IADVL

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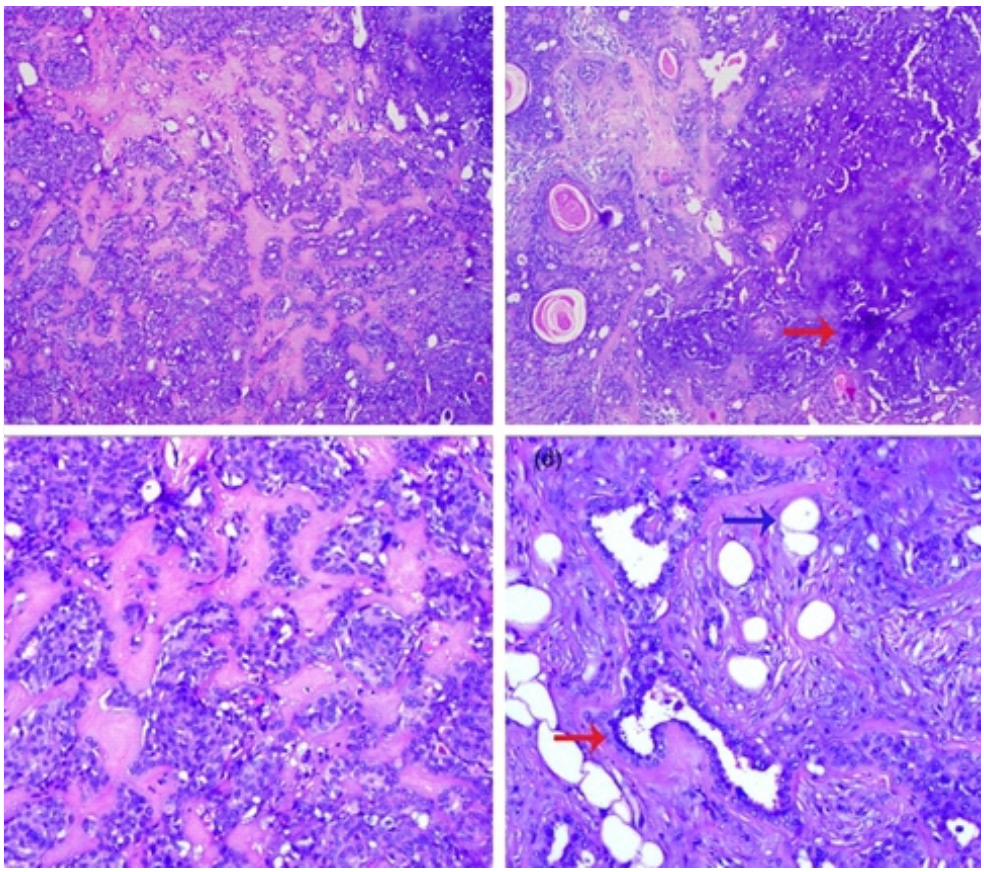

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FROM THE DESK OF THE EDITORIAL TEAM

Dr. Nandakumar Gopinathan Nair
SIG Dermatopathology Co-ordinator

Dr. Chirag Desai
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Dr. Geeti Khullar
SIG Dermatopathology Member

Dear All,

Greetings from the editorial team of SIG Dermatopathology newsletter.

As we are again fighting this second wave of the coronavirus pandemic with all our might and many of us are locked in our houses, it's time again to revise and revisit the academics in whichever way possible like webinars, discussions and SIG newsletters.

The highlight of this year's dermpath newsletter is that we invited articles from finest faculties to bring to you, a very interesting and enriching newsletter. The topics range from confocal microscopy to dermatopathology in social media, from digital imaging to fellowship experiences and interesting academic cases and from research options in dermatopathology to how to approach dermatopathology from exam view point. This newsletter has something for everyone, from post graduates to seasoned clinical practitioners.

So, let's drench ourselves in academics and learn from the experts in the field. We thank the IADVL Academy especially Dr.Deepika Pandhi maám for all the support for our endeavors and all the authors of the articles without whose contribution, this newsletter wouldn't have come to life.

Stay safe everyone.

Best wishes,

Dr. Nandakumar Gopinathan Nair

Dr. Chirag Desai

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Interesting case 1 – A skin coloured nodule on face

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Assistant Professor, AIIMS, Bhubaneswar

A 64-year-old female presented with a one-year history of slow-growing asymptomatic swelling on the right side of the face. It was not associated with an ulcer or discharge. Her medical history was unremarkable. The cutaneous examination showed a solitary 1cm x 1cm firm, nontender nodule with a mamillated surface over the right infra-orbital area (Figure 1). Other mucocutaneous, general, and systemic examinations were within normal limits. The lesion was excised and sent for histopathological examination. Histology revealed an atrophic epidermis and a well-circumscribed multilobulated deep dermal tumor surrounded by a fibrous capsule. The tumor lobules had epithelial components and stroma. The epithelial cells were round to oval and had abundant eosinophilic cytoplasm and round to oval basophilic nucleus. They were arranged in cords and nests and formed tubuloalveolar and ductal structures. A multicomponent matrix comprising chondroid, myxoid, and hyaline areas was evident. There was no cytological atypia, mitosis, or necrosis. Other features noted were apocrine decapitation, tadpole-like areas, mature fat cells, mucinous metaplasia, and keratocyst (Figures 2 and 3). A diagnosis of chondroid syringoma was made, and she was followed up for one year without any recurrence.

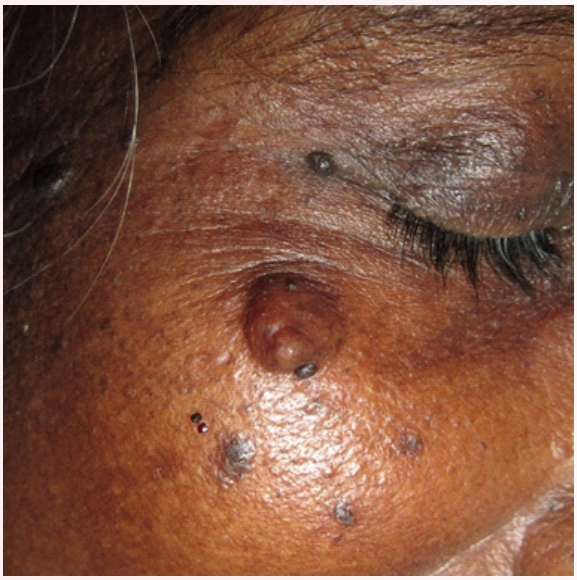

Figure 1: *Solitary firm, nontender nodule with a mamillated surface over the right infra-orbital area.*

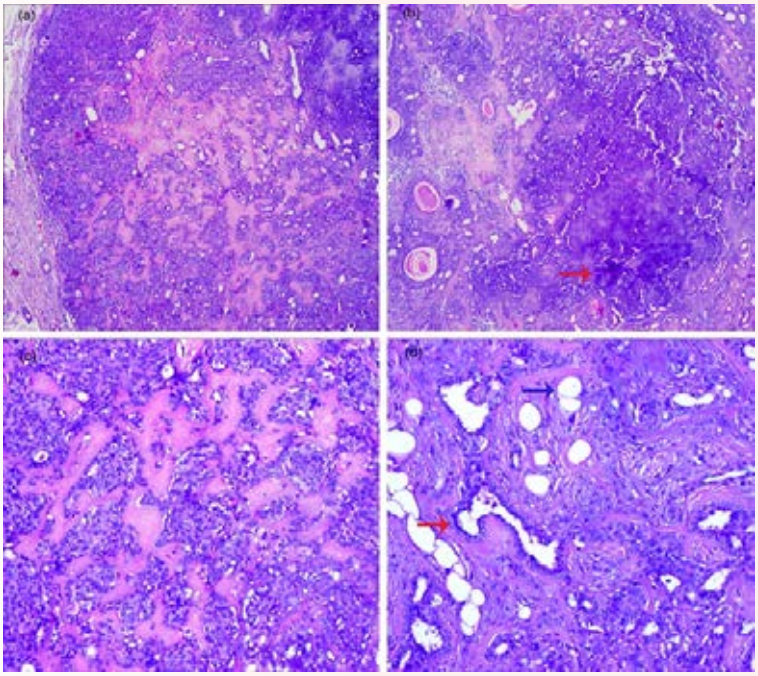

Figure 2: *(a) Histology shows tumor lobules with cords and nests of epithelial cells in a hyalinized to chondroid stroma (H & E, X50). (b) The characteristic homogenous bluish chondroid stroma (red arrow) (H & E, X50). (c) Cords and nests of epithelial cells in a densely collagenous, eosinophilic, and hyalinized stroma (H & E, X100). (d) Tubuloalveolar structures in a fibromyxoid stroma. Note the mature adipocytes (blue arrow) and apocrine decapitation (red arrow) (H & E, X100).*

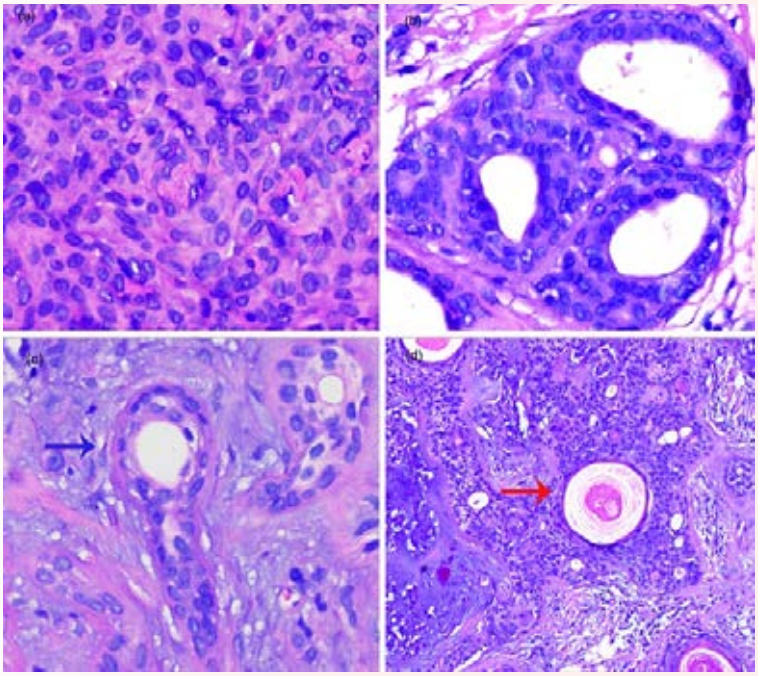

Figure 3: *(a) Epithelial cells with abundant eosinophilic cytoplasm and round to oval basophilic nucleus (H & E, X400). (b) Ductal structures are lined by two layers of cuboidal cells (H & E, X400). (c) Tadpole-like areas (blue arrow) (H & E, X400). (d) Keratocyst (red arrow) (H & E, X400).*

Chondroid syringoma, also called as mixed tumor of the skin, is a rare, slow-growing benign tumor of eccrine and, or apocrine origin. Middle-aged males in their fifties are commonly affected. The tumor has a predilection for the head and neck; nose, cheek, and upper lip are usually involved. Involvement of trunk, extremities, and genitalia are rare. [1]

It presents as a solitary, well-circumscribed, slow-growing, asymptomatic, firm, nontender, skin-colored, erythematous to bluish lobulated nodule of size 0.5cm – 3cm. [1] Giant variant with size > 3 cm has been rarely reported. [2] Ulceration is exceedingly rare. [3]

The clinical differential diagnoses of chondroid syringoma are many and will depend upon the color of the tumor and the skin color of the patient. For a skin-colored or erythematous nodule in a patient with skin of color, the differential diagnoses include sebaceous cyst, solitary neurofibroma, giant trichoepithelioma, pilomatrixoma, and hidradenoma. In fair-skinned patients, additionally, basal cell carcinoma and dermatofibroma can be considered as differential diagnoses.

The lack of specific clinical clues for chondroid syringoma requires a histopathological examination to reach a diagnosis. Chondroid syringoma can be apocrine, eccrine, or can have features of both. The scanning view shows a well-circumscribed multilobulated deep dermal or subcutaneous mass surrounded and separated by fibrous septa. The lobules constitute epithelial components and stroma. The former constitute cuboidal or polygonal cells with abundant eosinophilic cytoplasm arranged in cords and nests, as tubuloalveolar and ductal structures or distributed singly. Grossly dilated ducts with apocrine decapitation can be evident. The stroma can either be chondroid, myxoid, hyalinized, or mixed. Other features noted are clear cell change, mucinous metaplasia, foci of follicular and sebaceous differentiation, mature adipocytes, and foci of calcification and ossification. Features of cellular atypia, mitosis, and necrosis are characteristically absent. [1]

A proposed histopathological criterion requires the following five features for the diagnosis of chondroid syringoma: (i) Nests of cuboidal or polygonal cells; (ii) Ducts lined by one or two layers of cuboidal cells; (iii) Tubuloalveolar structures lined by two or more layers of cuboidal cells; (iv) A matrix of variable composition; and (v) The presence of keratocyst. [4]

A variant with atypical histopathological features and benign clinical course has been described. The atypical features include tumoral asymmetry, slightly infiltrative lower edge without capsular invasion, mild cytological atypia, and scattered multinucleated cells with pleomorphic and bizarre-looking cells. [5] The following histopathological features will help differentiate chondroid syringoma from its pathological mimics: the presence of serous and mucous acinar cells and the absence of cutaneous adnexal structures in pleomorphic adenoma of the salivary gland; no epithelial and myoepithelial elements in cutaneous chondroma; no true ducts and the presence of physalliferous cells in

parachordoma; and lack of chondroid matrix in hidradenoma papilliferum. Immunohistochemistry can be helpful in doubtful cases. The outer cells stain positive for mesenchymal markers such as vimentin and S-100 protein. The inner epithelial cell layer stain positive for epithelial markers like high and low molecular weight keratin (AE1/AE3), epithelial membrane antigen, carcinoembryonic antigen, and gross cystic disease fluid protein -15. Stromal cells stain positive for vimentin and S-100 protein. [1]

Surgical excision is the treatment of choice. Recurrence following excision is rare.

Malignant chondroid syringoma is very rare. It is usually primary or can be due to the malignant transformation of benign chondroid syringoma. Females are commonly affected, and trunk and extremities are the favored sites. The indicators of malignant transformation are the following: size more than 3 cm, rapid growth, and satellite nodules. The pathological features that indicate malignant nature are invasive margin, impaired tubular differentiation, increased or abnormal mitosis, pleomorphism, tumor necrosis, excessive mucoid stroma, poorly differentiated chondroid components, and chondrosarcomatous or osteosarcomatous differentiation. They are aggressive and can undergo lymph node and distant metastasis, commonly to the lung, bone, and brain. [6]

In conclusion, this report describes a rare sweat gland tumor. The presence of a skin-colored lobulated nodule on the head and neck area should raise suspicion of chondroid syringoma. A pathological examination is mandatory to reach the diagnosis.

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Interesting case 2 – Lipoid proteinosis – A case report with literature review

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Introduction

Urbach-Weithe disease or lipoid proteinosis is a rare autosomal recessive genodermatosis.[1] Genotypicially, a loss of function mutation in extracellular matrix protein 1 (ECM1) gene mapped to Chromosome 1q21, correlates clinically with widespread disease associated with variable degree of scarring and infiltration of skin, involving the oral cavity, larynx and mucosae.[2] In this case, we describe the various phenotypic variations encountered.

Case report

A 42-year male, oldest of the six siblings, born to parents of a third degree consanguineous marriage; asymptomatic at birth , developed hoarseness of voice in his infancy followed by spontaneous vesiculation over his face, arms, shoulders, back and over buttocks in childhood up till the age of 16 years which healed with atrophic scarring.

Further, he developed progressive thickening of his skin with the development of yellowish papules along the margins of his eyelids, neck and both hands and warty lesions over the sites of trauma. He gave history of increased discomfort during summer and episodes of seizures over the past 16 years. There was history of dysphagia and episodes of dyspnea that exacerbated with concurrent upper respiratory tract infections.

General Examination revealed short stature (height- 152.52 cm). Cutaneous examination revealed moniliform blepharosis (Figure. 1A) along with confluent yellowish-brown waxy papules over the face, neck, upper trunk, arms, forearms, legs, scrotum and dorsum of hands. Hyperpigmented verrucous lesions (Figure 1B) were seen over bilateral elbows, knees, axillae, intergluteal cleft and lateral malleoli. Scarring alopecia was noticed over the scalp along with lateral 1/3rd supraciliary madarosis. Thickened waxy skin over the face along with multiple variable sized pox-like scars rendered an appearance of leonine facies (Figure. 1C).

Oral mucosal examination showed induration of both lips, angular cheilitis, thickened infiltrated fissured tongue (Figure. 1D) and frenulum along with multiple dental caries and loss of teeth. The patient was not able to protrude his tongue.

The nails showed presence of ragged cuticles and onychoschizia. On dermoscopy, ragged cuticles over third and fourth fingers of right hand were observed (Figure. 2)

On slit lamp examination, features of dry eye were documented. Video-laryngoscopy showed thickened epiglottis and vocal cords with narrowed airway opening. X-ray skull showed radio-opacity in the pituitary region. There was history of similar affection with mild variations in four other younger male siblings suggestive of a familial pattern of involvement However, parents did not have any affection as per clinical history.

Histopathology of skin biopsy taken from verrucous lesions showed presence of amorphous eosinophilic hyaline material in the dermis, accentuated around the capillaries, sweat coils in an “onion skin arrangement” (Figure 3A, B C, D). These deposits stained positive on PAS (Figure. 3E, F) and negative for Congo red stain.

A diagnosis of lipoid proteinosis was made based on the characteristic clinical findings and histopathology.

Figures:

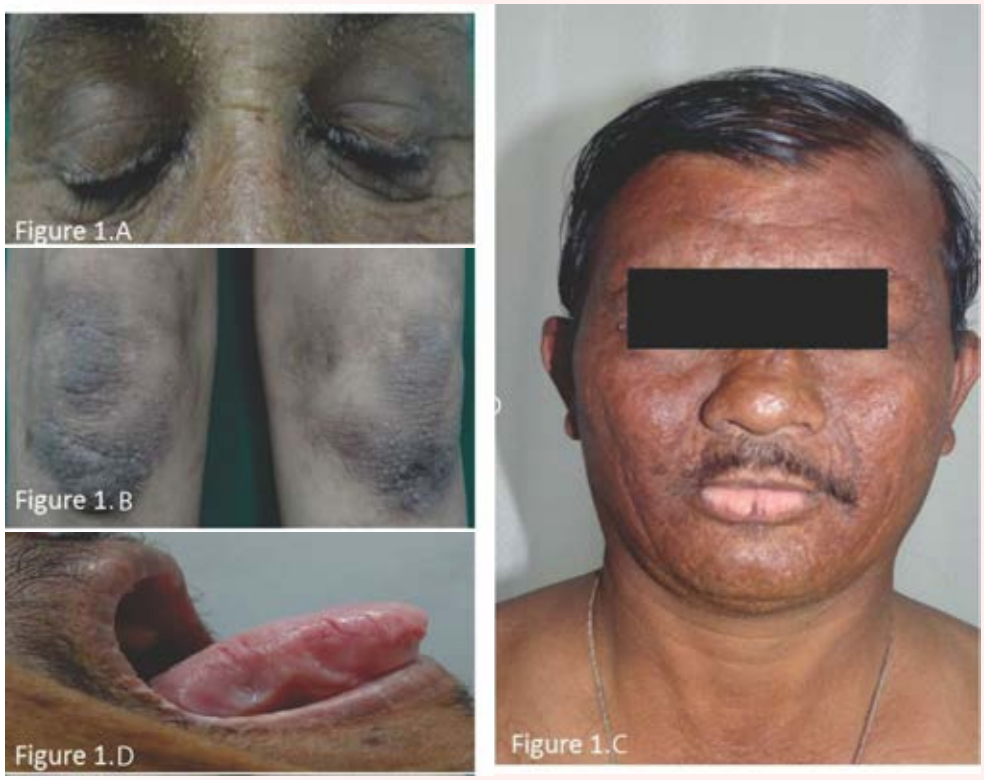


Figure 1: *Cutaneous features observed*

A) Moniliform blepharosis

B) Verrucous plaques over the knees

C) Pox-like scars over the face

D) Infiltrated tongue

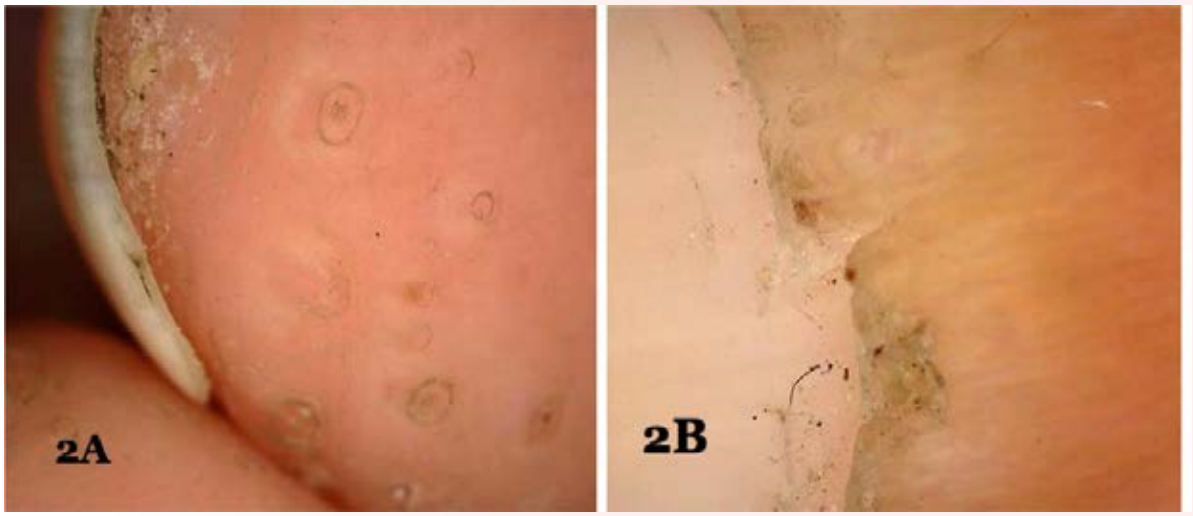
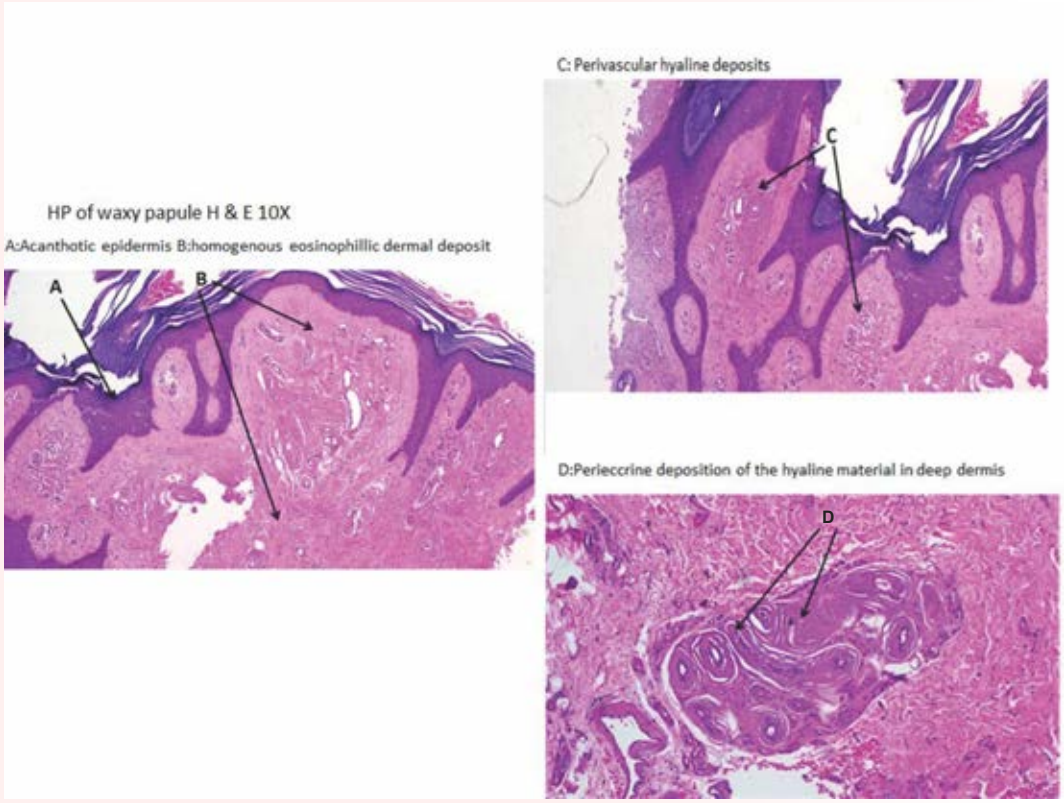


Figure 2: *Dermoscopy features (Dinolite, polarized, 150x)*

A) Pits and papules seen on finger tips

B) Ragged nail cuticles



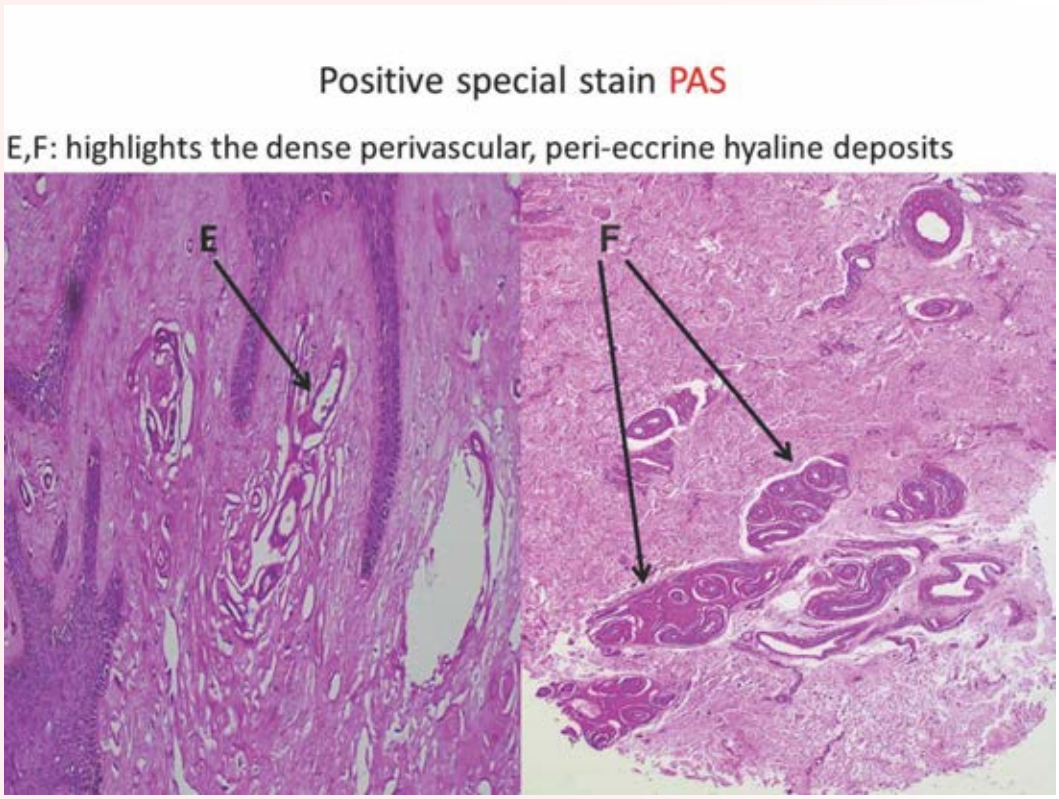


Figure 3AB: *Acanthotic epidermis and amorphous eosinophilic hyaline material in the dermis on H & E scanner view*
C,D: Hyaline material accentuated around the capillaries, sweat coils in an "onion skin arrangement" on H& E at 100x
E,F: PAS positive deposits in the dermis, highlighted along the capillaries and sweat coils.

Discussion

Lipoid proteinosis is an autosomal recessive. disorder, known to display considerable interfamilial and intrafamilial variation.[2]

Mucosal involvement manifesting as immobility of tongue, speech impediment, xerostomia and dental anomalies etc,[1,3] was seen in our patient. Infiltration of the pharynx, soft palate, tonsils, and lips lead to recurrent episodes of upper respiratory tract infections, parotitis and poor dental hygiene. However, clinical features such as angular cheilitis and fissured tongue were present additionally.

Extra mucocutaneous involvement, can manifest with ocular, psychiatric or neurological symptoms. Infiltration of Zeiss, Moll and Meibomian glands clinically present as madarosis, trichiasis, and distichiasis. Other commonly seen features are focal degeneration of macula and drusen formation in Bruch's membrane. Rare manifestations include glaucoma, cataract, subluxation, impaired color vision; corneal ulcerations, uveitis, epiphora, transient blindness etc.[4] Dry eyes was another new finding seen in our case.

The ECM1 gene encodes for a secretory glycoprotein and plays an important role in the structural and biological function of skin. [6,7] Mutations in this gene result in a disruption of collagen metabolism with decreased production of fibrous collagen and overproduction of basal membrane collagen. This presents clinically as the deposition of PAS positive hyaline material in dermis and submucosa.[1]

Skin lesions in lipoid proteinosis occur in two overlapping stages: Cell-poor subepidermal blisters with secondary acantholysis histopathologically which manifests clinically as spontaneous vesiculation that heals with scarring during early childhood followed by progressive PAS positive amorphous hyaline material deposition in the dermis, vessel wall and around eccrine glands presenting clinically as generalized thickened skin.[7,8]

Lipoid proteinosis is known to run a chronic and benign course with a normal life span but the patient suffers from various functional and cosmetic problems. Treatment options available are limited. Retinoids like acitretin modulates the metabolism of basement membrane and reduces the deposition of hyaline material in dermis. Facial lesions can be treated with dermabrasion or chemical peeling with CO2 laser surgery for vocal cords that helps in improvement of hoarseness.[8-10]

Along with the classical cutaneous features, some other new interesting features; like stunted growth, lateral one-third supraciliary madarosis, waxy papules over the scrotum and scalp with scarring alopecia , papular deposits on the fingertips with ragged cuticles of nails and findings of dry eyes which have not been mentioned in literature highlighted through this case.

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How to prepare for dermatopathology for MD/DNB exams?

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Approach a slide with an open mind and care not for the history! For the footprints of the disease have been left on the slide you are about to see. Just like travelling, what essentially matters is the journey to diagnosis and less does the diagnosis itself.

Dermatopathology section covers about 10-15% of practical examination marks but the anxiety it creates is a major concern for residents, for whom histopathology is more of a pink and blue slide affair. Earlier the access to histopathology slides, microscope and appropriate textbooks used to be cornerstone for good dermatopathology learning not to forget a guide/faculty fluent in dermatopathology. For self-learning one of the most essential part of residency requires spending time using a microscope to review slides already reported by pathologists or dermatopathologists and corelating with textbooks. With advent of time, it has become a routine portion of residency in a lot of medical colleges and it is interesting to see faculties giving importance to reviewing histopathology slides by obtaining them from pathology department and discussing along with residents.

So, during an exam, as a resident of course it would be the best thing to be able to diagnose a slide given in histopathology section for viva but what matters to an examiner is everything other than the diagnosis and how a resident approaches a slide, not the diagnosis. In fact, giving away diagnosis of a slide hints more at unfair play or puts off the examiner's enthusiasm(trust me that is the last thing you would like to do to an examiner, and the last thing you would like to experience as an examiner). Practically, for a resident to be able to make a spot diagnosis of all 5-10 slides out of approximately 1500 dermatologic diseases, just by looking at it for say 2 minutes is too extraordinary ana achievement. So, for a resident the million-dollar question on histopathology is DESCRIBE YOUR FINDINGS? The histopathology features point to a group of differential diagnosis and that approach is what matters to a faculty during exam because without clinical features it is difficult for anyone to make a sure shot diagnosis. How you look at the slide?(Table 1), what histopathology features you are able to identify, what clinico-pathologic correlation you could make between the short history and the features on slides, any special stains you would advise, any special investigation, associated clinical syndrome and thus give your probable differential diagnosis on its basis (Figure 1). The image at the top is a low power image of a section displaying granulomatous reaction pattern, which at higher power shows a macrophage predominant granuloma causing effacement of rete ridges thus narrowing down the possibility. When associated with clinical history it might guide us as to which special stain one may need to confirm our diagnosis and also stage the type of disease, know the bacillary load and anticipate the course and duration of treatment. So the credit question would be, if you are able to identify any special cells, features, sign which might narrow down your diagnosis or exclude other conditions which might display the same feature.

So, the rule number 1 from beginning of dermatology residency should be to spend time looking through microscope, get accustomed to its use and recognizing normal skin structures and cells such as lymphocytes, neutrophils, histiocytes, eosinophils, plasma cells and multinucleated giant cells. Once you know what is normal, you can then easily decipher the things that are abnormal. So, what to do when 3 months before your exams, you realize that there was probably too much to do in dermatology other than histopathology, well then just revise the basic reaction patterns of the skin and common dermatoses that you as a resident are expected to diagnose. You are not expected to diagnose a fixed drug eruption, cutaneous T-cell lymphoma, prurigo nodularis, photodermatitis, cutaneous lupus erythematosus etc. Some of the common differentials you are expected to know are given in Table 2.

Common slides belong to the following categories:

1) Spongiotic Dermatitis
2) Lichenoid / Interface Dermatitis
3) Psoriasiform Dermatitis
4) Autoimmune blistering disorders
5) Granulomatous Dermatitis
6) Disorders of Keratinization
7) Infectious Dermatoses (Viral or Fungal infections)
8) Tumors (Epithelial or Adnexal tumors)
9) Vasculitis and Vasculopathies
10) Cysts

With the advent of online websites, it has become quite easy to access the dermatopathology slides online than to access the microscope and hence websites like www.pathologyoutlines.com, dermnetnz.org, ISDP website, Dermatopathology groups on Facebook and other social media platforms, have made revision and discussions of dermatopathology slides easily accessible.

What an examiner requires is your ability to envision the possibilities that appear on the slide. Just like the possibilities that lie in you not just as a Dermatologist but as a Dermatology Expert! Or a future Dermatopathologist!

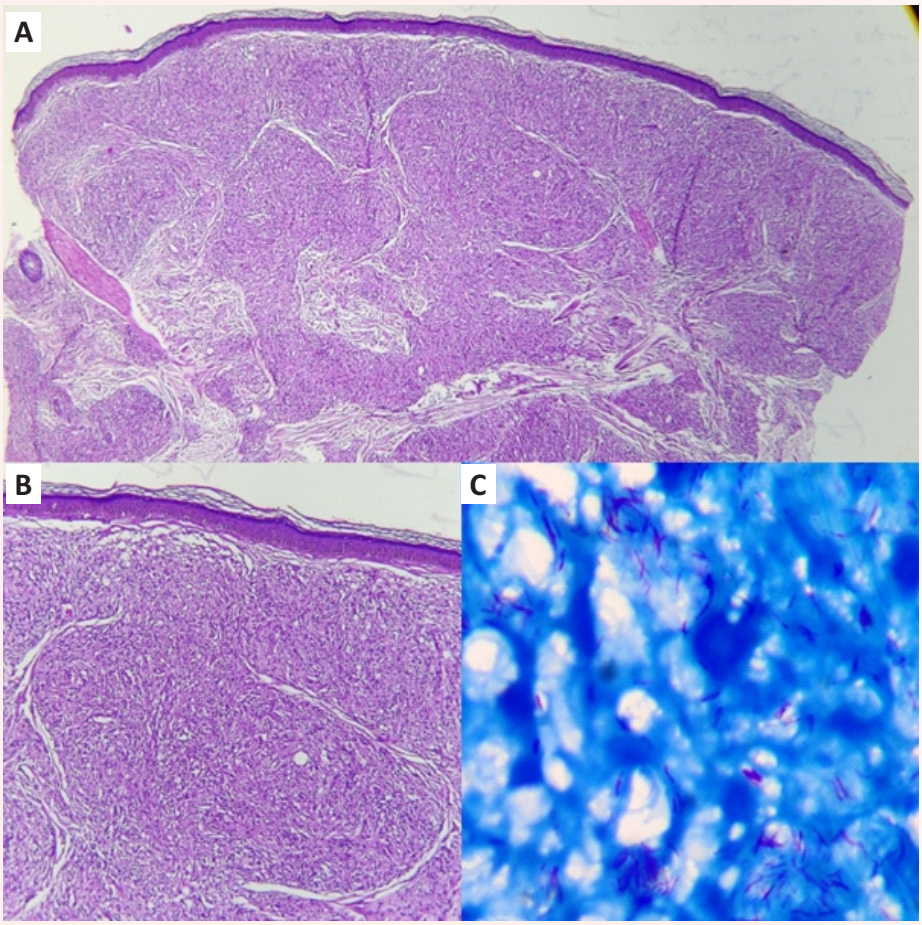

Figure 1: *Displays a granulomatous reaction on low power. (A) When you look at higher power it's a macrophage predominant granuloma. (B) The special stain displays elongated pink bacilli like structure which should fairly hint at diagnosis.(C)*

Table 1: *How do you look at a slide? There are some specific things to be seen in a specific sequence to realize the specific patterns and thus conclude a diagnosis.*

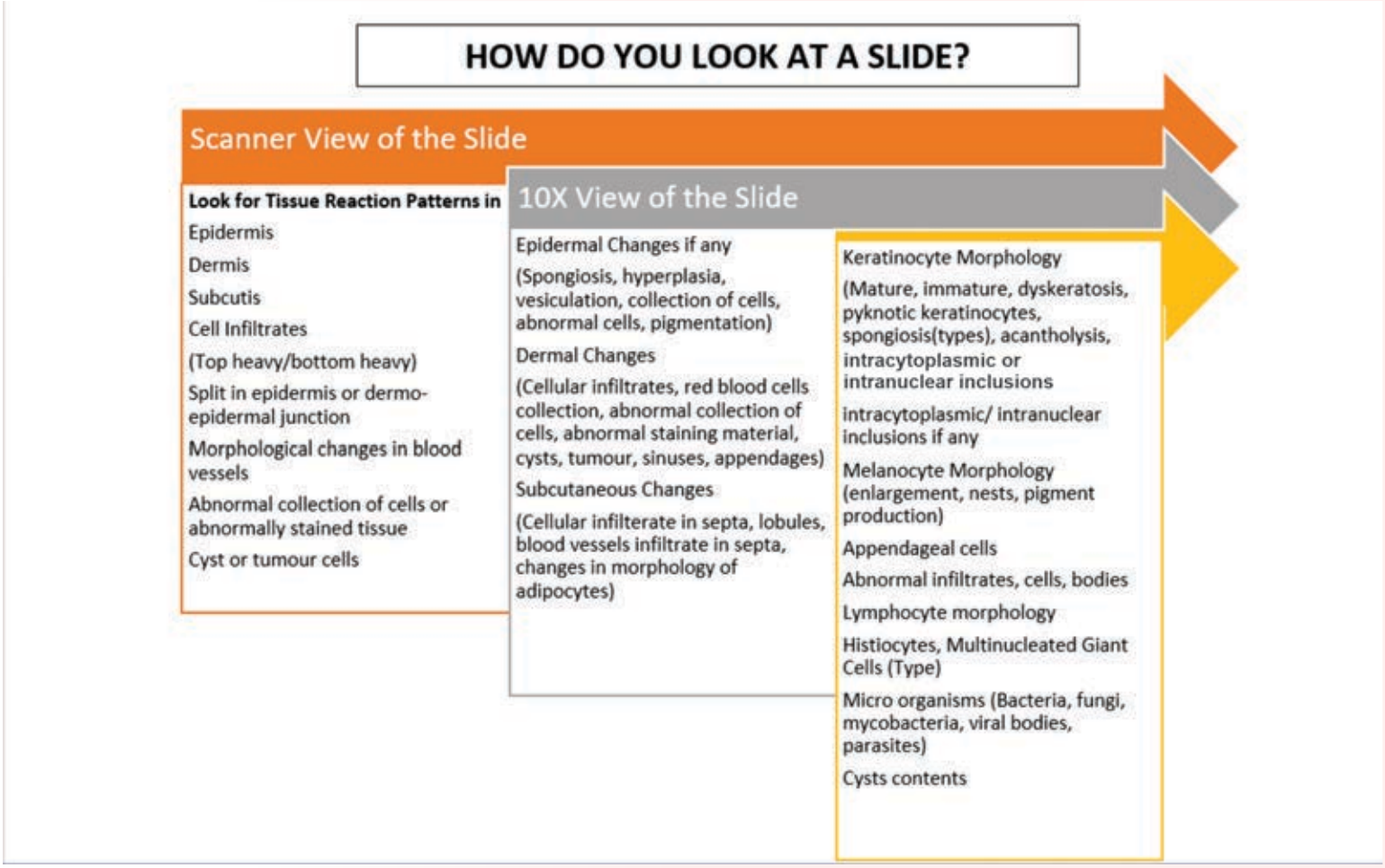

Table 2: *Differentials to common reaction patterns (Ref. Weedon's Skin Pathology)*

Reaction Patterns	Dermatoses
Lichenoid	Lichen Planus Lupus erythematosus Lichen sclerosus Porokeratosis Fixed drug reaction Erythema Multiforme
Psoriasiform	Psoriasis Parapsoriasis Pityriasis rubra pilaris Pityriasis Rosea Lichen Simplex chronicus Bowen's Disease

Spongiotic	Eczema Atopic Dermatitis Dermatophytosis Photodermatitis / PMLE Irritant Contact Dermatitis
Vesicobullous	**Intracorneal / Subcorneal** Impetigo Staphylococcal scalded skin syndrome Subcorneal pustular dermatosis Pemphigus foliaceous **Suprabasal** Pemphigus Vulgaris and vegetans Darier's Disease **Subepidermal** Bullous pemphigoid Epidermolysis bullosa aquisita Erythema multiforme Drug reaction
Granulomatous	Leprosy Tuberculosis Syphilis Leishmaniasis Deep fungal infection Granuloma Annulare Sarcoidosis Foreign body granuloma
Vasculopathic	Leukocytoclastic Vasculitis Livedoid Vasculopathy Henoch Schonlein purpura Sweet Syndrome Drug Reaction
Superficial and Deep Dermal Inflammation in absence of spongiosis	Dermatophytosis Chronic urticaria Viral Exanthem Drug reaction Pigmented purpuric dermatosis
Panniculitis Septal	**With Vasculitis** Leukocytoclastic vasculitis Superficial thrombophlebitis **Without Vasculitis** Erythema Nodosum Scleroderma Necrobiosis Lipoidica
Lobular	**With Vasculitis** Erythema nodosum leprosum Lucio phenomenon Erythema induratum **Without Vasculitis** Lupus profundus Sclerosing panniculitis Sclerema neonatorum

My dermatopathology fellowship experience

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I was fortunate enough to have been selected by the IADVL committee for the International observership program in the year 2018 and was the first one to have accomplished it. Probably because I chose an Asian country whose disease profile I expected to be similar to that of India.

Dr.Yu Hung Wu at Mckay Memorial Hospital Taipei, Taiwan was my mentor, and he has been my best mentor ever in my life. The dedication, teaching skills, discipline with which he works are something which we all have to emulate. He is a teacher par excellence.

There were regular sign out sessions for 2 to 3hours every day depending on the slide load. There was a review of interesting and difficult cases once a week. We also had weekly sessions of Direct immunofluorescence for autoimmune conditions like pemphigus group of disorders, cutaneous lupus and vasculitis. Another advantage was all Immunohistochemistry tests were readily done for required cases, which increased my knowledge and interest in it.

Regular Clinico-Pathological Correlation sessions were very interesting and great learning was happening during those sessions. There were weekly topic tests with extensive discussions across the deca-headed Microscope which had a great impact. Weekly case discussions, Journal clubs, web meets were all part of the training program. Every session is conducted on time with utmost discipline and at the same time there is freedom of expression and Dr.Wu encourages healthy discussions. He has a lot of publications in Dermatopathology, and all discussions happen with ready reference to the latest available literature in the dermatopathology journals. He is a very humble, friendly and approachable person which was very conducive for our learning. I got to present a case of Calciphylaxis which was much appreciated and also 2 journal club presentations.

The resource material provided is so immense. The slides are archived systematically into various topics, the collections are vast. Every entity in dermatology has a slide there, be it inflammatory, infectious, benign or malignant. We have the entire day at our disposal to view those slides at our comfort. There is also access to all the latest books and journals in Dermatopathology in the department Library.

I enjoyed the fellowship program with 3 other co-fellows, 2 from Phillipines and one pathologist from Kerala. Dr.Wu himself, drove us all to the Tamsui branch of Mckay Memorial Hospital and gave us hands on experience with the electron microscope, which was an exciting experience. We also got to see the entire pathology department where we saw the journey of the biopsy specimens to the glass slides. We also got to see the Immunohistochemistry section there.
Doing dermatopathology fellowship at Taipei is a very wonderful experience. All comforts are provided by the Taiwan International Health care Training Centre TIHTC with regards to accommodation which is very well furnished. It is a good place for nonvegetarians. Me being a vegetarian had to do minor cooking for myself. There is availability of plenty of exotic fruits and vegetables which can be explored.

People there are very friendly and go out of their way to help foreigners like us. Entire Taipei is very well connected with metro trains and there are lot of places to explore. I travelled the entire stretch of the city and enjoyed the place very much. Taipei 101 tower, Tamsui river are the spots of highlight. I also enjoyed shopping there. Dr Wu is also an 'Expert Viola artist'. He bought us tickets for his concert, which was an amazing experience. There are also lot of Indian associations there, conducting cultural programs, which engage you in the weekends.

During the last few days there I spent hours together at dermpath lab, trying to view all the slide collections, but I could not complete viewing them all. I long to go back there and spend my time endlessly in the microscopic world of skin slides. My perspective of dermatology changed. I learnt a lot more of clinical dermatology, because of dermatopathology. So my advice to all postgraduates is, dermatology can be enjoyed with dermatopathology. You get a hold on your diagnosis which ultimately leads to better treatment of your patients.

Dr.Wu is a saint like teacher. A wonderful person. Me being a faculty myself at Bangalore Medical College, became a better teacher and human being under Dr.Wu's influence. I also passed my FAADV fellowship exam in Dermatopathology, and luckily my examination centre was in Taipei itself, and Dr.Wu and Dr.M Ramam were among my examiners. Giving the exam was a joyful experience.

Last but not the least, I thank our IADVL, Dr.Venkatram Mysore, Dr.Ramesh Bhat, Dr.M.Ramam, Dr.Sujay Khandpur, my teacher Dr.Sacchidanand S and all my colleagues at BMCRI for giving me this opportunity to do the fellowship at Taiwan. Because of them , and their blessings we are also planning to start Dermatopathology fellowship at BMCRI shortly in collaboration with Pathology department. My Pranams to all my Gurus!!!.

Figure 1: *Dr. Eswari with her mentor Dr. Yu Hung Wu*

Figure 2: *Dr. Eswari at Mckay Memorial Hospital Taipei, Taiwan*

An interview with a dermatopathologist

Dr. Meera Thomas,
Professor,Department of Pathology,
Christian Medical College, Vellore

Q1 When and how did your interest in Dermatopathology begin?

During my post graduate days and as a very junior faculty, I had seniors like Dr. Sushil Chandi and Dr. Mary Jacob who seemed to make diagnosis out of thin air. They acted like Sherlock Holmes making diagnosis with just clinical details provided and an H&E slide in front of their microscopes. They pointed out intricate findings which in those days seemed invisible and honed in me the mantra "the eyes see what the mind knows", inculcating a seeking attitude.

Q2 How has been your journey in pursuing your passion?

It was very difficult initially as I didn't have adequate knowledge and my eyes had to learn to see the subtle variations. Many clinical diagnoses with a single histological picture and various changes in histological picture with aging of the lesion and the effects of drugs are some of the nuances you learn over the years.

CMC also provides us leave with pay to study and pursue the area of your interest anywhere in the world so that patient care in the institution can benefit. So I haved spent time with Dr. Almut Boer in Hamburg who was very patient with a novice like me and who spent many hours explaining small and seemingly silly doubts. I have also benefitted immensely spending time with experienced dermatopathologists like Dr. Jag Bhawan, Dr. Lyn Goldberg and Dr. Meera Mahalingam.

Just dermatopathologists alone are not enough. You need clinicians with good clinical acumen who will challenge you every day. Dr. Renu and Dr. Suzanne and various others in the department of Dermatology were the ones who sent us good cases, saw slides with us on the 10 header microscrope, when either we or they had a difference of opinion. We also got a good load of tumours and surgical cases from colleagues in the Plastic Surgery and Surgery department. Regular CPCs helped us to renew the way we reported for the benefit of our clinicians and hence in patient care.

Q3 How important is this subspeciality for pathologists and dermatologists?

It is a MUST KNOW for all Pathologists and Dermatologists. The nuances of Pathology honed over many years of seeing pathological aspects of diseases at various sites can help diagnose difficult cases for the pathologist. At the same time if clinical correlation is not done many diagnoses can go wrong. A dermatologist should know the various subtle differences in different histological conditions so that they can plan treatment accordingly.

Q4 What is the present overall state of dermatopathology training during postgraduate teaching in India?

I do not know about other centers. Dermatologists do have a one month posting in our institution in Dermatopathology. Two weeks in the first year and 2 weeks in the beginning of their final year. What I find most gratifying is after their posting the PG Registrar tends to write more clinical details for us the pathologist, which makes a huge difference in the way we make a diagnosis as we do not see the patient. Also we start writing the histopathology in such a manner so that the clinician can imagine the slide from our description. Unfortunately the pathologists do not have the luxury of doing some posting in the dermatology department during their postgraduation as the time is insufficient with many systems to cover and various aspects of Pathology to be covered in their 3 years.

Q5 What steps can be taken to reduce the knowledge gaps among postgraduates?

Regular Clinicopathological meetings, atleast once in 2 weeks of mundane and interesting cases can help to reduce the knowledge gap.

Q6 How does a fresh MD pass out build up on his knowledge of dermatopathology? Does he need any formal training and if yes, for minimum what duration?

For a fresh MD postgraduate in Pathology as well as Dermatology he/ she will need definite training as their 1 month posting and CPCs will just help them to recognize normal histology and may be differentiate it from abnormal. They may be able to diagnose simple cases like Basal cell carcinoma or Pemphigus Vulgaris. But subtle differences between a Sebaceoma or a Trichoblastoma from BCC or Pemphigus Vegetans or Dariers from Pemphigus Vulgaris takes time.
I would suggest a 1-2 year training programme with emphasis on clinicopathological correlation. The nuances of Dermatopathology will be strengthened with life long reading and regular application to the subject.

Q7 Which dermatopathology training centres you would suggest, both in India and abroad?
DNB has started a dermatopathology fellowship for Dermatologists in India from 2019. I do not know which are the centres in India which are affiliated to it.
Dr. Uday Khopkar from KEM Mumbai has a one year dermatopathology fellowship for Dermatologists.
IADVL has a dermatopathology observership for 2 candidates per year, one month of which they do come to CMC.
We in CMC have also have observers, between 18 to 20 per year, who come for a 2 week to one month posting. We did not have anybody last year due to the Covid pandemic.
We in CMC are planning to start a paid dermatopathology fellowship of 2 years duration for Pathologists from this year. This includes clinical postings of 6 months, dissertation and attending CPCs, conferences and paper presentation.
There are centres in Wakefield in the US, Boston Medical in the US, St. Thomas in UK and Hamburg in Germany which have dermatopathology fellowships.

Q8 What is your favourite dermatopathology textbook and any other learning source you would recommend for beginners?
Weedon is an all time favourite as is McKee's Pathology of Skin. Derm101 is a good internet resource as is dermpedia. Lectures by Jerad Gardner are very useful too.

Q9 How has dermatopathology in India grown over the years and in which aspects it is still lacking?
The type of biopsies we see has changed from larger biopsies to punch biopsies. The way we report has changed from single sentence diagnosis to using all the clinical material available to give a differential diagnosis so that the clinician has options for treatment. Newer techniques in immunofluorescence, new markers in Immunohistochemistry and molecular pathology has all helped in making dermatopathology more specific and interesting. Dermatopathology is still in its infancy in India. More people both pathologists and dermatologists need to take interest in it so that it becomes as important as hematopathology or Nephropathology.

Q10 Your tips and practice pearls for budding dermatopathologists.
Read voraciously, see continuously for the more you see the more you know and what the mind knows the eyes see.

← *Dr.Meera Thomas at her working station*

Will confocal microscopy replace routine light microscopy in diagnostic dermatopathology?

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https://www.mskcc.org/cancer-care/doctors/manu-jain
www.mskcc.org/ConfocalCourse

Dear Editor, thank you for this wonderful opportunity to express my views on confocal microscopy — a novel noninvasive microscopy technique. I have been extensively involved in this field over a decade now. When I first started my career in the field of noninvasive diagnosis: an eminent US pathologist asked me a curtly question “you are a pathologist but why you are helping to build technology which could potentially replace pathologist?”. Although this was my first encounter with pathologists' skepticism, I still face similar questions from the community. I responded at the time—and it stands true to this date—that if an innovation can improve patient care (“humanity”), I would embrace it.

Innovation has been a quintessential step for improving diagnosis and patient care in medicine. However, embracing a new technology can be challenging and generate speculation by clinicians — will this new technology replace the existing diagnostic workflow?

Traditionally, diagnosis of cancer and other non-neoplastic lesions rely on histopathological evaluation. Although histopathology is the gold standard, it requires time-consuming tissue processing, delaying diagnosis and management of patients. Currently, frozen section is the only modality for rapid histopathological evaluation; however, it still requires tissue sectioning and freezing, disrupting morphology. Furthermore, some fatty tissues such as breast are not suited for frozen section evaluation.

To overcome tissue processing limitations and provide rapid histopathological evaluation, several optical (light-based) imaging ex vivo and in vivo microscopes are built[1-13]. One such promising microscope is confocal microscope (CM). There are two types of CM devices: Ex vivo CM (EVCM) and In vivo Reflectance CM (RCM) (Figures 1,2). Both the devices can generate images at cellular resolution, equivalent to histopathology. EVCM device can rapidly (within 5 minutes) image freshly excised tissues, without any tissue processing[3]. It is being primarily used as rapid intraoperative tool for detection of residual basal cell carcinoma (BCC) in fresh Mohs surgical excisions. It has also been used for the evaluation of other neoplastic (melanoma, and keratinocytic neoplasms) and non-neoplastic (mucormycosis) skin lesions. The microscope is compact bench-top system that can be placed in the grossing room or in the surgical suite. Digitally colored purple and pink images are generated that resembles H&E images and can be readily read by a trained a pathologist (Figure 2b). This device can image freshly excised tissues from various organs such as prostate, bladder, breast.

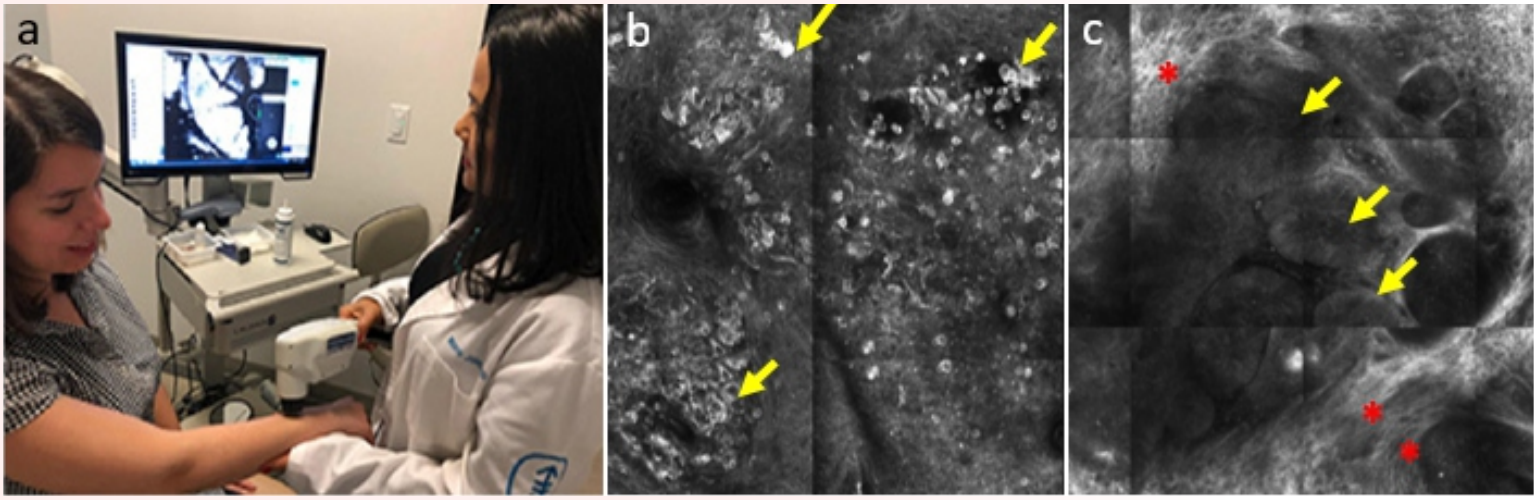

Figure 1: *In vivo imaging of a skin lesion using Reflectance Confocal Microscope: a) Vivascope RCM device, b) RCM image of a melanoma with clusters of big bright (melanin imparts strongest contrast on RCM) pagetoid cells in the epidermis, and c) RCM image of a BCC tumor nodule (arrows) with surrounding collagen stroma (*)[1]. 1. Cristian Navarrete-Dechent, Cristian Fischer, Eric Tkaczyk, Manu Jain. Principles of non-invasive diagnostic techniques in Dermatology. 4th edition of Moschella and Hurleys text book of dermatology. 2019*

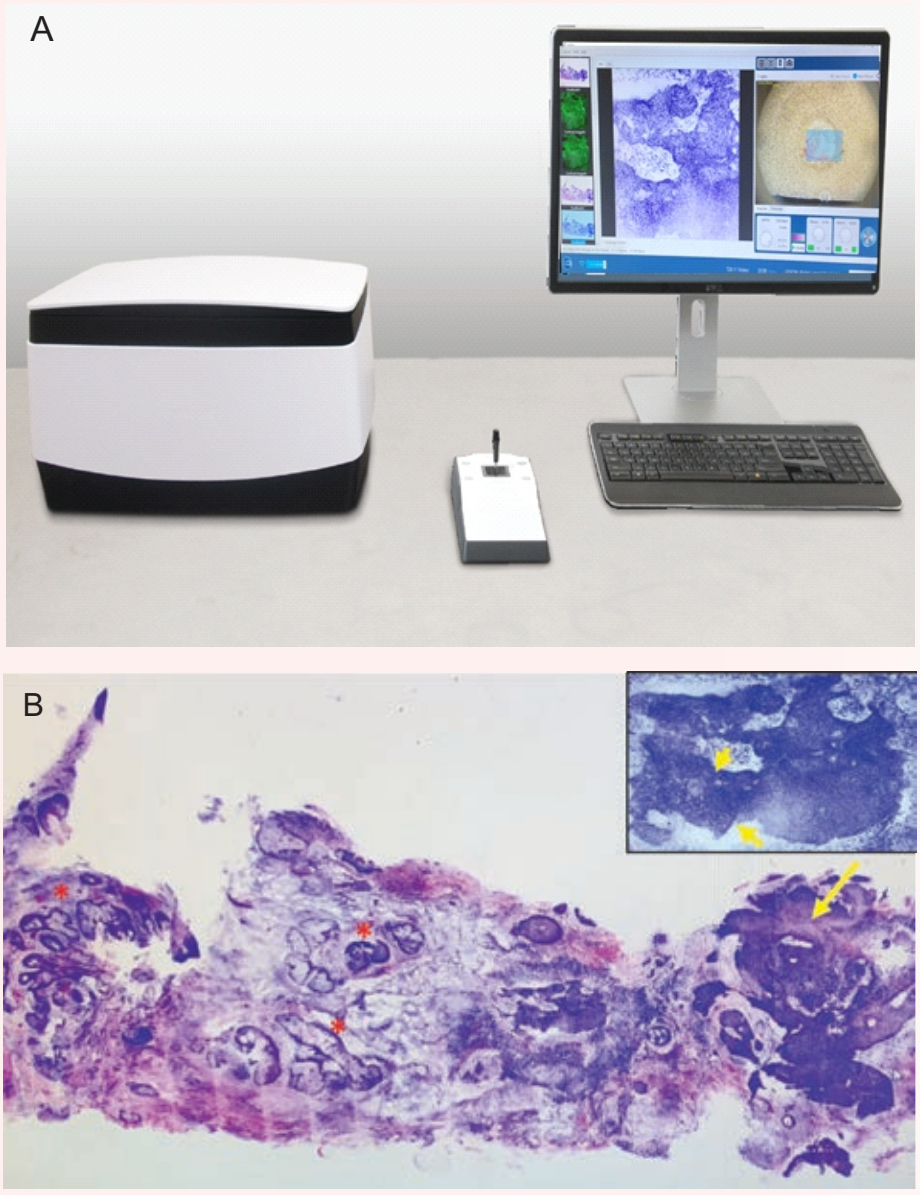

Figure 2: *Ex vivo imaging of a freshly excised, whole tissue (un-cut and un-processed) using a Confocal Microscope: a) Compact Vivascope Confocal device, b) Digitally colored purple and pink (similar to H&E-stained image) ex vivo CM (EVCM) image showing residual basal cell carcinoma (BCC; arrow) and surrounding normal skin structures (*). Inset: Image of another BCC acquired using EVCM device with palisading (arrow) and clefting (arrowhead).*

The in vivo CM device, called RCM, on the other hand is used to diagnoses skin lesions in patients, without the need for biopsy— "virtual" biopsy. RCM is a billable device in the US. It is being used for triaging neoplastic skin lesions as benign versus malignant such as differentiating nevi from melanoma, and BBC or SCC from their benign counterparts (Figure 2)[4,5]. RCM is used as an adjunct to clinical and dermoscopy and has significantly reduced the rate of benign biopsies. RCM is also used to determine various inflammatory dermatoses patterns and detection of infectious lesions (scabies, molluscum contagiosum etc.)[6–9]. RCM also plays an important role in non-invasive treatment monitoring and guiding scouting biopsies for large lesions and ill-defined lesions of lentigo maligna and extramammary Paget's[10]. As imaging is performed in vivo, RCM can provide information— not otherwise feasible with traditional pathology — such as dynamic phenomenon of leucocyte trafficking and can add a new perspective in diagnosis .

Circling back to the question "Will confocal microscopy replace routine light microscopy in diagnostic dermatopathology?". Absolutely not! History of pathology is a testimony to this fact. New diagnostic methods such as IHC, molecular markers have been added over centuries, but none have completely replaced the role of traditional light microscopy. Likewise, integration of confocal microscopy (and other noninvasive devices) would create their own niche in pathology. These techniques are here to expediate the pathological workflow and improve patient care. As these techniques generate "quasi-histopathology" images, pathologist should be the natural adopters of these techniques. Steve Jobs rightly stated: "Innovation is the ability to see change as an opportunity— not a threat".

Yes, these microscopes are expensive, but with ongoing efforts, cheaper and portable devices are being built, which would enable pathologists to sign-out reports all over the world sitting from the comfort of their living room[11]. To make this change, pathologists needs to be trained in reading these images, which is one of my ongoing goals— "Educate, Embrace, and Expand"[4,12,13].

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Digital Whole Slide Imaging in Dermatopathology

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Dermatopathology is a highly specialized branch of pathology where two streams of medicine, pathology and dermatology merge. Since these two subjects have high variability in exposure of postgraduates to basic pathology and dermatology, there is a need of constant training of dermatologists in pathological terms and morphology on one hand and training of pathologists in clinical presentation as well as pathology of dermatological conditions. Training in dermatopathology forms an integral part of dermatology and pathology postgraduate curriculum. This objective can be achieved by holding lectures, slide discussions in person, slide seminars, assessment programs and conferences at regular intervals by experienced faculty.

Of these various modalities, holding slide seminars is the most effective method of teaching dermatopathology. Traditionally, departments impart teaching by discussion of glass slides, usually on a 5 or 10 header microscope and by holding departmental slide seminars and quiz programs using glass slides of interesting cases at local level and during conferences and CME programs at state or national level.

However, as it is well known, glass slides have certain problems associated with them, the main being breakability, fading with time, physical space required for storage of slides and risk of pilferage of slides. For slide seminars and quiz programs, multiple sections are prepared, which is a problem in small biopsies as the actual pathology is many times lost on recutting the block.

Latest innovative technology of virtual microscopy uses whole slide imaging by which glass slides are scanned at the highest magnification of ×40 and a composite image of high resolution is formed (Figures 1 and 2). Specific areas of the whole slide image can be zoomed in and out at various magnifications and navigated from one field to another with image quality being retained. Scanning can also be done using ×100 objective to identify the microorganisms. These slides are then uploaded on the cloud server and grouped into different categories of dermatoses to prepare digital slide library (Figure 3). Clinical history is provided along with the digital images and salient findings are marked with annotations for ease of understanding. These slides can be accessed 24x7 from any location. Annotated and labelled slides are not only useful for teaching, but also for self-study by the postgraduates without restriction of time and space. One can add a section of quiz slides for self-assessment by the residents.

Digital slides are an excellent tool for conducting online slide seminars at national level since large number of residents without any limit and even in remote locations can be enrolled in the program. Recently there is an increasing trend of organizing online dermatopathology conferences, as online conferences do not require administrative and logistic problems of hiring expensive venue, arranging transport for pickup and drop of delegates and faculty to the conference venue and other destinations. Also, delegates do not have to spend on travel, stay and leave from department is not required, so 100% of the postgraduates can attend the conference without much problem.

Another big advantage is seeking second opinion from trained dermatopathologists using virtual slides since there is scarcity of expert dermatopathologists in the country. Traditionally for opinion, glass slides are couriered to the expert pathologist, which exposes the glass slides to breakage and loss during transit and takes 2-5 days to reach the destination

depending on the distance. On the contrary, using digital or virtual slides, link of slide is sent via internet which reaches the expert within minutes. Expert pathologist can view the slide immediately and give his / her opinion within hours instead of days. There is tremendous improvement in health care by providing early diagnosis validated by experts, reduction of anxiety period of patient, family and treating physician and early institution of therapy. All this is possible now by digital pathology which is being practiced to some extent in India too and is the future for second opinion and timely healthcare. Whole slide images are forming the mainstay of quantitative dermatopathology, comparative pathology, development of artificial intelligence and computational pathology in recent times and hope to play ever increasing role in interpretation of molecular pathology.

It is hoped that with time virtual microscopy will gain acceptance among dermatopathologists and residents and is going to be the future of teaching dermatopathology. Institutional digital slide libraries will be created and adopted in dermatopathology education by scanning the glass slides in the institution or by outsourcing scanning service from private establishments. Another advantage will be that rare cases can be shared by various institutions under interinstitutional collaboration without sending the glass slide physically as one image can be duplicated into 100s of images and can be viewed by million viewers at a given time.

The factors which have prevented the fast growth and acceptance of digital pathology in India have been high cost of slide scanners, unavailability of high-speed internet in most areas and general reluctance of dermatopathologists to adopt digital slides due to their deep attachment to glass slides, which have been the diagnostic tool used for centuries. It is hoped that with time, scanner prices will come down to make them affordable, high speed wi-fi facility will be available across the country including villages and far-flung areas and with more and more exposure through online slide seminars, dermatopathology conferences and quiz programs, dermatopathologists will be more responsive to digital pathology.

Fig.1 *– Showing scanning of the glass slide using slide scanner to create a whole slide image*

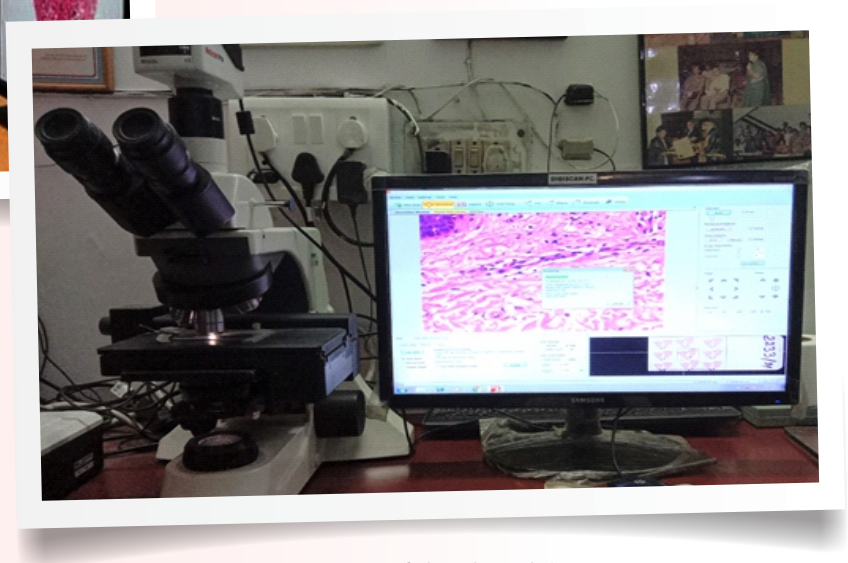

Fig.2 *– Scanning of the glass slide in progress*

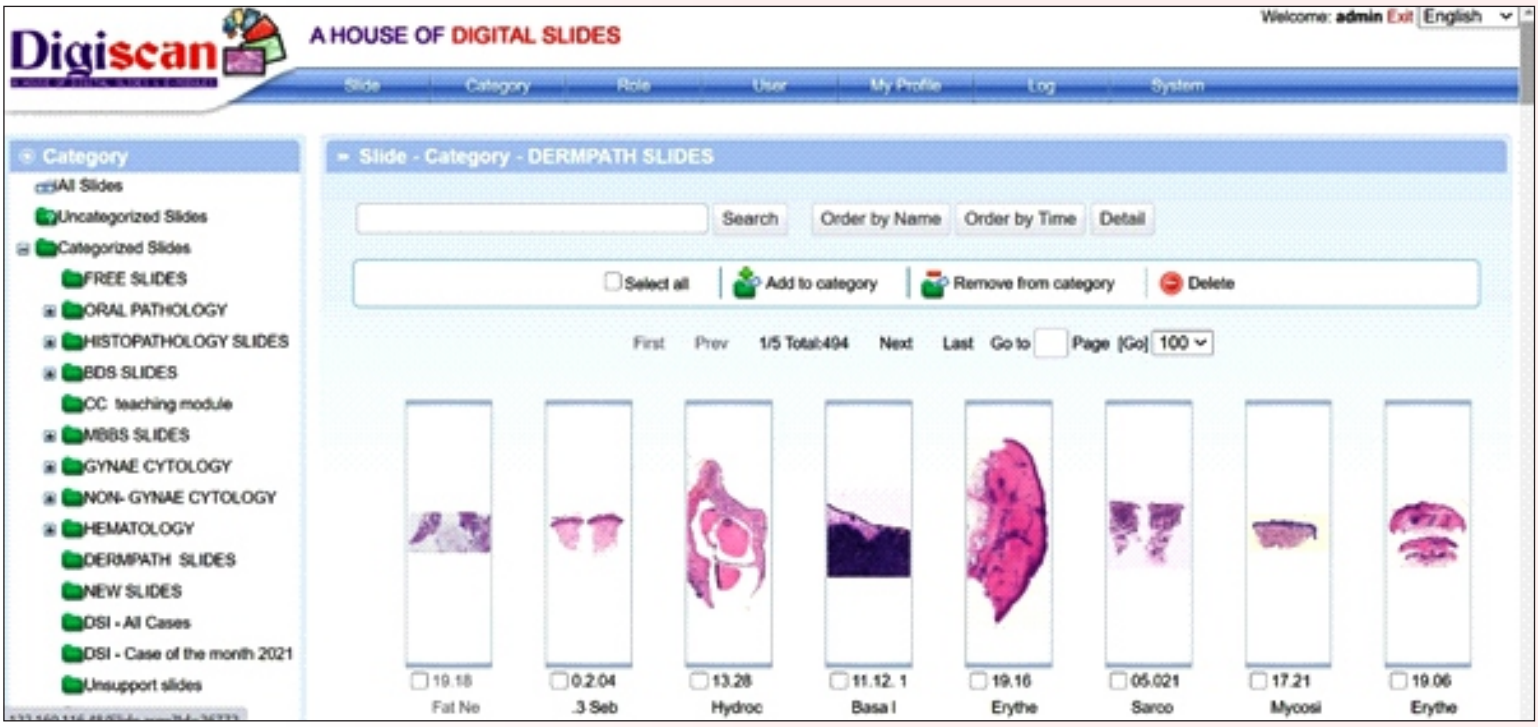

Fig.3 *– Creation of Digital library of Dermatopathology slides*

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Research in the field of dermatopathology in Asians - topics and how to proceed

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We, the medical fraternity understand the need for research well. It is claimed “Medicine will always remain an 'art', but with medical research and investigation, we can come closer to moving the practice of medicine away from empiricism to scientific discipline.” Both dermatologists and pathologists have a trait in common; both exhibit a commendable ability to observe. So, we know best the true sense of what Immanuel Kant once asserted “Concepts without Percepts are empty.”

Research in dermatopathology, I believe, is different for different people. Consistency in our observations could be research. We could consult literature based on our observations to see the uniqueness; if it is well reported, an opportunity for thorough reading helps us identify the missing information, that could be the starting point for a research question!

Conventional morphologic techniques (e.g., light microscopy, immunohistochemistry) and immunofluorescence are the most frequently used tools and widely available. Keen observation of pattern of immunoreactants in Direct immunofluorescence even in well-studied disorders like pemphigus, wherein, novel punctate pattern was observed amidst the well-known net-like pattern is an example. There is still scope for studying the serration patterns in subepidermal blistering disorders, the relevance of immune deposits for prognosis in leucocytoclastic vasculitis, utility of DIF in seronegative patients suspected to have a connective tissue disease and nondiagnostic findings on histological examination, etc. As of indirect immunofluorescence is concerned one could work on measures of increasing sensitivity of the test by working on the substates incorporated. Immunohistochemistry (IHC), we all would agree is an adjunct tool in the field of dermatopathology. IHC is an area in constant change. Some markers that seemed specific and reliable for diagnosis of certain diseases, after a while are described in lesions totally unrelated. I feel, observation of the normal structures highlighted by the stains is as essential as the studying the pathological area. I feel this could be a trigger for an idea to emerge as to how it could be employed in relevant disease conditions. IHC is an important research tool in the prognosis and the therapeutic approach to neoplastic diseases and is being used to screen many hereditary syndromes (eg: MSH2 and MSH6 protein expression as a predictor of mismatch repair deficiency in sebaceous neoplasia); this could be explored based on the profile of neoplasms encountered at the respective centres. We could transition from descriptive to quantitative methods for reporting IHC for reproducibility and documentation. One could consider research using integration of dermatopathological findings with dermoscopy or tools with a higher resolution like confocal reflectance microscopy – optical coherence tomography for a dermatoses or neoplasms that interest's them or relevant for their population if facilities are available. With the rise of molecular research, institutes having facilities for molecular studies could take to translational research to identify novel biomarkers in pathological tissues for diagnosis, prognosis or therapy. Cytology in dermatology is another area being explored.

Moving from research tools to research topics, the bottom-line I think should be interest driven. Choose a topic that aligns with your clinical interest and offer a fresh perspective on the topic! There are alternative ways to choose a research question, like in instances where a particular condition is more commonly encountered in a centre and yet to be elucidated pathologically (prevalence-driven) or technique-driven, that could be Plan B! We could decide if we need to study it retrospective or prospective. I always find the segment in research studies published- 'implications or recommendations for future research' very useful to derive a research question. Another source of research topic is Society meetings in dermatopathology or dermatology that provide good opportunities to hear about current research and hear from (collaborate with) national and international researchers. Histological characteristics of inflammatory dermatoses involving nail and mucosae, cutaneous toxicity of immune check-point inhibitors being used more often these days, rash in

COVID, exploring histopathological characteristics and biomarkers for prognosis in cancers like mycosis fungoides, histological and immunohistochemical characteristics of various infectious and non-infectious granulomatous conditions or any topic that one considers relevant is a good topic! When western literature is replete with information about malignant melanoma, Asian centres which have a high case load of acral melanomas could research the topic. The basis of many of the observations about subungual melanoma are yet to be understood in histology- eg:- dermal invasion pattern of the different areas of nail units in subungual melanoma-'concepts like dermal invasion in the nail matrix occur in later stages of subungual melanoma progression than that in other parts of the nail unit though the origin is the former'. Standardising assessment of dermal invasion of subungual melanoma due to its unique anatomy can be taken up.

Any time is a good time to start! I'm sure we all will agree it could begin with the post -graduate dissertation onwards. Identifying research mentors within/outside the medical centre is essential as for research in any other field. Funding from institutions or governing bodies could be reserved or preferred for Dermatopathology projects emerging from residents, faculty or consultants to encourage such work, something like 'Targeted funding for dermatopathologist-led, transdisciplinary research projects'.

As we all know for visibility of one's research, publication is necessary. The dedicated dermatopathology journals include Journal of Cutaneous Pathology, The American Journal of Dermatopathology, and The Indian Journal of Dermatopathology and Diagnostic Dermatology. Sections inviting dermatopathology papers in the form of Clinicopathological challenge are available in JAMA Dermatology, Clinical and experimental dermatology Clinicopathological Cases, International Journal of Dermatology, Indian Dermatology Online journal, to name a few and as dermatopathology Pearls in Indian Journal of Dermatology Venereology and Leprosy, Dermatopathology rounds in the Indian Journal of Dermatology.

Collaboration is the key! It starts with the dermatosurgeon sampling for us, technicians, pathologists, geneticist, molecular biologist, haematologist etc. We need to periodically evaluate our own practice, and to do that in a robust and meaningful way one needs to use the tools of research. We like any other researcher, need to be familiar with the research methodology and be able to critically review research done by others.

Happy researching!

Social media and Dermatopathology

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Skin physicians frequently perform skin biopsies on their patients and seek an expert opinion of dermatopathologist for their patients. Unfortunately dermatopathology is still in infancy stage in India and very few centres in India offer training in dermatopathology with good volume of cases. This has a cascading effect on presence of expert and experienced dermatopathologists in India. Currently India has only few well trained dermatopathologists whose opinion is well accepted among dermatology fraternity; however such dermatopathologists are over burdened and may not be easily available for a important aspect of diagnosis of skin disease i.e. clinico-pathological correlation.

Social media sites (Facebook, Twitter) are helping to bridge this gap of unavailability of expert dermatopathologist opinion. Many renowned and seasoned dermatopathologists are offering their opinion on slides posted on various social media, provided the slides are accompanied with enough clinical history and good quality photomicrographs. One must keep in mind that dermatopathologist gets to see only “4mm’" of a patient in contrast to primary skin physician. This aspect makes it imperative for primary skin physician to obtain a biopsy from a well-formed representative lesion, preferably upto the depth of subcutaneous fat. Processing of tissue and obtaining slides with good quality staining can be outsourced to a good pathology service having expert technical personnel. In skin pathology, a pristine quality H&E staining on thin tissue section is sufficient for routine clinical cases. Primary care physician should be able to reflexly order special stains in cases where an underlying infective process is suspected. A good quality trinocular microscope with image capturing facility is desirable to obtain high resolution photomicrographs.

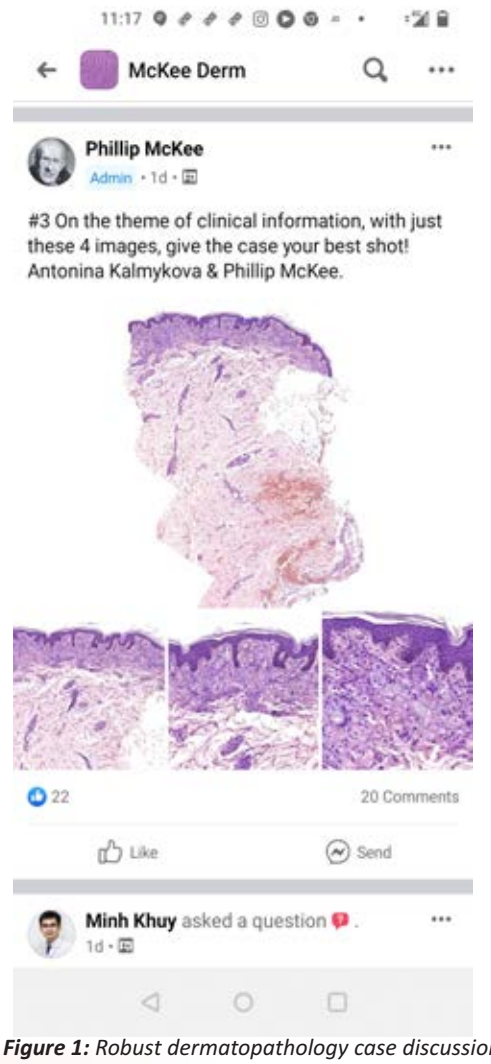

Figure 1: *Robust dermatopathology case discussion on one of the Facebook group*

Armed with clinical material and photomicrographs of interested areas of slides, primary care physician can seek opinion of experts on various social media platform. Many specially dedicated groups are formed on Facebook for the purpose of skin pathology. (Figure 1). However, primary provider should bear in mind to filter the responses obtained on their posts. Many early learners comment on the cases, which may be patently wrong and can divert the provider physician away from a correct diagnosis. Social media has vast reach across the globe and primary skin physician may be able to obtain an opinion of top notch skin pathologist of the day provided they are accessing social media. However; a time lag of three to four days need to be given in obtaining “a common consensus diagnosis" provided the different time zone of experts. Currently at the writing of this essay, author is aware of few expert dermatopathologists who are enthusiastically using social media for teaching dermatopathology.

However, Twitter algorithm is quite different form Facebook as former does not have any dedicated groups for a subject. Author of this essay suggest using Facebook groups to learn and get diagnosis on the cases. Twitter platform utilizes

various named hashtags (example #dermapath twitter#) 'to draw the attention of interested expert. Cases posted on Twitter have weak chance of getting commented on unless the primary skin physician knows that expert and tags the expert in the post.

WhatsApp platform provides an excellent means to share and seek opinion on photomicrographs. WhatsApp has proved to be very user friendly platform to teach and learn dermatopathology. (Figure 2) One of the main advantages of WhatsApp over Facebook and Twitter is allowing to share relevant literature in the pdf version which proves quite handy and useful. WhatsApp allows one to record their voice message and send the recording in a group allowing to share exact thoughts running in the mind. However, WhatsApp group has one major limitation of having only restricted number of members in a single group (256).

Fine nuances and in-depth technical details given by experts on skin pathology can be bit of taxing to a clinician. However it is advisable for primary skin physician to get well versed with various dermatopathological terminologies as it will allow better communication and comprehension in discussion. Working knowledge of various special stains and commonly used immunohistochemistry markers can prove handy during discussion.

Lastly it is to be kept in mind that 'Clinicopathological correlation is the king in diagnosis of skin diseases'

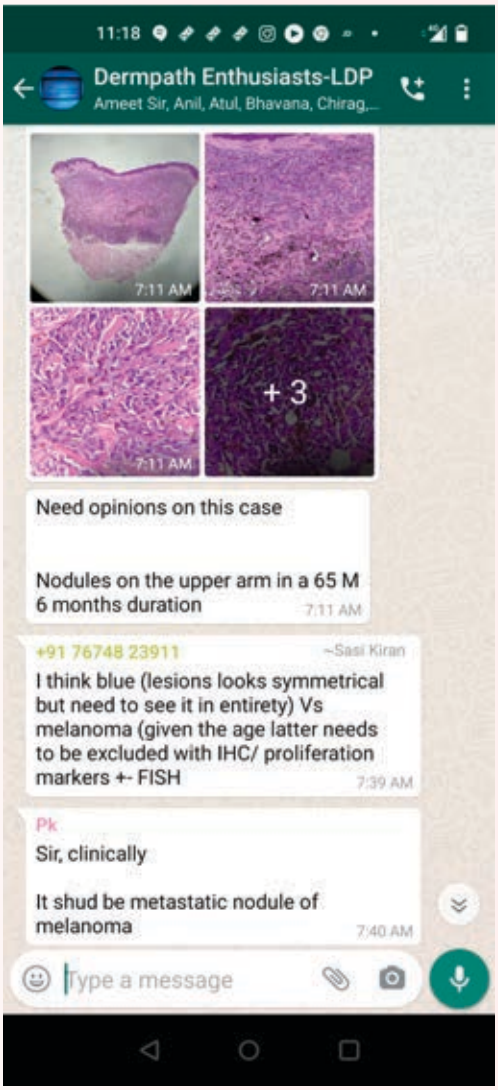

Figure 2: *WhatsApp discussion on a case in an Indian group*

Quiz

A long standing painful nodule on the thigh in a middle aged female

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A 44-year-old female presented with a minimally painful lump on the thigh since childhood. The lesion increased in severity of pain and extent since the last 6 months. She denied family history or similar lesions elsewhere. On examination, a compressible tender blue-black nodule with increased tenderness on cold application was noted **(figure 1).** The lesion was excised and histopathologic examination was performed which showed a well circumscribed dermal tumor with vascular spaces lined by cells with well-defined eosinophilic cytoplasm and round-ovoid nuclei **(figure 2a-c).** What would be the probable diagnosis?

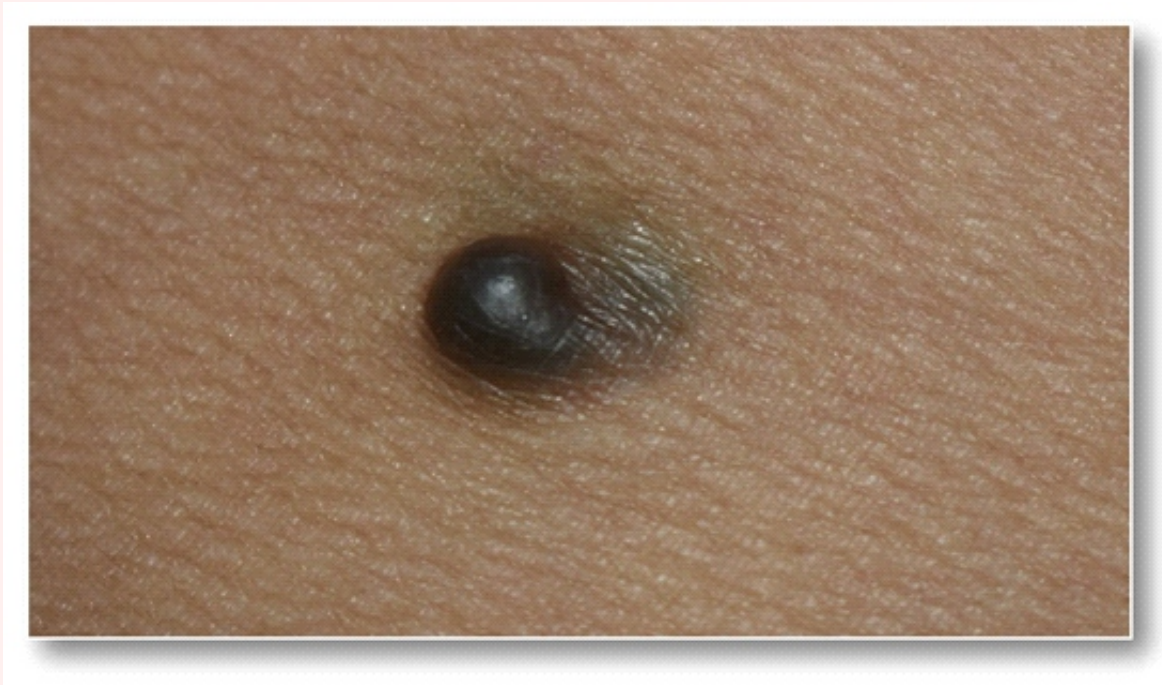

Figure 1*- A solitary blue-violaceous nodule on the thigh.*

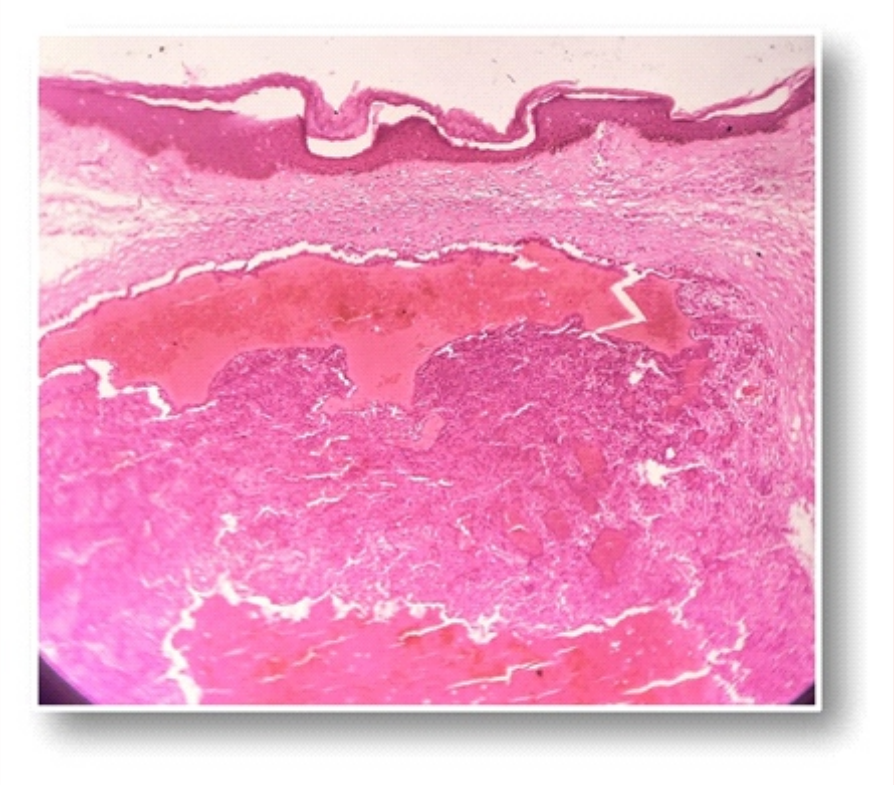

***Figure 2a**-An encapsulated vascular and cellular proliferation is seen in the dermis (H&E, 2.5x).*

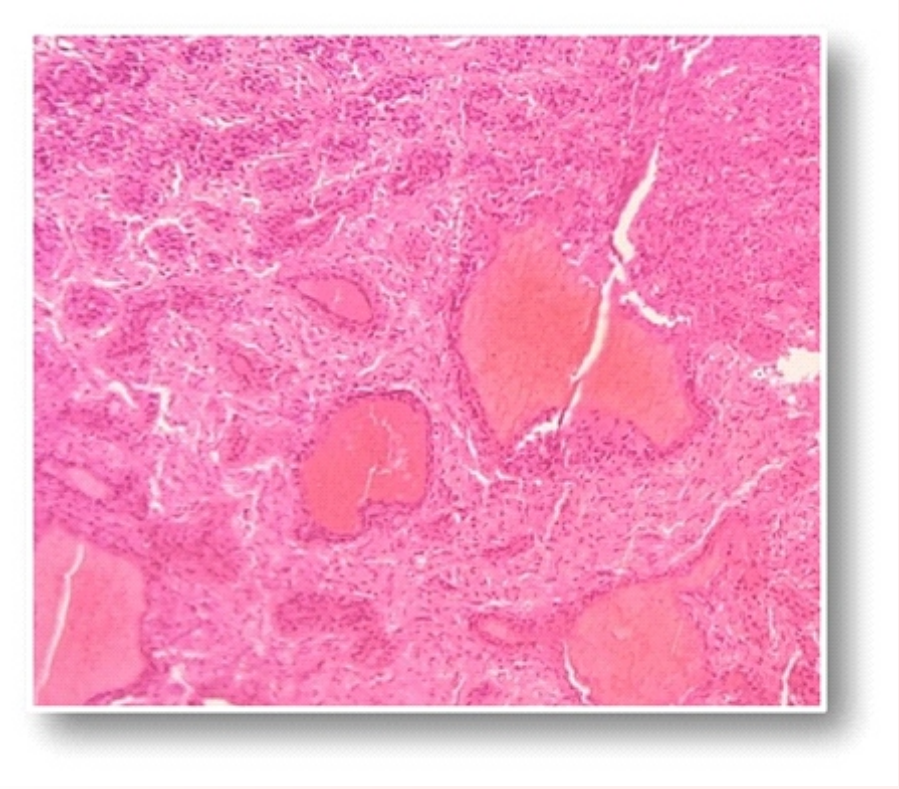

***Figure 2b**- Vascular channels are lined by a few layers of cells with eosinophilic cytoplasm and round nuclei (H&E, 5x).*

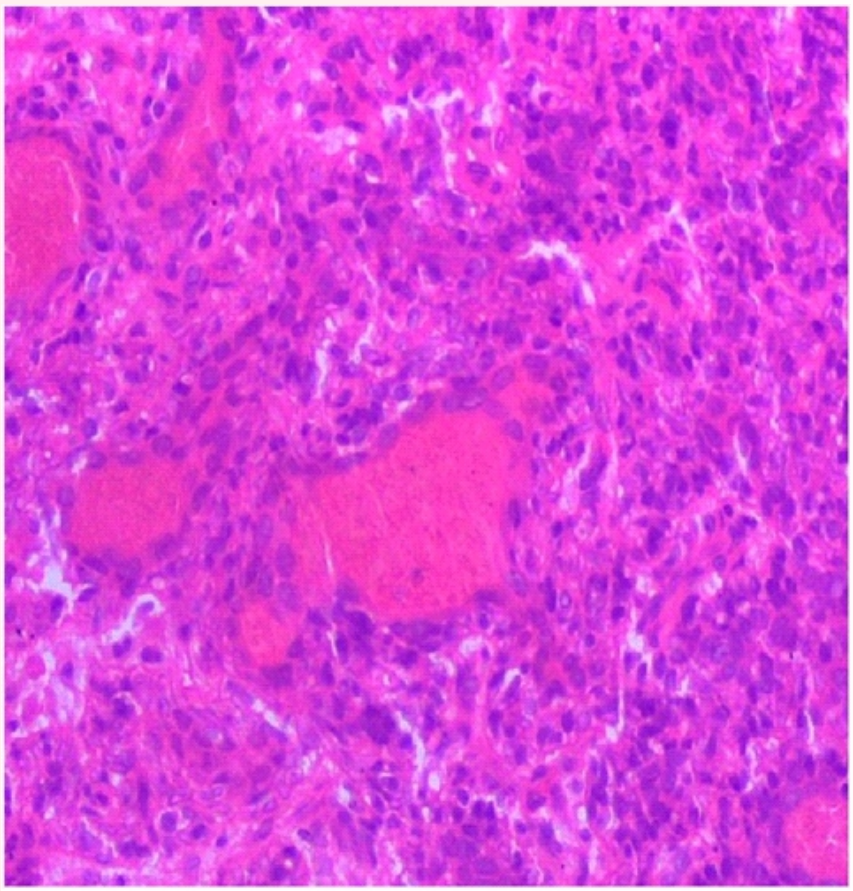

***Figure 2c**- Component glomus cells have eosinophilic cytoplasm and round-ovoid nuclei some having punched out appearance.*

A. Glomus tumor

B. Glomuvenous malformation

C. Venous malformation

D. Leiomyoma

Ans. B. Glomuvenous malformation

Presentation of patient with a painful skin tumor must provoke consideration of specific range of differential diagnoses.[1] Ascertaining the final diagnosis is incumbent on histologic analysis in many cases. In the present case, presence of the nodule since childhood, pain, tenderness and cold sensitivity hinted at the glomus cell origin of the tumor.

These tumors arise from smooth muscle cells of the arterial limb of the Sucquet-Hoyer canal.[1] They are divided into three types depending on their dominant histologic component: glomus tumors (with predominantly solid glomus cells), glomuvenous malformations (vascular spaces present), glomangiomyoma (smooth muscle cells).

Glomuvenous malformations (previously called glomangiomas) are uncommon soft tissue tumors which may be solitary or multiple, sporadic or inherited. Loss of function of glomulin gene is implicated.[2] Usually, glomangiomas arise in the pediatric age group. Unlike glomus tumors, they do not involve the subungual region. The limbs are commonly involved. They are usually blue-purple nodules or papules and are painful, tender and sensitive to cold.[3] Visceral involvement is rare.

Histology is the gold standard for diagnosis. It classically shows a well circumscribed dermal tumor with cavernous vascular spaces lined by one or more layers of glomus cells.[4] Glomus cells are distinctive by virtue of their pale eosinophilic cytoplasm, well defined cell membranes (highlighted by PAS stain) and round-ovoid punched out central nuclei.[5] Mitoses may be seen but obvious atypia is absent. Glomangiomyoma comprises spindle shaped smooth muscle cells adjacent to vascular spaces merging with glomus cells.

Two important histologic features to be looked for include infiltrating glomus tumor and glomangiosarcoma. The former is characterized by solid nests of glomus cells in deep soft tissue and frequently recurs. Criteria for glomangiosarcoma include size >2cm and subfascial or visceral location, atypical mitoses and moderate or marked nuclear atypia and 5 or more mitoses per 50 high power fields.[5]

Major differentials include eccrine spiradenoma, blue rubber bleb nevus and Mafucci syndrome. Eccrine spiradenoma is characterized by dermal cell nests (blue balls) with peripheral basaloid and central larger cells with pale nuclei.[6] Blue rubber bleb nevus syndrome, a vascular malformation, is characterized by dilated venous channels lined by flattened endothelium and attenuated smooth muscle wall.[7] A similar picture is also noted in Mafucci syndrome.[8]

Treatment includes surgical excision, sclerotherapy and lasers.[9] Recently, a combination of intense pulse light and NdYAG laser has shown reduction of lesion size with safety profile.[10]

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