Houston Dermatological Society
Thirtieth Annual

John M. Knox, M.D. Memorial Lecture

Saturday, November 12, 2022
Department of Dermatology
UTHealth McGovern Medical School

HOUSTON DERMATOLOGICAL SOCIETY
30th Annual John M. Knox, MD, Memorial Lecture
"In Memory of Excellence"

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Department of Dermatology, *UTHealth McGovern Medical School*

Program

8:30-8:35	**Welcome by Hung Quoc Doan, MD, PhD** Department of Dermatology, Assistant Professor
8:35-10:30	**Virtual Case Presentations** **Q&A, Case Presentations**
10:30-10:50	Break
10:50-11:00	**"Memories of John M. Knox, MD"** John E. Wolf, Jr., MD, MA *Professor and Chair Emeritus*, Dermatology, BCM
11:00-12:00	**Guest Lecturers** **Julia Dai, MD** Assistant Professor, Department of Dermatology, UTH-MDA **Auris Huen, MD, PharmD** Associate Professor, Department of Dermatology, UTH-MDA **Madeleine Duvic, MD** Deputy Department Chair, Department of Dermatology, UTH-MDA ***"Cutaneous T-Cell Lymphoma: Past, Present, and Future"***
12:00pm	Wrap-Up

Guest Lecturers

Julia Dai, MD

Dr. Julia Dai is an Assistant Professor in the Department of Dermatology at the University of Texas MD Anderson Cancer Center. Dr. Dai received her medical degree from the University of Pennsylvania Perelman School of Medicine. She went on to complete a clinical fellowship in cutaneous T-cell lymphoma at Stanford University under the mentorship of Dr. Youn Kim. She completed dermatology resident at the University of Chicago, where she served as chief resident. Dr. Dai was recruited to The University of Texas, MD Anderson Cancer Center in 2021. She has received national awards and recognition from the Medical Dermatology Society and the Society for Investigative Dermatology. In her spare time, you can find her running, cycling, and rock climbing around Houston

Auris Huen, MD. PharmD

Dr. Auris Huen is an Associate Professor in the Department of Dermatology at the University of Texas MD Anderson Cancer Center. Prior to medical school, she attended pharmacy school at the University of Texas at Austin and pharmacy residencies at the University of California, San Francisco and MD Anderson. Dr. Huen practiced as a clinical pharmacist at MD Anderson prior to attending medical school at University of Texas Medical School in Galveston. She then went on to complete dermatology residency at the University of Pennsylvania and joined the faculty at MD Anderson in 2015. Dr. Huen is the chair of the multidisciplinary T-cell lymphoma group at MD Anderson and the medical student director for the cutaneous lymphoma course. Outside of work, she enjoys traveling and exploring Houston's diverse food offerings!

Madeleine Duvic, MD

Dr. Madeleine Duvic is a Professor of Internal Medicine and Dermatology and Deputy Department Chair of the Department of Dermatology at The University of Texas, MD Anderson Cancer Center. She is internationally recognized for her work and leadership in cutaneous lymphoma. She has led numerous clinical and translational studies, including investigational trials of novel therapeutics such as denilleukin diftitox, bexarotene, vorinostat, and mechlorethamine gel that have led to FDA approval. Dr. Duvic operates a robust ongoing database of cutaneous lymphoma patients that has allowed longitudinal study to better understand the clinical and biological behavior of disease and response to treatment. She has served on the medical and scientific boards of national and international organizations, including the United States Cutaneous Lymphoma Consortium, Cutaneous Lymphoma Foundation, and Society for Investigative Dermatology. She has been awarded an K24 award and continues to direct an NIH-funded molecular biology lab. She has a substantial history of mentoring successful students, residents, and junior faculty – including Dr. Huen and Dr. Dai!

In Memoriam
John M. Knox, M.D.
(April 11, 1925-February 28, 1987)

When John Knox died suddenly on the Hawaiian Island of Maui, Texas dermatologists lost one of their most gifted and compassionate leaders. For over thirty years Jack was not only a dynamic force for clinical and educational excellence in our profession, but also a forceful voice for our often- timid collective conscience; he was not afraid to oppose what he thought to be wrong or to stand up for what he felt was right – and he was right more often than wrong. When Jack spoke, the room fell very quiet, and we listened.

Most of us live out our lives near the intersection of "Prudence" and "Paranoia", preferring not to "disturb the universe." John Knox was more courageous, and therefore more vulnerable. We will miss that courage, and his relentless honesty, even more than his numerous, well-documented contributions to dermatology. Jack was author or co-author of more than 300 publications. He served as president of the Houston Dermatological Society, the Texas Dermatological Society, the South Central Dermatologic Congress, the American Venereal Disease Association, and the American Board of Dermatology; he was chairman of the Council of the National Program for Dermatology and on the Board of Directors of the American Academy of Dermatology, the Society for Investigative Dermatology, and the American Dermatological Association. When he died suddenly, Jack was in Hawaii to be named President of the American Dermatological Association, an honor which was graciously awarded to him posthumously.

John Knox received a B.S. degree from Texas A&M University in 1946 and an M.D. from Baylor University College of Medicine in 1949. He received his dermatology training at the University of Michigan and became the first full-time Chairman of the Department of Dermatology at Baylor College of Medicine. After retiring from Baylor, Jack continued his superb teaching as a Clinical Professor at Baylor, UTMB Galveston, and the University of Texas Health Science Center in Houston. To his enormous pleasure, he was joined in the practice of dermatology by his son, J. Marshall Knox, II.

However, the measure of a man is not the list of his accomplishments but how he lived. John Knox was a decent man who loved his family and was fiercely loyal to his friends; his enemies should have chosen a different adversary. To me, he was teacher, friend, and valued counselor. If you ask me how I know that John Knox will be both missed and remembered and that his contributions to dermatology will be enduring ones, I can only say that I just know. In Jack's own words, "A thumb is a thumb."

John E. Wolf, Jr., M.D.
May 1, 1987

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Case # 1
RED, WHITE, AND BLUE-GRAY BABY

Presented by: Chelsea Steele MD MPH and Adelaide Hebert MD

History: A 7-month-old female patient was admitted to the PICU for status epilepticus. Dermatology was consulted for cutaneous pigmentary abnormalities including red patches on the face and blue-gray patches on the trunk and extremities, both of which had been present since birth. Parents reported that the baby was born at term with no abnormalities, but did experience her first seizure on second day of life. Patient's seizures had been previously controlled on single agent anti-epileptic up until this admission. The patient was not meeting age appropriate milestones. Family history revealed no dermatologic or neurologic abnormalities in either parental line. Neurology and ophthalmology were consulted as well. Continuous EEG on admission showed diffuse encephalopathy. CT of the brain showed moderate cerebral atrophy but no acute intracranial abnormality. MRI of the brain with and without contrast showed diffuse cerebral atrophy as well as leptomeningeal enhancement along the left cerebral convexity. Ophthalmology findings were significant for elevated intraocular pressures bilaterally, indicative of congenital glaucoma. GeneDx single gene slice of cells cultured from skin biopsy were negative for mutations in GNAQ, PIK3CA, and PTEN.

Medications: Phenobarbital, levetiracetam, timolol eye drops

Physical exam: On the central forehead, a triangular, well-demarcated erythematous patch that crossed midline. On the trunk and all four extremities, aberrant blue-gray patches. Notable macrocephaly and no discrepancy in size of upper and lower extremities.

Diagnosis: Phakomatosis Pigmentovascularis Type IIb & possible Sturge Weber Syndrome

Discussion: Phakomatosis pigmentovascularis (PPV) is a rare congenital syndrome that describes a capillary malformation with an associated pigmentary nevus and the possibility of extra-cutaneous manifestations. There have been less than 250 cases published in the literature. PPV is divided into 5 subtypes according to the associated pigmentary nevus, and is further sub-divided into whether extra-cutaneous signs are absent (a) or present (b). Types I through IV are characterized by a nevus flammeus, or port wine birthmark, most commonly on the face, and types II, III, and IV may have an additional nevus anemicus. Type I has an associated pigmented linear epidermal nevus, type II has associated dermal melanocytosis (most commonly aberrant dermal melanocytosis but may also be a nevus of Ota or Ito), and type III has an associated nevus spilus. Type IV is a combination of type II and III. Type V is distinct in that the capillary malformation is instead cutis marmorata telangiectatica congenita with associated dermal melanocytosis. The extracutaneous findings that characterize the "b" subtype include neurologic, ocular, or musculoskeletal findings.

The most common subtype is type II, and is associated with extracutaneous findings in over 50% of cases, as in the case presented. The most commonly reported associated syndromes with type IIb are Sturge Weber Syndrome (SWS) and Klippel-Trenaunay syndrome. A diagnosis of PPV requires careful clinical examination, in addition to appropriate radiographic studies and additional referral to subspecialties such as neurology and ophthalmology. This patient case highlights the multidisciplinary approach to patients with PPV.

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2. Al Robaee, Ahmad, Nusrat Banka, and Abdullah Alfadley. "Phakomatosis Pigmentovascularis Type IIb Associated with Sturge-Weber Syndrome." Pediatric dermatology 21.6 (2004): 642–645. Web.

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4. Cruz, Helena Vidaurri-de et al. “Phakomatosis Pigmentovascularis II A and II B: Clinical Findings in 24 Patients.” Journal of dermatology 30.5 (2003): 381–388. Web.

Case # 2
New-onset Pustular Rash in an Immunocompromised Patient

Presented by: Ashley Brown MD and Megan Rogge MD

Examine: Full body, including genital exam

History: This is a 50-year-old man who presented to the emergency department with a two-week history of skin lesions on the neck, face, scalp, back, penis, and sole of the foot. He reported five days of cough, low grade fevers, and rhinorrhea prior to eruption of skin lesions. All lesions are pruritic, lesions of the sole and genitals are painful. He has a history of poorly controlled HIV (CD4 48 cells/dL) as well as a recent emergency visit with similar skin rash, diagnosed as syphilis and treated with penicillin. Additionally, he had been sexually active with multiple male and female partners in the weeks prior. No known sick contacts nor relevant travel history.

Medications: Currently off all medications, including anti-retroviral therapy

Physical exam: Indurated erythematous plaques with overlaying firm pustules with central serous or necrotic crust of the forehead, nose, scalp, neck, back, left sole, scrotum, penile shaft, pubis. Cervical lymphadenopathy noted, right chain with overlaying erythema and necrotic nodule

Histopathology: Ulcer and suppurative folliculitis. Findings are non-specific and could be consistent with monkey pox

Lab results: Positive monkey pox PCR swab from lesion on forehead

Diagnosis: Monkeypox

Discussion: The 2022 monkeypox global outbreak is an ongoing health crisis, with the first case in the United States reported in May 2022. Given the quick spread of disease and level of public interest in the outbreak, there is a need to characterize the manifestations of monkeypox clade II (the current clade spreading in the United States). Classically, monkeypox occurs in three stages; incubation of 1-2 weeks, prodrome fever and lymphadenopathy, rash lasting from 2 to 4 weeks that develops from macular to papular to pustular to finally crusted lesions that desquamate. We describe a severe case of monkeypox disease in an immunocompromised patient who was treated with multiple rounds of tecovirimat (T-poxx) due to recalcitrant disease lasting multiple months.

Currently, the FDA has no approved treatment for monkeypox. The CDC has outlined the use of T-poxx, an FDA approved smallpox antiviral agent, for emergency use for severe cases of monkeypox. In limited case studies, T-poxx has been shown to decrease viral shedding and duration of monkeypox disease. This case demonstrates a severe presentation of monkeypox that necessitates T-poxx treatment.

References:

1. Adler H, Gould S, Hine P, Snell LB, Wong W, Houlihan CF et al. Clinical features and management of human monkeypox: a retrospective observational study in the UK. Lancet Infect Dis. 2022;22(8):1153-62. doi:10.1016/s1473-3099(22)00228-6.
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Case # 3
THE GREAT IMITATOR

Presented by: Julianna Martel MD, Meryl Musicante BS, Shelby Kubicki MD, Anisha Patel MD

History: A 61 y.o. male with chronic lymphocytic leukemia (CLL) maintained on venetoclax initially presented to the emergency department with oral lesions, worsening lymphadenopathy, and fever. CT imaging demonstrated new enlarged submandibular and submental lymph nodes, and fine needle aspiration revealed an atypical lymphoid proliferation. The patient was diagnosed with CLL relapse and was referred for CAR T-cell therapy.

Over the next several weeks, the patient developed a rash on his trunk, extremities, palms and soles. The rash was asymptomatic and persistent. The patient also reported unilateral blurred vision and bilateral floaters. He denied any new medications or environmental exposures. He was admitted with dermatology consulted for further evaluation.

Medications: Venetoclax, entresto, eplerenone, escitalopram, oxycodone, furosemide

Physical exam: Exam was significant for erythematous macules and few thin papules with fine scale involving the trunk, extremities, palms, and soles. There was also a purple indurated and scar-like papule with rolled boarders on the distal tongue and submandibular lymphadenopathy.

Histopathology: Punch biopsy of the abdomen showed interface dermatitis with plasma cells, and treponema pallidum immunostaining was positive for spirochete organisms.

Labs: The patient had a reactive RPR, positive TP-PA, and positive CSF-VDRL

Diagnosis: Neurosyphilis

Discussion: Ultimately, this case highlights the diagnostic overlap between syphilis and leukemia. An atypical lymphocytic proliferation in lymph nodes of patients with a history of CLL does not preclude the possibility of other causes of lymphadenopathy as CLL cells can persist at low levels in these patients despite chemotherapy. Therefore, additional work-up of lymphadenopathy is indicated for infectious and inflammatory disease, especially in the setting of rash and vision changes. Syphilis, in particular, can mimic malignancy as seen in our patient.

References:

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Case # 4
VERRUCOUS PLAQUES ON THE FEET

Presented by: Keemberly Kim MD and Omar Pacha MD

Examine: Genitalia, lower extremities, and feet

History: This is a 39 y.o. Caucasian male with a history of Bowen's disease of the right foot s/p Mohs surgery 3 years prior who presented to dermatology for evaluation of painful verrucous plaques involving the toes of his bilateral feet for 5 years. He had been following with a local podiatrist and dermatologist who had performed multiple biopsies of the areas consistent with squamous cell carcinoma in situ (SCCis). They recommended surgical excision of the areas. On further evaluation, the patient was found to have multiple verrucous papules involving the genital area.

Medications: None

Physical exam: Verrucous exophytic plaques involving the toes of the bilateral feet, most pronounced in the interdigital spaces. Multiple verrucous papules on shaft of the penis and scrotum

Histopathology: Full thickness epidermal keratinocytic atypia with verrucous features. Lesional cells are positive for high-risk HPV (subtypes tested: 16, 18, 31, 33, 35, 45, 52, 58)

Diagnosis: High-risk Human Papillomavirus induced squamous cell carcinoma in situ

Discussion: Cutaneous and mucosal HPV infections are common and generally cause benign papillomas. Persistent infection with high-risk HPV subtypes, predominantly HPV 16 and 18, can lead to intraepithelial neoplasia that can proceed to invasive carcinoma. HPV associated SCC and SCCis is most often reported in the genital area, however it can rarely involve the distal digits. Diagnosis is typically delayed, and lesions may undergo years of therapeutic attempts without a biopsy.

While Mohs micrographic surgery is the most effective treatment, recurrence rates are reported to be as high as 23%. This could be due to being unable to eliminate oncogenic HPV from surrounding skin. Several local destructive adjuvant treatments may be considered following surgery: CO2 laser, curettage and electrodesiccation, cryotherapy or imiquimod.

Due the patient's extensive involvement of his feet, neoadjuvant treatment was started with cryotherapy and topical imiquimod 5% cream to the genital and foot lesions. He is being closely monitored and pending evaluation for further surgical management.

References:

Alam M, Caldwell JB, Eliezri YD. Human papillomavirus-associated digital squamous cell carcinoma: literature review and report of 21 new cases. J Am Acad Dermatol 2003; 48: 385–393.

Case # 5
Benign lesions in a dangerous condition

Presented by: Shelby L. Kubicki MD and Valencia Thomas MD

Examine: Face, trunk, and extremities

History: This patient is a 45-year-old Caucasian man with Cowden syndrome with known PTEN mutation and history of multiple malignancies including thyroid cancer, non small-cell lung cancer, renal cell carcinoma, meningioma, and cutaneous B cell lymphoma. History of multiple cutaneous lesions including trichellilomas, BCC, SCC, DSFP, and multiple other benign skin lesions. He presented with multiple painful skin lesions.

Medications: Levothyroxine, hydrochlorothiazide

Physical exam: A. Right pectoralis with 7x7mm firm pink papule, B. left lateral sacrum with 9x7mm firm pink papule, C. left inguinal fold with 1.5x1cm tan nodule and D. left mid flank with 2x1.5cm tan nodule.

Histopathology: A, B. Dermatofibromas (benign fibrous histiocytomas); C, D. Angiolipomas

Diagnosis: Dermatofibromas associated with Cowden syndrome

Discussion: Cowden syndrome is a rare genetic disorder caused by an autosomal dominant mutation in PTEN, a tumor suppression gene located on chromosome 10. Mucocutaneous manifestations include trichellimomas, acral keratoses, and mucosal papules. Cowden syndrome is also associated with an increased risk of internal malignancy, most commonly breast cancer.

The NCCN has developed diagnostic guidelines based on the presence of major and minor criteria. Fewer criteria are required when the patient has a family member with Cowden syndrome either diagnosed clinically or with a known PTEN mutation. Malignancy screening is the major focus of management and the NCCN provides modified guidelines for Cowden syndrome patients. Excision, cryotherapy, curettage, or laser destruction are commonly used for symptomatic mucocutaneous lesions. For more widespread lesions, systemic treatments including acitretin and sirolimus have demonstrated efficacy.

While there are a number of cutaneous findings associated with Cowden Syndrome, dermatofibromas and angiolipomas are not commonly reported. While neither are rare lesions even in healthy patients, this patient has had three dermatofibromas and nine angiolipomas excised over the last twelve months. It is important to characterize lesions commonly found in genetic conditions in order to optimize treatment.

References:

Lopes S, Vide J, Moreira E, Azevedo F. Cowden syndrome: clinical case and a brief review. Dermatol Online J. 2017;23(8):13030/qt0023k3x0.

Case # 6
A CASE OF CONRADI-HUNERMANN-HAPPLE SYNDROME

Presented by: Quoc-Bao Nguyen MD MBA and Adelaide Hebert MD

History: An 18-day old female patient presented to the pediatric dermatology clinic with scaly, brown, whorled fine macules and papules noted to be present at birth at 36 weeks gestation.

Physical exam: Scaly, brown, whorled fine macules and papules in a blaschkolinear pattern on the trunk and extremities.

Imaging: Epiphyseal stippling involving the bilateral femurs.

Histopathology: Hyperkeratosis and no significant acanthosis. Dyskeratosis and eosinophils were absent. The granular layer was not attenuated and there was no dermal inflammation.

Diagnosis: Conradi-Hunermann-Happle Syndrome (confirmed with genetic testing)

Discussion: Conradi-Hunermann-Happle (CHH) syndrome, also known as X-linked chondrodysplasia punctata, was first described by Dr. Happle in the 1970s. CHH syndrome occurs almost exclusively in females. The disease is most often fatal in male fetuses, but there have been some rare reports of living males. This rare genodermatosis is caused by a mutation in the emopamil-binding protein (EBP) gene, which encodes a 3β-hydroxysteroid-δ8, δ7-isomerase.

Cutaneous findings occur in about 95% of CHH syndrome cases. Common cutaneous findings noted at birth include a generalized ichthyosiform erythroderma following the lines of Blaschko. The erythroderma resolves substantially within the first few months of life and is replaced by follicular atrophoderma and dyspigmentation. Cataracts are the most common ocular abnormality, are present at birth or develop within the first months of life. Stippled epiphyses are the most characteristic radiologic finding detected during early infancy and becomes less apparent over time once bone maturation progresses, potentially making radiologic diagnosis more difficult later in life. Other clinical findings include abnormal curvature of the spine, short stature, asymmetric limb shortening, microphthalmia, microcornea, frontal bossing, macrocephaly, and a flat nasal root.

Histopathology is non-specific with hyperkeratosis and parakeratosis as the most common findings. An important test to confirm the diagnosis of CHH syndrome is evaluating the plasma for elevated levels of 8(9)-cholesterol, which can be measured by gas chromatography-mass spectrometry. The diagnosis of CHH syndrome can also be confirmed through molecular genetic testing.

Treatment is focused on symptomatic management. Orthopedic consultation for scoliosis or leg length discrepancy, ophthalmologic management of cataracts with possible lens implant, and support for respiratory problems, hearing loss, and hydronephrosis may be necessary. Skin manifestations may require emollients, keratolytics, and sun protection. Patients often require a team of interdisciplinary specialists for follow-up and continued monitoring. Furthermore, family support and genetic counseling are of paramount importance. The life expectancy for patients with CHH syndrome is usually normal barring any significant cardiac or pulmonary compromise due to scoliosis or decrease in cognitive function.

References:

Happle R. X-Linked Dominant Chondrodysplasia Punctata Review of Literature and Report of a Case. Hum Genet. 1979; 53(1):65-73.

Case # 7
Eccrine syringofibroadenomatosis associated with epidermodysplasia verruciformis

Presented by: Raghavendra L. Girijala MD and Valencia D. Thomas MD MHCM

Examine: Face, neck, trunk, upper extremities

History: A 59-year-old man with a history of epidermodysplasia verruciformis presented for evaluation of eruptive neoplasms of uncertain behavior on the scalp for 1 year. He noted a distant history of Grenz ray therapy and in-office salicylic acid treatments for verruca. He denied a prior history of skin cancer. Given the number of lesions at presentation, he was only able to undergo Mohs-assisted excision of three neoplasms on the scalp (right anterior parietal, right frontal, and left temporal). Intraoperative suspicion for an adnexal origin to the neoplasms prompted a debulk.

Physical exam: Numerous exophytic nodules were observed on the right anterior parietal scalp, right frontal scalp, left temporal scalp, right scalp, and left parietal scalp 7 cm superior to the helix. Numerous hypopigmented scars were noted on the trunk, neck, and upper extremities.

Histopathology: Multifocal basaloid and reticulated epithelial neoplasm consistent with syringofibroadenoma. Keratinocytic changes consistent with epidermodysplasia verruciformis were present.

Labs: Human papillomavirus (HPV) genotyping demonstrated positivity for HPV-5, -10, and -16

Diagnosis: Eccrine syringofibroadenoma associated with epidermodysplasia verruciformis

Therapy: Intralesional 5-fluorouracil (50 mg/mL)

Discussion: Epidermodysplasia verruciformis (EDV) has been associated with the development of non-melanoma cutaneous neoplasms, most commonly squamous cell carcinoma. The etiology of eccrine syringofibroadenoma (ESFA) is unclear, with reports linking it to genodermatoses such as Clouston syndrome and reactive processes such as erosive lichen planus, bullous pemphigoid, epidermolysis bullosa, and venous stasis. There are a handful of reports linking ESFA to human papillomavirus (HPV) related keratinocyte changes.

ESFA associated with Clouston's syndrome has been associated with HPV-10, suggesting a viral-mediated epithelial proliferation. ESFA has also arisen within squamous cell carcinoma, with subsequent genotyping revealing human papillomavirus (HPV)-107 in the dysplastic epithelium. In our case, keratinocyte abnormalities consistent with viral-induced EDV were seen along with the development of eruptive ESFA, supporting a possible link between the two entities.

Treatment options for ESFA are limited. For solitary ESFA, excision is feasible; however, it is not a realistic option for patients with numerous lesions. A review of the literature notes attempts at treatment with cryotherapy, CO2 laser therapy, electrodesiccation, topical and intralesional retinoids, and imiquimod. Given the possible contribution of HPV-induced changes in ESFA, we propose intralesional 5-fluorouracil as a treatment modality for this rare condition.

References:

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Case # 8

TENDON SHEATH ERYTHEMA

Presented by: Daniel Morse MD and Natasha Klimas MD

Examine: Face, neck, trunk, upper extremities, lower extremities

History: A 49 y.o. Hispanic female with one year history of breast cancer, s/p neoadjuvant chemo with Doxorubicin/Cyclophosphamide/Paclitaxel, mastectomy, and adjuvant radiation who presented to the dermatology clinic. She noted a red rash on her arms, hands, chest, and thighs that appeared eleven months ago around one month before she started chemotherapy. She noted generalized pruritus but denied muscle weakness or dysphagia. Notably her rash began prior to her chemo regimen and before she started preventative tamoxifen.

Physical exam: 1-2mm erythematous, dome shaped, keratotic papules at the bilateral forearms. Thin pink plaques of MCPs and PIPs and symmetric erythema of the skin overlying the extensor tendon sheaths of the hands. No mucosal or nail involvement.

Histopathology: Interface dermatitis with mucin consistent with dermatomyositis

Labs: Positive for transcription intermediary factor 1-gamma (TIF1-γ) antibodies

Diagnosis: Wong type, Amyopathic Dermatomyositis

Therapy: 15 mg of methotrexate weekly with significant improvement

Discussion: Wong-type dermatomyositis (DM) is a rare variant exhibiting concomitant clinical and histopathological features of pityriasis rubra pilaris (PRP). It is characterized by keratotic follicular papules that mimic PRP. It can manifest in the context of myopathic or amyopathic DM and may rarely present with erythroderma.

Histopathologic examination shows follicular and non-follicular epidermal invaginations filled with keratin. In addition, a distinctive histologic pattern of tiered parakeratosis with dyskeratosis or “peacock plumage”, has been described in Wong-type DM. This “peacock plumage”, has been associated with human polyomavirus (HPyV) 6 and HPyV7. Further studies are needed to elucidate the connection between Wong-type DM and HPyV infection.

Treatment options include azathioprine, methotrexate, and mycophenolate mofetil. Tamoxifen, which our patient was taking, has been shown to accelerate antimalarial associated retinopathy. We were thus careful to avoid antimalarials.

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Case # 9

AN OVERLOOKED CUTANEOUS COMPLICATION AFTER INTERVENTIONAL CARDIOLOGIC PROCEDURES

PRESENTED BY: Yamila Goenaga MD and Adelaide Hebert MD

HISTORY: 73-year-old white male patient requested re-evaluation of an area of on his back due to new-onset of bleeding and itching. He described a dry, pink patch that had been present for years. It was previously asymptomatic but now it had become somewhat itchy and irritated. He denied previous cutaneous eruptions. Previous treatments included emollients as needed and topical steroids.

PMH: coronary artery disease status post percutaneous coronary intervention x 2 (10 years ago).

MEDICATIONS: losartan, aspirin, clopidogrel, hydrochlorothiazide, atorvastatin.

EXAM: Midline lower back with a well demarcated erythematous plaque with telangiectasias, fine dry scale, hyper and hypopigmentation, and mild ulceration with hemorrhagic crust at 7 o' clock.

DIAGNOSIS: Fluoroscopy-induced radiation dermatitis.

THERAPY: regular wound care including emollients and hydrogel dressings.

DISCUSSION: The short- and long-term effects of radiation on the skin have been extensively described. However, fluoroscopy-induced radiation dermatitis (FIRD) resulting from interventional cardiologic procedures is an underreported entity that carries high morbidity. As the leading cause of mortality around the globe, coronary atherosclerosis is requiring more widespread diagnostic and therapeutic procedures using fluoroscopy such as angiography and percutaneous coronary intervention (PCI). Furthermore, complex procedures have continued to emerge as well as their repetition leading to higher lifelong cumulative radiation doses. As such, the incidence of radiation-induced skin injuries such as FIRD is increasing and expected to continue doing so.

Three patterns of FIRD have been described: Acute FIRD usually occurs within 90 days of exposure, subacute FIRD occurs weeks to months, and chronic FIRD occurs months to years after. The total dose and volume and surface area exposed to radiation influence the risk and subsequent manifestations of FIRD. Skin changes typically simulate a burn injury varying from erythema, dry to moist desquamation, blistering, ulceration, or necrosis. Secondary infection may occur and pain and pruritus are common.

The diagnosis is mostly clinical and the most important clues to the diagnosis is that the skin changes are sharply demarcated limited to the irradiated area which is typically on the patient's back at the site of beam entry. Biopsy is not required in the majority of cases but the primary histological feature of FIRD is a toxic interface dermatitis with mononuclear cells in direct apposition to necrotic keratinocytes. Differential diagnosis mainly includes acute graft-versus-host disease, contact dermatitis, dermatophyte infection, or fixed drug reaction. Diagnostic challenges include the variable onset interval from week to months, concomitant treatments that may lead to misleading symptoms, and lack of awareness so a high level of suspicion is required by both the dermatologist and dermatopathologist. Treatment is based on the wound care literature which require a multidisciplinary approach not specific to this entity. However, progression and malignant transformation into squamous cell carcinoma or basal cell carcinoma at the site of the injury is an important consideration that justifies close dermatologic surveillance of patients who have had an interventional cardiologic procedure.

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Case # 10

Treatment of Refractory Cutaneous B-cell Pseudolymphoma with Intralesional Rituximab

Presented by: Caroline Starling MD, Areebah Ahmad BA, Woo Cheal Cho MD, Meghan Heberton MD

History: A 61-year-old woman presented with a four-year history of dermal plaques of the bilateral lower eyelid margins and cheeks. Medications at the time included cetirizine, prednisolone, lotemax, olopatadine, and tobradex eye drops. Biopsy of the left lower eyelid showed atypical B-cell lymphoid infiltrate. Prior patch testing was positive for tixocortol-21-pivalate. Past treatments included three excisions, topical steroids, intralesional steroids, radiation to the eyelids (4 Gy), and hydroxychloroquine without long-term improvement.

Physical exam: Violaceous dermal plaques of the bilateral lower eyelid margins and cheeks

Histopathology: Punch biopsy of the left cheek showed dense dermal lymphoid B-cell infiltrate associated with reactive lymphoid follicles. Additional studies with immunoglobulin heavy chain gene rearrangement polymerase chain reaction showed a polyclonal B-cell population.

Diagnosis: Cutaneous B-cell pseudolymphoma (B-cell CPL)

Treatment: Methotrexate 15 mg weekly was poorly tolerated and did not result in improvement. Systemic rituximab was discussed and declined by the patient due to concerns for immunosuppression during the Covid-19 pandemic. Intralesional rituximab injections for the plaques on the cheeks were initiated. She received four cycles of weekly 10-20 mg intralesional rituximab over the course of one year with marked decrease in the size and thickness of the plaques as well as pruritus. She had no systemic side effects and tolerated the treatments well.

Discussion: B-cell CPL is a benign disorder that can be challenging to differentiate from malignant primary cutaneous B cell lymphoma without immunohistochemical and molecular studies [1]. Therapies may include excision, corticosteroids, antibiotics, biologic agents, immunosuppressive agents, or radiotherapy [2,3]. Rituximab is a monoclonal antibody against the CD20 surface antigen on B cells. There has been one other case report of CPL treated with intralesional rituximab injections at 10 mg/mL given weekly for 18 weeks. In both cases, there were marked areas of clearing of the pseudolymphoma patches and plaques though not complete resolution. This case highlights the potential utility of intralesional rituximab for refractory B-cell CPL cases.

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Case # 11
PINK PLAQUES AND PATCHES ON A 68-YEAR-OLD WOMAN

Presented by: Sahira Farooq MD and Julia Dai MD

History: A 68-year-old woman from Mexico presented to dermatology clinic for 6 months of widespread pink edematous papules and plaques on the face, trunk, and extremities. The lesions were associated with intermittent pruritis, but she otherwise felt well and denied significant constitutional symptoms. A prior skin biopsy from an outside hospital was reviewed which showed findings concerning for a lymphoproliferative disorder.

Medications: Amlodipine-valsartan, celecoxib, empagliflozin-metformin, levothyroxine

Physical exam: Multiple pink to violaceous patches and edematous papules and plaques involving the face, trunk, upper extremities, and lower extremities with sparing of the palms and soles. No palpable preauricular, cervical, axillary, or inguinal lymphadenopathy.

Histopathology: Atypical perivascular, periadnexal, intravascular lymphoid infiltrate involving superficial and deep dermis with follicular helper T-cell phenotype. Immunohistochemistry revealed CD3+ T-cells with cytologic atypia and CD20+ B-cells forming reactive germinal centers. Additional findings included CD4:8 ratio of 5:1 and expression of follicular helper T-cell markers PD1, Bcl-6, and ICOS.

Additional studies: PET CT showed new regional lymph node involvement and subsequent lymph node biopsy was consistent with T-cell lymphoma with follicular helper T-cell phenotype.

Diagnosis: Primary cutaneous follicular helper T-cell lymphoma with associated lymph node involvement

Treatment: After discussion at multidisciplinary T-cell lymphoma consensus panel, she was initiated on brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone (BV-CHP) under clinical trial protocol.

Discussion: Primary cutaneous follicular helper T-cell lymphoma is a rare, newly proposed variant of cutaneous T-cell lymphoma. Of the limited number of cases reported in the medical literature, most presented as multiple papules, nodules, and plaques predominantly occurring on the trunk and extremities. Most did not have evidence of extracutaneous signs or symptoms. Histopathology findings of reported cases overall showed a lymphoid infiltrate involving the superficial and deep dermis with minimal or absent epidermotropism and expression of a combination of follicular helper T-cell markers such as CXCR5, CXCL13, CD10, Bcl-6, PD-1, and ICOS.

Treatment is variable given the limited number of reported cases. Most reported cases are limited to skin and have shown variable response to therapies such as multiagent chemotherapy, radiotherapy, and allogeneic stem cell transplant.

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Case # 12

Mucosal and acral pigmentation in an ovarian cancer patient

PRESENTED BY: Eugenio Galindo MD, and Fiorinda Muhaj MD

HISTORY: 60 year old Caucasian female with recurrent high grade serous ovarian cancer s/p cryoreductive surgery and adjuvant carboplatin+doxorubicin presents with blue-brown spots on the lips, inside the mouth, and fingertips:

PMH: Ovarian cancer, GI polyps

LABS: GeneDx testing negative for *STK11* and *PTEN*

COLONOSCOPY: 2 Tubular adenomas, one sessile serrated adenoma

EXAM: Lower mucosal lip, buccal cheeks, dorsum of tongue with gray-brown macules, right labia minora with one round brown macule and left distal fingetips with few brown macules

DIAGNOSIS: Provisional: Laugier-Hunziker

DISCUSSION: Laugier-Hunziker syndrome is an acquired benign pigmentary disorder involving the oral mucosa, digits and sometimes longitudinal melanonychia. It is a diagnosis of exclusion and other systemic conditions should be worked up prior to making a diagnosis.

Here we present a unique case of provisionally diagnosed Laugier-Hunziker syndrome in a patient with a past medical history of high grade serous ovarian cancer and GI polyps. Her diagnosis of exclusion was made after review and lack of genetic and diagnostic criteria for both Peutz-Jeghers Syndrome and PTEN Hamartoma syndrome (Cowden disease, Bannayan-Riley-Ruvalcaba syndrome) described in this case presentation.

Peutz-Jeghers syndrome(PJS) is an autosomal dominant disorder associated with mutations in *STK11*. It's hallmark features include mucocutaneous lentigines at birth or during childhood and multiple hamartomatous gastrointestinal polyps. Patients with PJS are at a higher risk of pancreatic, ovarian and testicular malignancies.

PTEN hamartoma tumor syndrome refers to a spectrum of disorders caused by mutations in the *PTEN* tumor suppressor gene. These disorders are characterized by multiple hamartomas that can affect various areas of the body and include conditions such as Cowden disease and Bannayan-Riley-Rulvacaba syndrome.

Cowden disease carries an autosomal dominant inheritance pattern in mutations for *PTEN* and usually manifests clinically in adolescence or adulthood. its predominant findings include multiple cutaneous papillomatosis and rarely can be associated with perioroficial and acral lentigines. Patients with this disease have an increased risk of thyroid, breast, gastrointestinal and genitourinary cancers.

Bannayan-Riley-Rulvalcaba syndrome carries an autosomal dominant inheritance pattern in mutations for *PTEN* and usually manifests clinically at birth or during childhood in contrast Patients with this syndrome usually have genital pigmented macules and can have other findings such as lipomas, vascular malformations and hamartomatous intestinal polyps

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Case # 13

INDETERMINATE DENDRITIC CELL NEOPLASM

Presented by: Padmavathi Karri MD, Jessica Tran MD, Julia Dai MD, Fiorinda Muhaj MD

Examine: Scalp, neck, chest, back, upper extremities, lower extremities

History: Patient is a 82 y.o female with medical history notable for primary myelofibrosis on hydroxyurea and ruxolitinib daily. She presented with a 6-7 month history of cutaneous painful nodules that began on the scalp and progressed to the trunk. The lesions were previously biopsied and showed histiocytic infiltrate with central area of a caseation, suspicious for unusual sarcoidosis. To rule out other etiologies, an infectious disease and rheumatology workup was complete and negative. The lesions were thought to be a granulomatous reaction to her myelofibrosis and would improve with time on the hydroxyurea and ruxolitinib. However, about 6 months after her initial presentation, she presented with worsening skin lesions to her perivulvar, perianal, and perineal areas. Her lesions did not improve with the hydroxyurea and ruxolitinib prompting additional biopsies.

Medications: Hydroxyurea, Ruxolitinib

Physical exam: Purple to erythematous nodules of varying sizes on the scalp, posterior neck, back, chest, arms, vagina, perineum, and buttocks

Histopathology: Extensive non-Langerhans cell histiocytic proliferation involving dermis and subcutaneous adipose tissue. The dermal histiocytes were positive for CD68, CD1a, and S100, negative for CD207 (langerin) consistent with indeterminate cell histiocytosis

Diagnosis: Indeterminate dendritic cell neoplasm (IDCN)

Discussion: IDCNs present as pink-to-brown variably sized papulonodules and typically only involve the skin; however, there have been reported cases with lymph nodes or spleen involvement. The clinical course can vary widely, but most cases are indolent and have a good prognosis.

In a case review by Horna et al. (2017), 22% of published cases of indeterminate dendritic cell neoplasms have been associated with a secondary hematopoietic neoplasm. The most associated neoplasms are lymphoma, chronic myelomonocytic leukemia, and acute myeloid leukemia.

Indeterminate dendritic cell neoplasms are almost exclusively cutaneous in presentation, so therapy is predicated on symptoms/extent of involvement. There is not an established treatment protocol for this skin disorder; however, several cases report improvement with phototherapy and radiotherapy. We opted for low-dose radiation for the most symptomatic areas including her perineum and will likely consider nbUVB therapy for other skin areas. The patient had a significant clinical response after treatment and reports less discomfort and increase in quality of life.

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Case # 14

When Skin and Heart Are Not Far Apart

Presented by: Rachel Graubard MD and Auris Huen MD PharmD

History: 71-year-old male with a history of bullous pemphigoid on dupilumab and AV heart block, requiring pacemaker implantation who presented to the hospital with a four-month history of intermittent fevers, night sweats, unintentional 8-pound weight loss, and new skin lesions. Each lesion began sporadically as an erythematous papule in varying locations and grew to become an exquisitely tender, indurated plaque before spontaneously involuting.

Physical exam: Scattered lesions throughout the body in various stages as follows:

- Erythematous, dome-shaped papules on right lateral index finger and right paraspinal back
- 3 cm flesh-colored, vascular plaque on left medial thigh. Exquisitely tender to palpation
- Erythematous papule with central depression and surrounding halo of hyperpigmentation on right flank

Skin Histopathology: CD30+ Lymphoproliferative Disorder

Heart Histopathology: Neoplastic process of similar characteristics to previous skin lesion biopsy. Tumor cells strongly positive for CD30 and EMA, consistent with anaplastic large cell lymphoma

Diagnosis: Primary Cutaneous Anaplastic Large Cell Lymphoma

Therapy: Brentuximab vedotin infusion every 3 weeks x6 cycles with 11-month survival

Discussion: Primary cutaneous lymphoproliferative CD30+ disorders, including lymphomatoid papulosis and primary cutaneous large cell lymphoma (pcALCL), are a common subtype of cutaneous T-cell lymphomas (CTCL), which generally have a good prognosis overall. Although CTCLs are generally confined to the skin upon diagnosis, pcALCL is associated with the greatest likelihood of extracutaneous involvement, occurring in approximately 10% of patients and most commonly within regional lymph nodes. Extensive cutaneous disease at presentation, age over 60, and progression to lymph nodes or visceral organs are considered poor prognostic factors and require a more aggressive treatment strategy with systemic therapy.

Brentuximab vedotin is an anti-CD30 antibody drug conjugate, which is FDA-approved for treatment of mycosis fungoides and anaplastic large cell lymphoma. In recent studies, when compared to traditional treatment with methotrexate or bexarotene, brentuximab has shown to lead to a greater objective response lasting at least 4 months and, in some patients, a complete response has been observed.

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Case # 15
A Case of an Eruption of Blisters

Presented by: Matthew Dallo, MD; Richard Jahan-Tigh, MD

Examine: Upper Extremities, Lower Extremities

History: This is an 11-year old Caucasian male patient who presented to Pediatric Dermatology for complaints of multiple, pruritic, blisters that have come and go for the last 5 years on his dorsal hands, forearms, and lower extremities. He reports that the blisters would burst and result in ringed-shaped lesions that tended to spread. He was previously seen by a Pediatric Rheumatologist and was diagnosed with cutaneous lupus 3 years prior. He was started on hydroxychloroquine with minimal improvement. He had tried topical mupirocin and had also taken oral antibiotics without improvement.

Medications: Hydroxychloroquine, Mupirocin, Clindamycin

Physical exam: Multiple 1 – 2 cm erythematous annular plaques with raised borders clustered on the bilateral dorsal forearms and hands. One erythematous annular plaque on the right lower extremity. Scattered hypopigmented patches on the bilateral dorsal forearms and hands.

Histopathology: Some foci of vacuolar interface dermatitis. Aggregate of mostly lymphocytes and neutrophils near the area of vesiculation. The papillary dermis has scattered interstitial lymphocytes and histiocytes with an occasional eosinophil present.

Diagnosis: Bullous Systemic Lupus Erythematosus

Discussion: Bullous Systemic Lupus Erythematosus (BSLE) is a rare, autoimmune, subepidermal, vesiculobullous disease that occurs in patients with a previously known or concurrent diagnosis of systemic lupus erythematosus (SLE). The occurrence of BSLE among children and adolescents is around 1%. The condition is characterized by an eruption of tense vesicles or bullae that can occur at any cutaneous site or mucosal region.

Diagnosis is supported by histology and immunofluorescence testing. Histology typically reveals a subepidermal blister with neutrophil-predominant inflammatory infiltrates below the bullae formation. Immunofluorescence demonstrates linear IgG staining along the basement membrane and occasional granular IgA, IgM, and C3 deposits. Treatment includes dapsone, glucocorticoids, or immunosuppressants.

Given the clinical and histological findings, there is a high clinical suspicion for BSLE. Other differential diagnoses considered include bullous impetigo, bullous fixed drug eruption, epidermolysis bullosa acquisita, dermatitis herpetiformis, chronic bullous dermatosis of childhood, and bullous pemphigoid. Patient will be treated with topical steroids and observed for a response before considering systemic therapy.

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Case # 16
Hyperkeratosis and Blistering of the Hands and Feet

Presented by: Tayler Parker MD and Anisha Patel MD

Examine: Hands, palms, feet, and soles

History: This is a 71y.o. Caucasian man with a past medical history of non-melanoma skin cancers, hypertension, and cholangiocarcinoma who presented to dermatology with a two-week history of painful lesions on the hands and feet. These lesions were located on the pressure surfaces of the hands and feet and elicited pain upon pressure. About six weeks prior to presentation, he was started on chemotherapy with Capecitabine for cholangiocarcinoma. He had not tried any treatments.

Medications: Capecitabine, sildenafil, ondansetron, pancrelipase, pantoprazole, senna-docusate

Physical exam: Hyperkeratosis and hemorrhagic blisters on the pressure surfaces of the plantar feet. Erythematous papules on the lateral nail folds on the 1st and 2nd toes of both feet and the 4th right finger. Peeling and fissuring of the distal fingers on bilateral hands.

Histopathology: Epidermal acanthosis, papillomatosis, spongiosis, dispersed dyskeratotic cells and keratinocyte vacuolar degeneration

Diagnosis: Hand Foot Skin Reaction

Discussion: Hand foot skin reaction is an uncommon dermatosis that affects patients on certain chemotherapy agents, most commonly multikinase inhibitors. The mechanism of injury occurs via defects in repair of friction-related trauma from medication-induced inhibition of multiple pathways including VEGFR. Skin manifestations include tender, erythematous focal plaques, hyperkeratosis, and bullae in areas of weight-bearing and friction. Under histology, bullae can be seen as an intraepidermal vesicles and hyperkeratotic plaques can be seen as epidermal acanthosis, and papillomatosis. Capecitabine is a prodrug of 5-fluorouracil and is known to cause hand foot syndrome and rarely causes hand foot skin reaction. The mechanism of Capecitabine causing hand foot skin reaction in this case is unknown.

It is important to recognize this condition early to avoid progression of disease and dose reduction in the chemotherapy agent. First line treatment is topical steroids, such as clobetasol. Other therapies include topical vasodilators such as sildenafil and topical minoxidil. There are ongoing clinical trials assessing the efficacy of topical nitroglycerin paste.

The patient underwent initial treatment with topical clobetasol 0.05% ointment and topical minoxidil 5% solution bid to the hands and feet. He returned to clinic after one month of therapy and reported significant improvement in pain and improvement in the hyperkeratosis and blistering.

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Case # 17
A Rare Case of Congenital Ichthyosis

Presented by: Anna Zanot MD and Adelaide Hebert MD

Examine: Head, neck, trunk, upper extremities, lower extremities

History: This is a 15-hour old female patient born at 37 weeks gestation via C-section. At birth, she presented with diffuse, hyperkeratotic plaques with fissures, edema of hands and feet, and severe ectropion. She also had transient tachypnea of the newborn and metabolic acidosis. Dermatology, ophthalmology, plastic surgery, otolaryngology, nutrition, wound care and genetics were consulted. The patient was admitted to the NICU and placed in a humidified chamber (50-70% humidification) on a burn mattress. Vaseline single use packets, ocular lubricant ointment, and Cetaphil cleanser were utilized. She was started on acitretin 1 mg/kg/day on day 7 of life. Patient's blood cultures were positive for *Klebsiella pneumoniae* and *Candida albicans* and she was started on gentamicin, cefepime, and amphotericin B.

Medications: Acitretin 1 mg/kg/day, acetaminophen, morphine, ocular lubricant ointment, ofloxacin otic solution, gentamycin, cefepime, amphotericin B

Physical exam: Generalized plate-like hyperkeratotic plaques separated by fissures involving the head, neck, trunk, upper and lower extremities. Edema of hands and feet. Ectropion (upper>lower eyelids), eclabium, flattened nose, rudimentary ears.

Diagnosis: Harlequin Ichthyosis

Discussion: Harlequin Ichthyosis is a rare congenital ichthyosis caused by a mutation in the lipid transporter adenosine triphosphate binding cassette A 12. Patients present with extensive, plate-like keratotic scale separated by fissures, ectropion, eclabium, flattened nose, rudimentary ears, and pseudocontractures with progression to necrosis of the digits during the neonatal period. Genetic testing is performed shortly after birth to confirm the diagnosis. Harlequin ichthyosis carries a high mortality rate, with sepsis and respiratory failure being the most common causes of death. Patients are managed in the NICU and placed in humidified chambers (50-70% humidity) on a burn mattress. Single use petrolatum packets and ocular lubricants are applied. Patients must be carefully monitored for infection, electrolyte abnormalities, pain, respiratory compromise, nutritional demands, limb and digit perfusion, and impaired thermoregulation. Patients are also at risk for long term complications, including developmental delay, chronic pain, conductive hearing loss, arthritis and frequent hospitalizations. Rajpopat S et al. recommends initiating systemic retinoids within the first 7 days of life to promote desquamation. Acitretin 0.5-1.0 mg/kg/daily is most utilized. Topical retinoids may be initiated if oral therapy is unavailable.

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Case # 18

A CASE OF JUVENILE DERMATOMYOSITIS

PRESENTED BY: Michael Ryan MD, Emma Villamaria BSA, Adelaide Hebert MD

HISTORY: A 7-year-old healthy female patient presented to Pediatric Dermatology clinic as a referral from an outside dermatologist for a rash on the face and dorsal hands for 2 months. The patient had no significant past medical history and took no medications. The eruption developed shortly after a non-specific fever and respiratory illness. The patient's mother noted that the patient had been more fatigued, slower to move, and experienced difficulty getting dressed and walking up stairs. Otherwise review of systems was negative.

EXAM: Erythematous confluent patches involving the forehead, nasal bridge, upper cutaneous lip, and cheeks with minimal overlying scale. Subtle bilateral upper eyelid edema/erythema was present. There were pink, scaly papules with excoriations over the bilateral dorsal interphalangeal and metacarpophalangeal joints. Diminished proximal muscle strength on extension and flexion of the upper extremities (⅗) and lower extremities (⅘) was noted. The Childhood myositis assessment scale score was 28/52.

LABS: CBC, ESR, and CRP were within normal limits. Creatine kinase was elevated at 1366 U/L (nl<143 U/L). CMP revealed elevated AST of 85 U/L (nl 12-32 U/L) and ALT of 67 U/L (nl 8-24 U/L). Aldolase was elevated at 10.7 U/L (1-7.5 U/L). Myositis-specific panel was negative, which included Jo-1, Pl-7, Pl-12, EJ, OJ, SRP, Mi-2 alpha, Mi-2 beta, MDA-5, TIF-1y, NXP-2.

IMAGING: MRI of the femur without contrast showed findings consistent with systemic inflammatory myositis.

DIAGNOSIS: Juvenile dermatomyositis

TREATMENT: Prednisolone 30mg daily and Methotrexate 12.5 mg weekly

DISCUSSION: Juvenile Dermatomyositis (JDM) is a very rare form of inflammatory myopathy with an incidence of only 2 to 4 per million children annually. Notable clinical features of JDM include symmetrical proximal muscle weakness and characteristic cutaneous manifestations. While the etiology is unclear, JDM is proposed to be an autoimmune reaction in genetically susceptible individuals in response to a trigger, such as infectious agents.

The initial evaluation for suspected JDM includes total body skin examination, objective muscle strength examination, and laboratory studies. Total body skin examination often reveals characteristic cutaneous manifestations including heliotrope rash, Gottron's papules, dilated proximal nail fold capillaries, and skin ulceration. Additionally, proximal muscle weakness is a characteristic finding. The Childhood Myositis Assessment Scale (CMAS) is an objective measure used to assess muscle function. CMAS uses various physical exam maneuvers to assess overall muscle strength and has been shown to be a valid measure of physical function in children with JDM.

Muscle enzyme testing including creatine kinase, lactate dehydrogenase, aspartate aminotransferase, and aldolase should be obtained in suspected cases of JDM. Additionally, antibody testing for JDM-specific autoantibodies as well as other connective tissue disease-related autoantibodies, such as antinuclear antibody and anti-Sm, should be obtained. Due to the invasive nature, electromyography (EMG) and muscle biopsy are no longer used frequently as diagnostic techniques, especially in patients who present with characteristic symptoms. MRI is important to obtain to assess muscle involvement and disease activity. Workup for associated malignancy in JDM is not typically required, as there is not a strong association between JDM and malignancy as seen in adult dermatomyositis.

Multidisciplinary care with a pediatric rheumatologist is highly recommended in cases of JDM. Early initiation of treatment for JDM is essential, as complications such as ulceration, calcinosis, gut vasculopathy, and nervous system disease can ensue. The goal of therapy is to minimize inflammation, improve function, and prevent disability. This goal is accomplished through pharmacological treatment with high-dose steroids and adjuvant methotrexate. Intravenous immunoglobulin may be a useful adjunct for resistant disease, particularly when skin features are prominent. Lastly, physical therapy and strict sun protection are important measures to minimize morbidity.

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Case # 19
TATTOOS SAY A THOUSAND WORDS

Presented by: Jamael Thomas, MD, MPH and Sirunya Silapunt, MD

History: This is a 25 y.o. African-American man who presented to dermatology clinic with a 6-day history of multiple mildly pruritic papules involving the bilateral upper extremities and chest. All lesions developed within independent tattoos obtained over a 7-year period at two separate tattoo parlors. Associated symptoms included fevers, chills, headache, myalgias, and eye redness associated with pain, blurry vision, and photophobia.

Medications: None

Physical exam: Conjunctiva were injected. There were multiple erythematous to violaceous papules both with and without scale along with a several scattered pustules all limited to black tattoo ink scattered across bilateral upper extremities and anterior trunk. The few areas of red tattoo ink were not involved.

Histopathology: Sarcoidal non-caseating dermal granulomatous inflammation with tattoo ink

Infectious Rule Out: Negative Fite, AFB, PAS stains + negative tissue cultures (AFB, bacteria & fungi)

Diagnosis: Tattoo-Associated Sarcoidosis with Severe Uveitis

Discussion: Sarcoidosis is a multisystem, inflammatory condition of unknown etiology. While able to manifest in virtually any organ system, common structures affected include lungs, lymphatics, skin, and eyes. Cutaneous morphology expresses impressive variability ('great imitator') including propensity to involve tattoos. Prognosis varies from spontaneous resolution to prolonged chronic inflammation complicated by fibrosis and end-organ damage. Pulmonary followed by cardiac complications are most common causes of death.

Treatment is dependent on organ involvement and severity of presentation. Initial treatment often involves systemic glucocorticoids with early taper and transition to glucocorticoid-sparing antisarcoidal agents. Common agents include methotrexate, azathioprine, leflunomide, mycophenolate, and hydroxychloroquine. For refractory disease, alternatives include TNFα inhibitors.

Given concern for atypical mycobacterium, he was initially started on empiric antimicrobials, which were discontinued upon rule out. Subsequently started on prednisone 60 mg daily and ophthalmic and topical steroids with rapid improvement of ocular symptoms and progressive resolution of cutaneous papules along with constitutional symptoms. Prednisone has since been tapered to 20 mg daily with plan to transition to methotrexate as a steroid-sparing agent. Co-managed with ophthalmology and rheumatology at VAMC.

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Case # 20
PAINFUL PINK PAPULES

PRESENTED BY: Brandy Maphet MD, Misha Koshelev MD PhD

HISTORY: A 47-year-old female presents to clinic with 10 years of papules on the chest and buttocks. The patient has continued to develop papules, which are intermittently painful.

PMH: Uterine fibroids leading total hysterectomy (age 45)

Physical Exam: Clustered pink papules and nodules on the chest and left buttock.

Histopathology: Dermal aggregates of interlacing smooth muscle fibers. Stains positive for desmin and smooth muscle actin. Consistent with leiomyoma.

Diagnosis: Hereditary leiomyomatosis and renal cell carcinoma (HLRCC) or Reed syndrome

Discussion: Hereditary leiomyomatosis and renal cell carcinoma is caused by a mutation in the fumarate hydratase gene and is inherited in an autosomal dominant pattern. The clinical presentation includes multiple cutaneous leiomyomas, uterine leiomyomas, and type 2 papillary renal cell carcinoma. With HLRCC, the lesions arise from proliferation of the arrector pilli muscle, classifying them more specifically as piloleiomyomas. On average, leiomyomas first appear in the third decade, are skin colored to pink/brown, and are painful secondary to smooth muscle contraction.[1] Treatment is focused on symptomatic relief, but often proves difficult due to number of lesions. Systemic treatment options include calcium channel blockers, gabapentin, and alpha1-blockers. A clinical trial showed improved quality of life with intralesional botulinum toxin as well as improved pain at rest when compared to placebo.[2] Another treatment option includes removal or destruction via excision, cryotherapy, electrodessication or laser ablation.

Genetics referral should be ordered and genetic counseling considered due to the risk of renal cell cancer and uterine leiomyomas. A reported 90% of female HLRCC patients will develop uterine leiomyomas.[3] Uterine leiomyomas in HLRCC arise in the 4th decade of life leading to infertility, uterine bleeding, or pain, prompting a need for gynecology referral. Type 2 papillary renal cell carcinoma develops in 15% of HLRCC patients.[1] This classically arises in the 5th decade and has a high mortality rate.[1,3] Yearly screening with computerized tomography (CT) scan or magnetic resonance imaging (MRI) is recommended.

This case highlights the importance of recognizing skin lesions as part of a larger systemic disease. In general, high suspicion of HLRCC should be present in a patient with multiple cutaneous leiomyomas. Dermatologists play an essential role in this situation and are integral to initiation of multidisciplinary care.

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