concordant
Cutaneous lymphoid hyperplasia. Comment: For further immunohistochemical stains to exclude lymphoma.	1	Concordant
Cutaneous pseudolymphoma (needs CD3 and CD20 IHC for confirmation)	1	Concordant
Dermal nodular lymphoid infiltrates, differentials include cutaneous lymphoid hyperplasia and low-grade lymphoma. Suggest for immunohistochemical stains to exclude low-grade lymphoma.	1	Concordant
Lymphoid hyperplasia	1	
Angiolymphoid hyperplasia with eosinophilia (Epithelioid hemangioma)	1	

EDUCATIONAL NOTES:

1) The skin biopsy on low power examination reveals a diffuse, vague nodular infiltrate that fills the dermis and involves the subcutis. There is moderate to marked nodular lymphoid infiltrates which tend to be perivascular and periadnexal in distribution within the dermis and subcutis. A grenz zone is present. The B cell lymphoid infiltrates are composed of variable sizes of primary and secondary follicles in which some have reactive and polarized germinal centres. The germinal centres are comprised of an admixture of centroblasts, centrocytes and tingible body macrophages. The mantle zones are prominent and polarized. The interfollicular areas are populated by polymorphic infiltrates of small lymphocytes, histiocytes, plasma cells and occasional eosinophils. The overlying epidermis is within normal limits. There is no evidence of malignancy.
2) Distinction between primary cutaneous follicle center cell lymphoma and primary cutaneous marginal zone B-cell lymphoma requires IHC workup due to overlap of features. Immunohistochemical confirmation (IHC) as well as clinical correlation are recommended in this case.
3) Recommended IHC: Germinal centre markers [CD10 and BCL6] are limited within the germinal centres in which they demonstrate lack of BCL2 expression. Kappa and lambda show no clonality. There is no significant cluster of plasmacytoid cells present in CD123. Distinction between these disorders requires clinical correlation.
4) The classical clinical presentation of a cutaneous B-cell lymphoid hyperplasia is erythematous or red brown to red-purple solitary nodules with a smooth surface. Idiopathic cutaneous B-cell pseudolymphoma probably constitutes the largest group and is most frequent on the face (cheek, nose, earlobe) (70%), chest, and upper extremities. Children and adults may be affected. The course of cutaneous B cell lymphoid hyperplasia varies. The lesions may resolve with or without treatment. In some instances, a precipitating cause can be identified. The clinical features depend to a certain extent on the situation in which the B-cell pseudolymphoma arises.

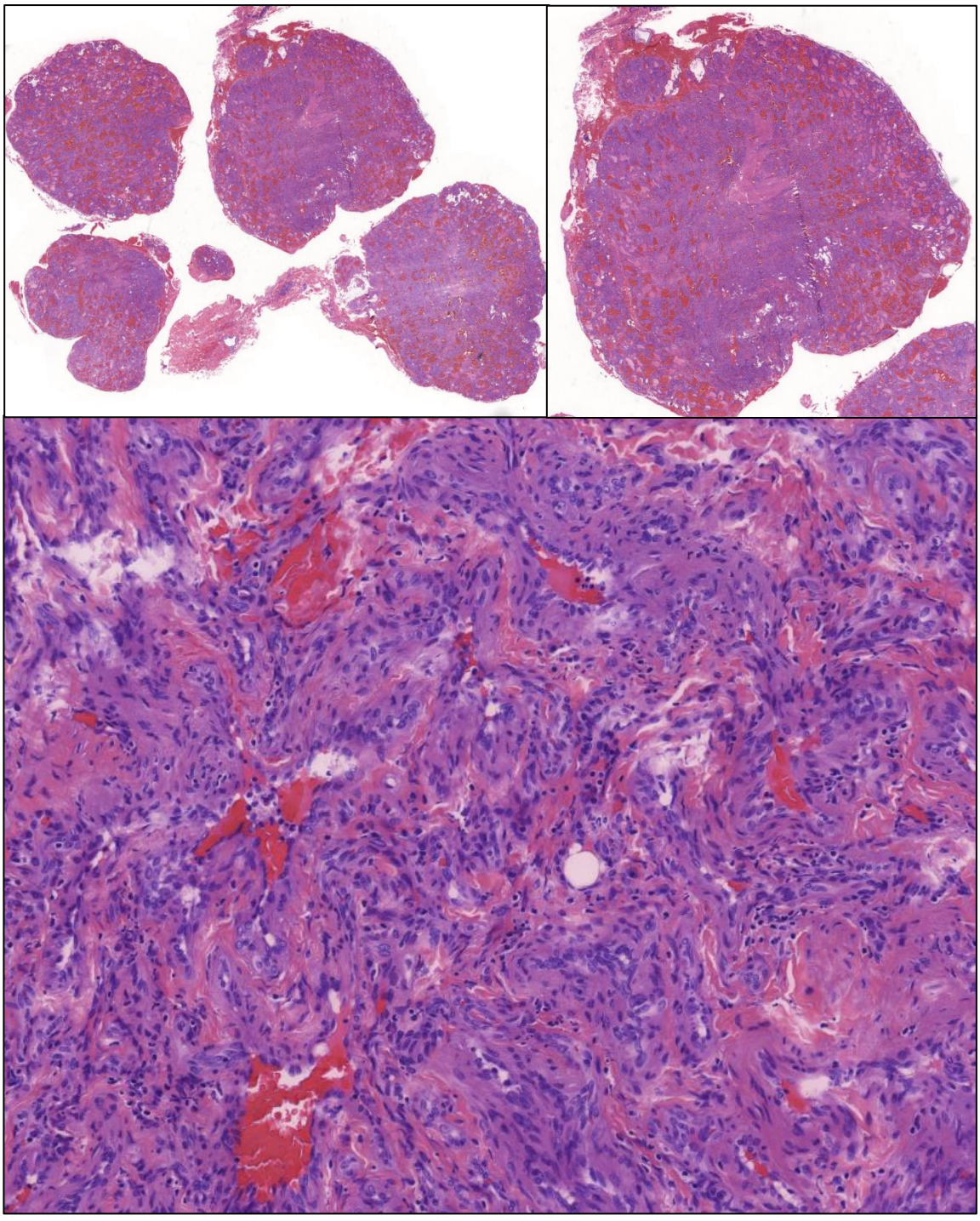
5) Various stimuli may induce lesions of cutaneous B cell lymphoid hyperplasia, including insect bites,persistent nodules of scabies, drugs(antidepressant therapy), vaccinations, injections for hyposensitization and tattoos. Cases of cutaneous B cell lymphoid hyperplasia are often associated with infection by Borrelia burgdorferi. In many cases however, a precise cause is not found.

REFERENCES:

- McKee's Pathology of the Skin, 4th edition 2012, Elsevier Limited
- Weedon’s Skin Pathology, Fifth edition
- Barnhill’s Dermatopathology Review

CASE 7

HISTORY: 49-year-old female with lesion over the back.
TARGET DIAGNOSIS: Myopericytoma
MINOR DISCORDANT:
MAJOR DISCORDANT:



Submitted Diagnoses by Participating Institutions	Number	Assessment
Benign vascular lesion, in favour of myopericytoma	1	Concordant
Benign vascular lesion, with differentials include hemangioma, angioleiomyoma, myopericytoma or hamartoma.	1	Concordant
Haemangioma	1	
Spindle cell hemangioma	1	
Cavernous haemangioma	1	
Haemangioma, features are favouring spindle cell haemangioma.	1	
Benign vascular neoplasm.	1	
Benign vascular tumour, favour cherry haemangioma.	1	
Benign vascular tumor suggestive of sinusoidal hemangioma	1	
Angiomyolipoma.	1	

EDUCATIONAL NOTES:

1) Myopericytoma is a rare type of soft tissue tumour that originates from pericytes which are cells that surround blood vessels and play a role in regulating blood flow.
2) The skin biopsy shows a well circumscribed but non-encapsulated nodule of cytologically bland oval to spindled cells with concentric multilayered perivascular growth. In the section, uniform ovoid cells with concentric onion skin -like perivascular growth is appreciated. The cytoplasm is eosinophilic, with myoid features. The nuclei are round to ovoid. The cellularity varies greatly, as does the vasculature. The presence of thin-walled communicating vessels may mimic solitary fibrous tumour, while lesions with thicker vessels result in an appearance reminiscent of angioleiomyoma. Histologically myopericytoma can be differentiated from other soft tissue tumours by their perivascular arrangement of cells and lack of atypia and mitotic activity.
3) Myopericytoma typically presents as a solitary, painless slow-growing mass, most commonly occurring in middle-aged adults (mainly in the fifth decade) with a predilection for the limbs, particularly the distal lower limb followed by the head and neck (including the oral cavity). Exceptional tumors may occur in the kidney, lung, parotid gland, within the cranium, or in the thoracic spine. Males are more frequently affected than females. Lesions are small (less than 2 cm in diameter), long-standing, usually asymptomatic, and may be single or (less frequently) multiple. Rarely, tumors are painful. Recurrence is rare and frequently represents either persistence or the development of a new tumor. Very rare malignant examples of myopericytoma have been described which have aggressive behavior.
4) Differential diagnosis includes myofibroma, angioleiomyoma and solitary fibrous tumour. Myopericytoma was considered to form a spectrum with myofibroma, angioleiomyoma and glomus tumour, but recent studies suggest these are rather distinct at the molecular level, albeit having significantly overlapping morphological and phenotypic features. Recurrent PDGFRB alterations have been documented, similar to those seen in infantile myofibromatosis/myofibroma, supporting a close pathogenetic link between the entities. A small number of myopericytomas show BRAF(V600E) mutations and anti-BRAF(V600E) agents

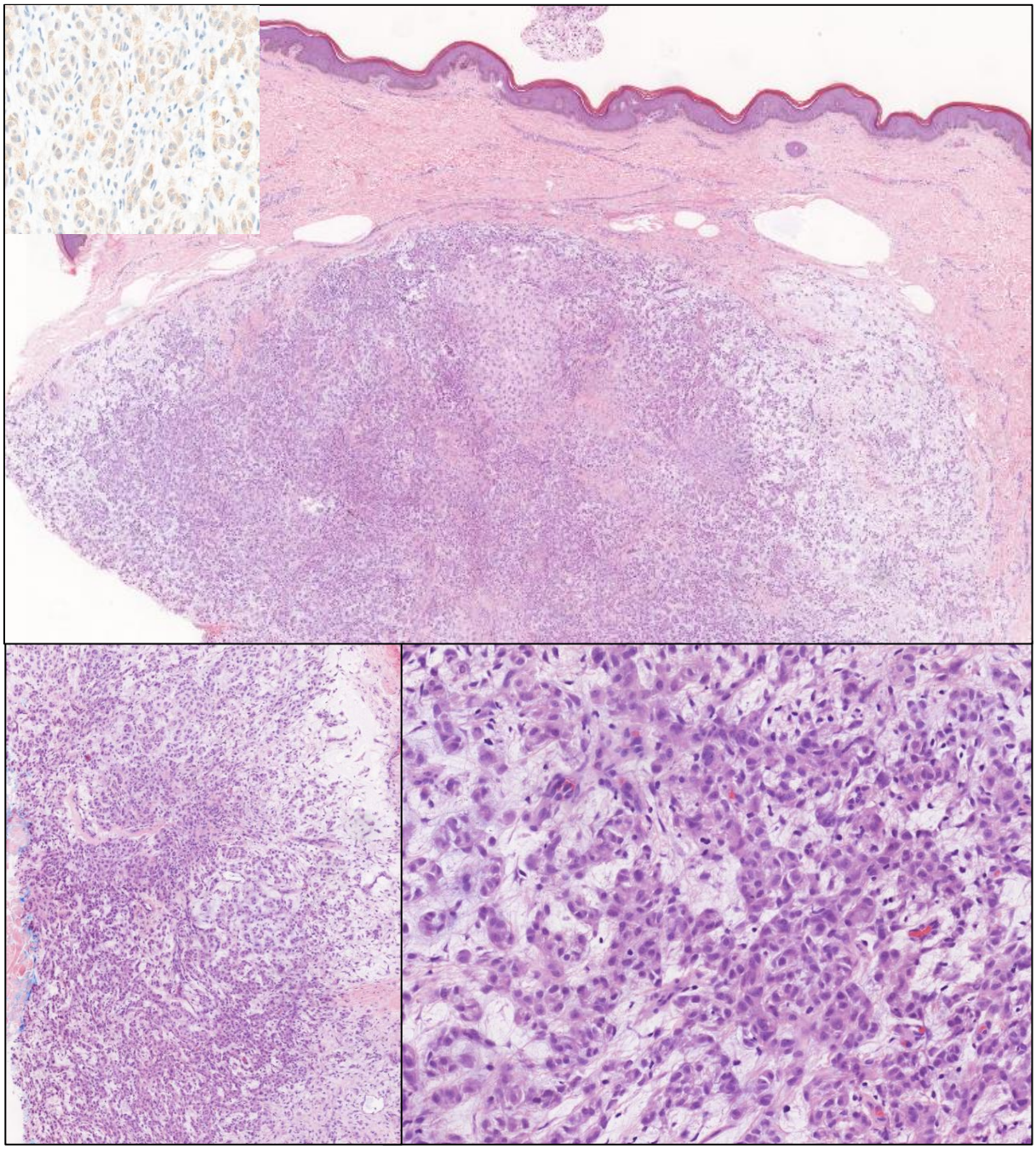
have been suggested as a treatment for multifocal, infiltrative and recurrent tumor bearing this mutation.

REFERENCES:

- McKee's Pathology of the Skin, 4th edition 2012, Elsevier Limited
- WHO Classification of Skin Tumours 5th Edition

CASE 8

HISTORY: 68-year-old Indian lady ? dermatofiroma
TARGET DIAGNOSIS: Epithelioid fibrohistiocytoma
MINOR DISCORDANT: -
MAJOR DISCORDANT: -



Submitted Diagnoses by Participating Institutions	Number	Assessment
Epithelioid fibrous histiocytoma.	8	Concordant
Epithelioid dermatofibroma	1	Concordant
Benign mesenchymal tumour with epithelioid differentiation possible epithelioid fibrous histicytoma, with differential of epithelioid inflammatory myofibroblastic tumour.	1	Concordant

EDUCATIONAL NOTES:

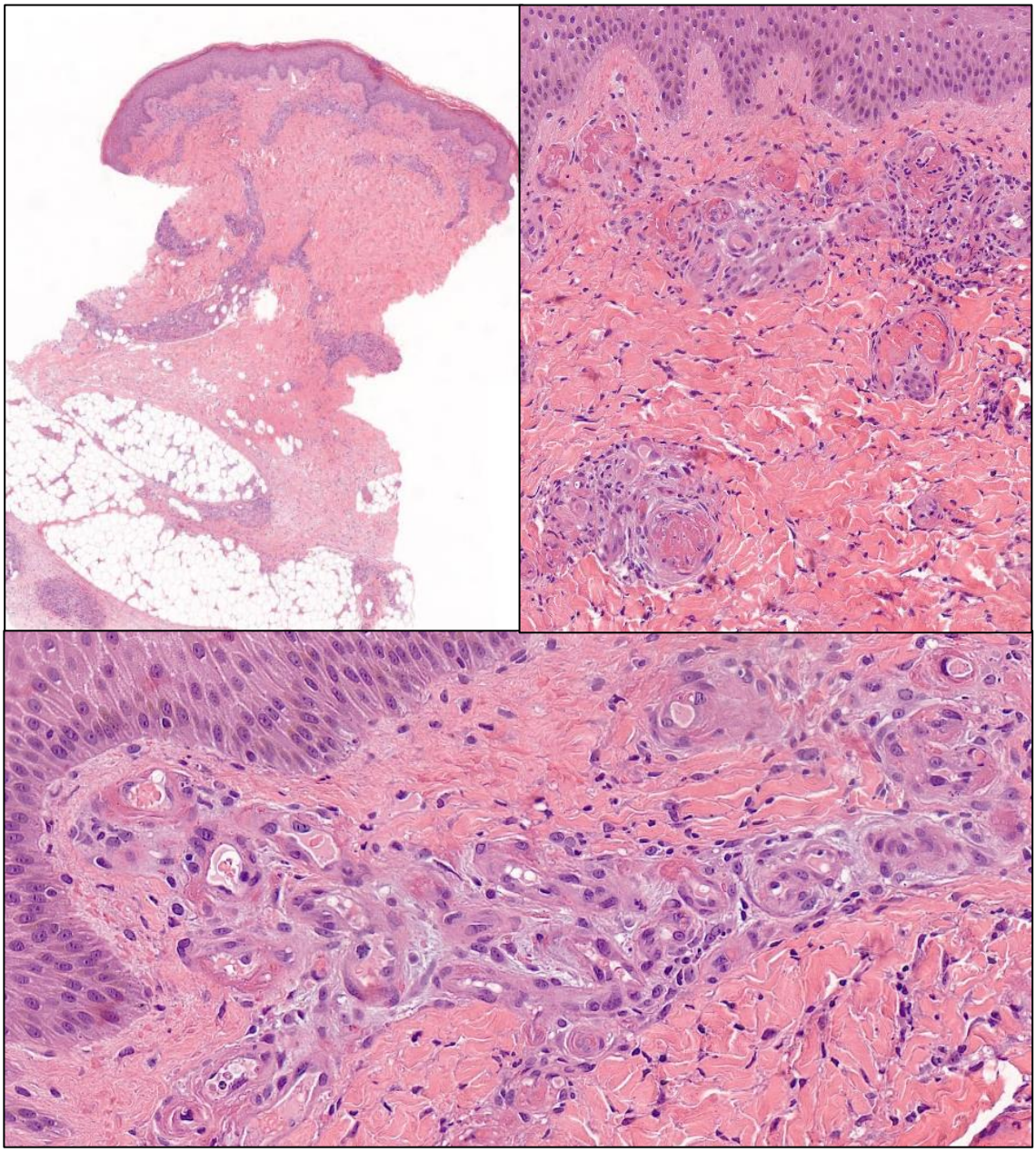
1) Section from the excision biopsy of the skin lesion shows a well circumscribed intradermal proliferation of epithelioid cells arranged in sheets. Individual cells show abundant eosinophilic cytoplasm with round vesicular nuclei and prominent nucleoli. Some cells display some nuclear atypia. There is no atypical mitosis observed.
2) Immunohistochemical studies show that the cells are reactive toward ALK (anaplastic lymphoma kinase).
3) Epithelioid fibrous histiocytoma (EFH) is a rare lesion believed to arise from dermal microvascular unit fibroblasts and dendritic histiocytes. EFH has long been considered a morphologic variant of benign fibrous histiocytoma (dermatofibroma), with prominent epithelioid cytomorphology that can mimic both vascular and melanocytic neoplasms. Recent molecular studies have identified the presence of recurrent anaplastic lymphoma kinase (ALK) gene rearrangements, a phenomenon that has not been described in benign fibrous histiocytoma. These new molecular findings highlight the uniqueness of this rare tumor and may prove useful as a diagnostic tool for differentiation from other histologic mimics.
4) EFH usually presents as polypoid red nodules or flesh-coloured nodules which can be confused with pyogenic granuloma. The classic histologic features of EFH are exophytic, well circumscribed tumours, consisting of an intradermal proliferation of relatively uniform epithelioid to polygonal cells with vesicular nuclei and moderate amounts of eosinophilic or amphophilic cytoplasm. The tumour cells are frequently binucleate. Immunohistochemically, the cells are CD34 positive, factor XIIIa positive, S100 negative. EMA and ALK expression are seen in 65% and 90% of cases respectively.

REFERENCES:

- McKee's Pathology of the Skin, 4th edition 2012, Elsevier Limited
- Weedon's Skin Pathology, Fourth edition
- WHO Classification of Skin Tumours, 4th Edition
- Felty CC, Linos K. Epithelioid fibrous histiocytoma: a concise review. Am J Dermatopathol. 2019;41:879–883

CASE 9

History: 23 years old female presented with recurrent painful ulcerated lesion both lower legs.
TARGET DIAGNOSIS: Livedoid vasculopathy (Synonyms: Atrophie blanche, livedo vasculitis, Livedoid vasculitis, segmental hyalinizing vasculitis)
MINOR DISCORDANT: Leukocytoclastic vasculitis, small vessel vasculitis, vasculitis
MAJOR DISCORDANT: -



Submitted Diagnoses by Participating Institutions	Number	Assessment
Livedoid vasculopathy	2	Concordant
Atrophie blanche (livedoid vasculopathy)	3	Concordant
Vasculopathic lesion suggestive of livedoid vasculopathy.	1	Concordant
Thrombotic vasculopathy consistent with livedoid vasculopathy (atrophie blanche)	1	Concordant
Segmental hyalinizing vasculitis	2	Concordant
Vasculitis	1	

EDUCATIONAL NOTES:

1. Livedoid vasculopathy (LV) is a common vasculopathic condition which preferentially involves the cutaneous small blood vessels of the lower extremities, usually occurs in the elderly particularly females. The lesions consist of one or more irregular, smooth and atrophic plaques surrounded by a hyperpigmented border and telangiectases.
2. Small ulcerative lesion of 2 types may precede it. The small lesion (1 -5 mm diameter) consists of very painful erythematous purpuric areas that ulcerate and heal slowly. Chronic large areas of ulceration up to 5 mm in diameter, which after a long period of time, heal to form extensive areas of small, white, punched out, atrophic stellate scars. Features of livedo reticularis are frequently seen in the background.
3. There is seasonal variation, typically worsening in the summer months. Lesions recur at periodic intervals and are predominantly located at the lower legs and ankles and the dorsal surface of the feet. Occasionally found around the forearms, fingers and hands. The disease is often associated with signs of venous stasis.
4. Although previously considered to be caused by vasculitis, LV is best regarded as a manifestation of thrombogenic vasculopathy in which occlusion of the small dermal vessels by fibrin thrombi is the primary event.
5. The pathogenesis is not well understood but it appears the ischaemia may be the end result. Although increased hydrostatic pressure contributes to the development of this condition, the finding of immunoglobulin (usually IgM, less often IgG and IgA) and complement within the blood vessel walls raises the possibility of an immunological pathogenesis. It has been associated with a localized defect of tissue plasminogen activator from the vessel walls. The location of the lesions suggests that trauma may also play some role in the development of the lesions.
6. Patients with LV and disorders of coagulation such as factor V Leiden mutation, raised anticardiolipin antibodies, deficiency in protein C or protein S, prothrombin mutation and raised level of fibrinopeptide A have been described, suggesting that at least in some patients, an underlying coagulopathy is the basis of the disorder.
7. Histopathology: Early and ulcerative lesions are characterized by the presence of increased numbers of dermal vessels containing fibrin within their walls in addition to intraluminal fibrin plugs in the upper and mid dermis. The fibrin plugs are diastase-resistant and periodic acid-Schiff (PAS) positive.

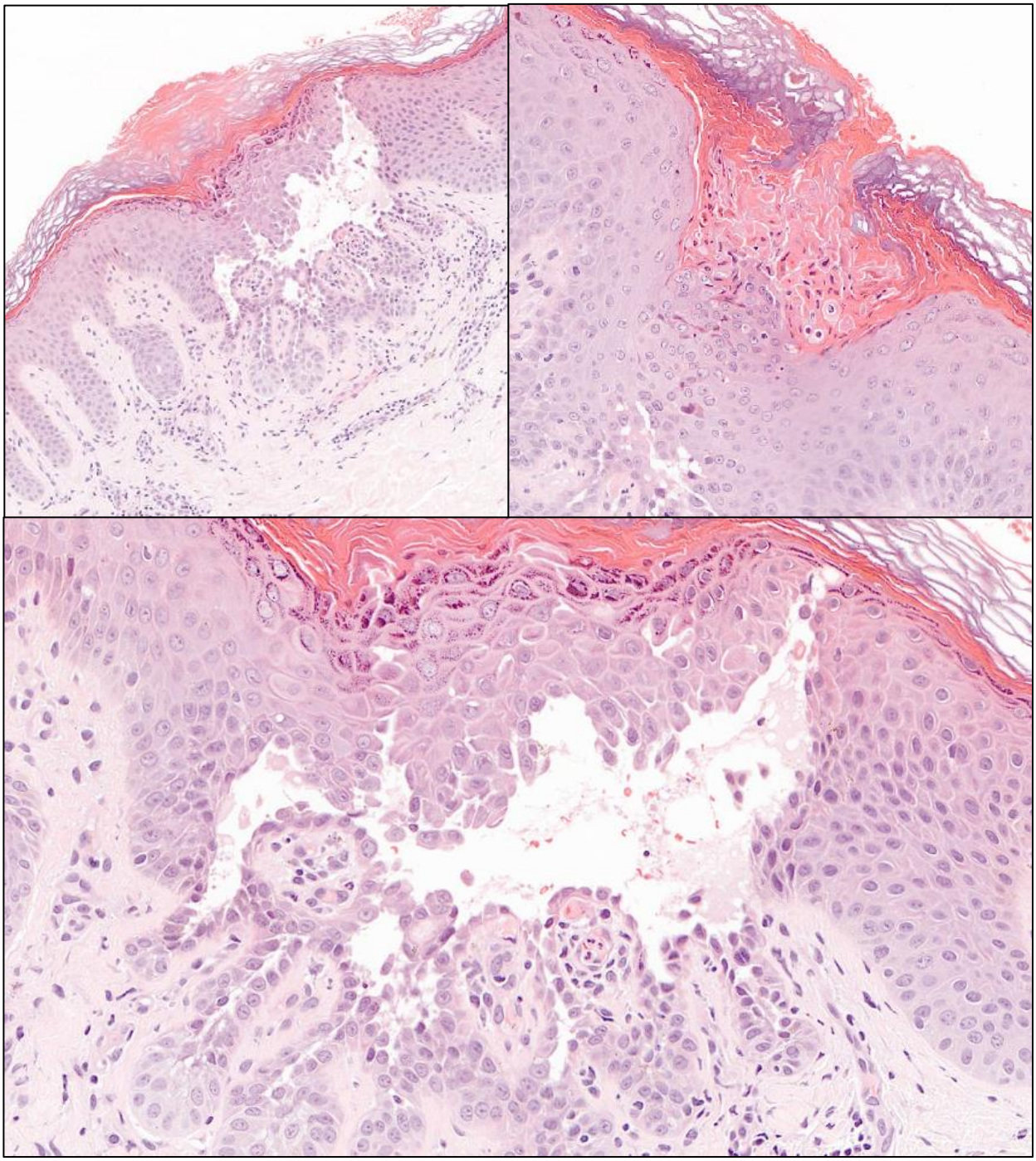
8. Inflammatory destruction of blood vessels is not a feature, and this disorder is not a true vasculitis. Variable degrees of red blood cell extravasation are evident and haemosiderin pigment is often present in the upper dermis.
9. A perivascular lymphohistiocytic infiltrate of varying intensity is usually found and dermal mast cells are often increased in number, but there is no vasculitis. Neutrophils, if present are usually sparse and confined to the infarcted upper dermis and ulcer base.
10. Ulcerative lesions show infarction of the superficial dermis and epidermis. A thin parakeratotic layer is present overlying the infarcted or atrophic epidermis. The epidermis adjacent to the ulceration may be spongiotic.
11. In the fully established atrophic plaque, in addition to the thickening and hyalinization of vessels in the dermis with some endothelial cell oedema and proliferation, fibrinoid material may also be present in the vessel walls. The epidermis is atrophic, and the dermis shows dense scleroderma-like scarring.
12. The histological features in the appropriate clinical setting are diagnostic. Coagulopathies are associated with intraluminal fibrinoid plugs but not extensive fibrinoid change of the vessel wall. LV shows some of the features seen in stasis dermatitis such as clustering vessels in the superficial dermis. However, uncomplicated stasis does not show fibrinoid change.

REFERENCES:

- McKee's Pathology of the Skin, 4th edition
- Weedon's Skin Pathology 3rd Edition
- Pearls and pitfalls in Inflammatory Dermatopathology, Asok Biswas 2017

CASE 10

History: 42-year-old female with 1 year history of itchy rashes on scalp, face, and neck.
TARGET DIAGNOSIS: Darier disease
MINOR DISCORDANT: Warty dyskeratoma, Hailey-hailey disease, Pemphigus vulgaris, Grover disease
MAJOR DISCORDANT: Superficial pemphigus



Submitted Diagnoses by Participating Institutions	Number	Assessment
Darier disease	5	Concordant
Acantholytic dyskeratosis consistent with Darier disease	1	Concordant
Suprabasal blister with dyskeratosis, differential diagnosis Darier's disease and Grover's disease	1	Concordant
Suprabasillar acantholysis. Differential diagnoses include Darier disease, Grover disease, Hailey- Hailey disease and Pemphigus vulgaris. To correlate with IF study.	1	Concordant
Intraepidermal acantholysis, consistent with pemphigus, differentials include pemphigus foliaceus and pemphigus vulgaris. Immunofluorescence required to confirm.	1	Minor Discordance
Bullous pemphigoid	1	Minor Discordance

EDUCATIONAL NOTES:

1) Section shows acanthotic epidermis with suprabasal acantholysis and clefting. There is associated dyskeratosis forming corp ronds and grains. Immunofluorescence study is negative.
2) Darier's disease, which is characterized by abnormal keratinocyte adhesions, is a rare hereditary disorder, usually transmitted in an autosomal dominant pattern. It is usually ascribed to a defect in the synthesis, organization, or maturation of the tonofilament-desmosome complexes. The sex incidence is equal, although males appear to be more severely affected than females. The lesions are frequently itchy and less commonly painful. They are characterized by greasy, crusted, keratotic yellow brown papules and plaques found particularly on the 'seborrheic' areas of the body.
3) The histological features of Darier's disease depend upon a variable interplay between acantholysis and abnormal keratinization(dyskeratosis), the acantholysis resulting in suprabasal cleft formation and dyskeratosis manifesting as corps ronds and grains of Darier. Corp rond is a rounded keratinocyte in superficial spiny and granular layer with basophilic/pyknotic nucleus, perinuclear halo and often a rim of eosinophilic cytoplasm. Grain is an elongated keratinocyte in the stratum corneum with small basophilic nuclei and intensely pink cytoplasm, appear as plump parakeratosis and may form tiers.

REFERENCES:

- McKee's Pathology of Skin 4th Edition
- Weedon's Skin Pathology