Chicago Dermatological Society

Monthly Educational Conference

Program Information
CME Certification
and
Case Presentations

Wednesday, November 5, 2014

Conference Location & Host:
Department of Dermatology
Feinberg School of Medicine
Northwestern University
Chicago, Illinois

Program

Conference Locations

- Feinberg Pavilion Conference Center, 3rd Floor; 251 E. Huron St.; Chicago
- Dermatology Clinic, 676 N. Saint Clair Suite 1600

8:30 a.m.	**Registration & Continental Breakfast with the exhibitors** *Feinberg Pavilion Foyer outside conference room "A" - 3rd Floor*
9:00 a.m. - 10:00 a.m.	**Resident Lectures** – *Feinberg A - 3rd Floor* "Neonatal Dermatology: 101, 411, 911" *Lawrence Eichenfield, MD*
9:30 a.m. - 10:45 a.m.	**Clinical Rounds** Patient, Poster & Slide Viewing *Dermatology Clinic, Suite 1600, 676 N. Saint Clair*
11:00 a.m. - 12:00 p.m.	**General Session** - *Feinberg A - 3rd Floor* BLUEFARB LECTURE "Acne Update: What's Erupting?" *Lawrence Eichenfield, MD*
12:00 p.m. - 12:30 p.m.	**Box Lunches & visit with exhibitors** *Feinberg Pavilion Atrium*
12:30 p.m. - 12:45 p.m.	**CDS Business meeting** – *Feinberg A*
12:45 p.m. - 2:20 p.m.	**Case Discussions** – *Feinberg A*
2:20 p.m. - 2:30 p.m.	**MOC Self-Assessment Questions** – *Feinberg A*
2:30 p.m.	**Meeting adjourns**

Mark the Date!

Next CDS monthly meeting – Wednesday, December 3, 2013 at the Gleacher Conference Center, 650 N. Cityfront Plaza (near the NBC Tower) in downtown Chicago. **Please note this new location!**

The conference host is the University of Chicago, and the guest speaker is Wayne Grayson, MD from the University of the Witwatersrand, Johannesburg, South Africa

Watch for details on the CDS website: www.ChicagoDerm.org
Save time and consider registering online!

Guest Speaker

Delivering the Samuel Bluefarb Lecture

LAWRENCE EICHANFIELD, MD

Chief of Pediatric and Adolescent Dermatology, University of California; Director, Division of Pediatric and Adolescent Dermatology, Rady Children's Hospital; San Diego, CA

Dr. Eichenfield earned his medical degree from Mount Sinai School of Medicine in New York (1984). He completed his residency in dermatology in 1991 at the University of Pennsylvania after also completing a pediatric residency at Children's Hospital of Philadelphia in 1988 (chief resident, 1987-1988).

Dr. Eichenfield is a Professor of Clinical Pediatrics and Medicine (Dermatology), University of California-San Diego School of Medicine and also is an Adjunct Professor, Departments of Pediatrics and Medicine (Dermatology), University of California-San Diego School of Medicine. He was honored as a member of Alpha Omega Alpha Medical Honor Society during medical school and is a recipient of the Benjamin Ritter Award at Children's Hospital of Philadelphia. He has been named one of the "Best Doctors in America" since 1994.

Dr. Eichenfield has held a number of editorial positions and has numerous publications to his credit. His clinical interest include atopic dermatitis, vascular lesions, laser surgery, acne and neonatal dermatology.

ONSITE HANDOUT

Chicago Dermatological Society

Presents

"2014 - 2015 Chicago Dermatological Society Monthly Meeting"

November 5, 2014 *Chicago, IL*

Please complete the CME claim form included in your meeting materials and return to the registration table before you leave the conference. A certificate of credit will be sent to you following the meeting. Participants must attend entire session to receive full credit. Also, we ask that you complete the evaluation form and return to the registration table. The information collected as part of this process represents an important part of the CME planning process.

Colorado Foundation of Medical Care will retain a record of attendance on file for six years.

JOINT SPONSOR STATEMENT

This educational activity is jointly provided by Colorado Foundation for Medical Care and the Chicago Dermatological Society.

GOAL / PURPOSE

To educate participants on the new regulations and research surrounding dermatology.

EDUCATIONAL OBJECTIVES

Upon completion of the activity, participants will be able to:

1. Discuss key factors in the diagnosis and treatment for a variety of dermatologic diseases and conditions, including psoriasis, hair disorders, and dermatological symptoms of systemic diseases.

2. Describe the manifestation of skin cancers and the efficacy of treatments available to the dermatologist.

3. List the therapeutic options available to the dermatologist for a variety of skin diseases, both medical and surgical, and discuss how new emerging treatments can be successfully incorporated into a dermatology practice.

CREDIT STATEMENTS

CFMC ISO 9001 Certified Office of Continuing Education

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Colorado Foundation for Medical Care and the Chicago Dermatological Society. Colorado Foundation for Medical Care is accredited by the ACCME to provide continuing medical education for physicians.

Colorado Foundation for Medical Care designates this live activity for a maximum of 4.5 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

DISCLAIMER STATEMENTS

The content, views and opinions presented in this educational activity are those of the authors and do not necessarily reflect those of Colorado Foundation for Medical Care and Chicago Ophthalmological Society. The authors have disclosed if there is any discussion of published and/or investigational uses of agents that are not indicated by the FDA in their presentations. Before prescribing any medicine, primary references and full prescribing information should be consulted. Any procedures, medications, or other courses of diagnosis or treatment discussed or suggested in this activity should not be used by clinicians without evaluation of their patient's conditions and possible contraindications on dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities. The information presented in this activity is not meant to serve as a guideline for patient management.

DISCLOSURE STATEMENTS

Colorado Foundation for Medical Care insures balance, independence, objectivity, and scientific rigor in all our educational activities. In accordance with this policy, CFMC identifies conflicts of interest with its instructors, planners, content managers, and other individuals who are in a position to control the content of an activity.

The following ***faculty, planner and/or content manager*** reported the following financial relationship with commercial interests whose products or services may be mentioned in this CME activity:

Dr. Eichenfield has provided the following disclosure:
Grants/Research Support - Galderma (no compensation); Consulting Fee - Galderma, Medicis/Valeant; Speakers' Bureau - Galderma

All other members of the faculty and planning team have nothing to disclose nor do they have any vested interests or affiliations.

Fee Information - There is no fee for this educational activity.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #1**

Presented by Lauren Graham, MD, PhD and Maria Colavincenzo, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
This 66-year-old Caucasian female with a history of scleroderma presented with a 3-year history of subcutaneous nodules diffusely over her body that had developed over time. The nodules initially started as small flesh colored papules, enlarging over several months. Recently she has developed more large nodules. The nodules were asymptomatic at first, until 1-2 months ago, when they became progressively pruritic. Patient also complained of shortness of breath, acid reflux, dysphagia, dry cough, dyspnea on exertion, and fingertips turning blue in the cold.

PAST MEDICAL HISTORY
HTN, chronic kidney disease

MEDICATIONS
Amlodipine, carvedilol, fenofibrate, ferrous sulfate, lansoprazole, lisinopril, sildenafil

PHYSICAL EXAM
Her face has numerous non-blanchable telangiectasias. On the back, chest, abdomen, ventral arms, dorsal feet, and upper legs were numerous flesh colored to reddish brown papulonodules. Several were rubbery while others were firm. She has sclerodactyly on bilateral hands. She has a slight decrease in range of motion of abduction in her shoulders and wrist extension.

LABs/Imaging
Abnormal: Hgb 10 g/dL (11.6-15.4 g/dL), Hct 32 % (34-45%), PT 13.9 seconds (9.2-13 seconds), INR 1.3 (0.8-1.2), ESR 40 mm/hr (2-25 mm/hr), CRP 0.7 mg/dL (0-0.5 mg/dL), Cr 1.8 mg/dL (0-1.3 mg/dL), B-Natriuretic peptide 1659 pg/ml (0.2-100 pg/ml), urinalysis: total protein 100 mg/dL (0 mg/dL), ANA positive 1:1280, anti-dsDNA 135.8 IU/mL (</= 29.9 IU/mL), anti-RNA polymerase III > 80 Unit/mL (< 21 Unit/mL)
PFTs: FEV1 74 L, DLCO 39%
High resolution CT of chest: increased reticulonodular opacities peripherally in both lungs, slightly more pronounced at the lung bases. Scattered ground glass opacities throughout the lungs, most pronounced within the upper lungs. Esophagus is mildly enlarged without wall thickening.
Right heart catheterization: moderate pulmonary hypertension
Echocardiogram: moderate to severe right ventricle enlargement with moderate right atrium enlargement. Severe tricuspid regurgitation and moderate mitral regurgitation

Normal/Negative: WBC, ALT, complement C3 154 mg/dL (75-179 mg/dL), complement C4 39 mg/dL (10-40 mg/dL), anti-centromere Ab, anti-ribosomal Ab, anti-Sm Ab, anti-Scl-70 Ab, anti-SSA Ab, anti-SSB Ab, beta-2-glycoprotein IgG, IgA, IgM

HISTOPATHOLOGY
Square-shaped punch biopsy with marked thickening of deep dermal collagenous bundles and a deep perivascular and interstitial lymphohistiocytic infiltrate with some plasma cells. There was depletion of the peri-adnexal fat pad. Colloidal iron stain was negative. Masson's trichrome shows thickened collagen.

DIAGNOSIS
Nodular scleroderma

TREATMENT AND COURSE

The patient was started on cetirizine and fexofenadine daily with some improvement of her pruritus. Her shortness of breath and kidney function declined over the next 6 months. She was started on treprostinil, a prostaglandin I_2 analog, with improvement of her lung symptoms. She is currently being managed by pulmonologist and nephrology. She is concentrating on her lung treatment and is not receiving any specific cutaneous treatment at this time.

DISCUSSION

Nodular scleroderma is a rare variant of scleroderma where patients present with numerous nodules or papulonodules. Nodular lesions also have been seen in morphea. These lesions are often firm, asymptomatic or pruritic, and can be generalized, linear, or in a localized pattern. Most often, nodules are found on the trunk and proximal extremities with sparing of the face. Nodules can be found in areas already affected by scleroderma or in unaffected skin. Patients often have scleroderma for many years before developing nodules, although there are a few case reports where nodules are the primary scleroderma skin lesion. Nodular scleroderma often affects younger women.

The first reported case was in 1894 and several case reports have been published since, although it is still considered a rare variant. Biopsies of the nodules are consistent with the histopathological findings of scleroderma with sclerotic, thickened collagen bundles. Some groups consider nodular scleroderma to be the same as keloidal scleroderma, whereas others view it as a separate entity. In keloidal scleroderma, patients can develop keloid-like lesions, often spontaneously in areas without known previous trauma. Histopathological findings of these lesions have features more consistent with keloids.

Scleroderma is an autoimmune disease that can affect numerous organs including the skin, lungs, heart, vascular system, and kidneys. There are limited published data on nodular scleroderma, limited to cases studies and retrospective case series. Therefore, there is little data showing whether patients with nodular scleroderma have different systemic findings than other variants. Cannick et al. looked at 14 patients with nodular scleroderma or nodular morphea and found that eight patients had a positive ANA antibody. All of the patients with nodular scleroderma had sclerodactyly, Raynaud's phenomenon, arthralgias and many had pulmonary and/or renal involvement.

The pathogenesis of scleroderma is believed to involve vascular endothelial injury, autoimmunity, and fibroblast dysfunction. There is limited data on the mechanism of nodule development within the context of scleroderma. Isolated reports of nodular scleroderma have suggested that acid-fast bacteria, organic solvent, or hepatitis C may play a role. A recent study by Moinzadeh *et al* compared the biopsies of the nodule and the sclerotic skin adjacent to the nodular lesion. They found that the nodule had reduced elastic fibers and increased collagen XII, fibrillin-1, and cartilage oligomeric matrix than the adjacent sclerotic skin. Treatment for nodular scleroderma is the same as for the more common variant, and is based on the most prominent organ system involved.

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2. Heath CR et al. Nodular Scleroderma presenting as multiple spontaneous keloidal scars. JAAD 2012, 66(6): e245.
3. Labandeira et al. What is Nodular-Keloidal Scleroderma? *Dermatology* 2003, 207:130-132.
4. Moinzadeh P et al. Systemic Sclerosis with multiple nodules: characterization of the extracellular matrix. Arch Dermatol Res 2013, 305:634-652.
5. Stadler B, et al. Systemic sclerosis with keloidal nodules. An Bras Dermatol. 2013,88(6 Suppl 1):S75-7.
6. Wriston CC, et al. Nodular Scleroderma: A Report of 2 cases. Am J Dermatopathol 2008, 30(4):385.

CHICAGO DERMATOLOGICAL SOCIETY **Case #2**

Presented by Pedram Yazdan, MD, Johnathan Cotliar, MD, Ahmad Shatil Amin, MD, Murad Alam, MD, and Pedram Gerami, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

CASE A

HISTORY OF PRESENT ILLNESS

This 45-year-old female presented with a new pigmented skin lesion on the left forehead, developed 1 week after initiation of pazopanib (MEK inhibitor) and dabrafenib (BRAF ^{V600E} inhibitor) trial in May 2014 at Ohio State University for her widely metastasized *BRAF*^{V600E} positive follicular variant of papillary thyroid carcinoma (FVPTC). Skin biopsy of the lesion was performed.

PAST MEDICAL HISTORY

FVPTC (diagnosed in 2011, now with metastases to the lungs, liver, skin, spine, and brain); no prior personal history of primary skin cancer

FAMILY HISTORY

Cousin with melanoma

PHYSICAL EXAM

Left forehead, a 4 mm brown reticulated macule with irregular pigment network throughout and asymmetric darkening at inferior pole.

LABs/Imaging

Abnormal: Hgb 10.9, ALT 125, AST 97, ALP 253. PET/CT: uptake in metastatic disease in the liver, right arm, right hip, and lung. MRI Spine: osseous metastases without spine compression

Normal: WBC and platelets, BMP, and LDH

HISTOPATHOLOGY

There was an irregular proliferation of atypical melanocytes involving the epidermal compartment with irregular and expansile junctional nesting as well as notable pagetoid changes. There was focal involvement of the papillary dermis by the atypical melanocytes extending to a Breslow depth of 0.17mm and Clark's level II. An associated dermal nevus component was also noted. Epidermal ulceration or dermal mitotic figures were not identified. The lateral margins were involved. The melanoma cells were negative for BRAF^{V600E} immunohistochemical staining.

DIAGNOSIS

Primary cutaneous wild-type *BRAF* melanoma secondary to combination therapy with BRAF inhibitor and MEK inhibitor

TREATMENT AND COURSE

She underwent excision of the primary melanoma via slow Mohs technique with advancement flap reconstruction after histopathologic margin clearance was obtained. She also developed Grade I hand-foot syndrome that was being effectively treated with topical fluocinonide. She has continued treatment with pazopanib and dabrafenib for metastatic thyroid carcinoma, and is undergoing total body skin examination every 6 weeks.

CASE B

HISTORY OF PRESENT ILLNESS

This 57-year-old male presented with a new pigmented growth on his left abdomen 4 weeks after the initiation of *BRAF*^{V600E} inhibitor, LGX818 (Encorafenib), for metastatic lung adenocarcinoma harboring the *BRAF*^{V600E} mutation. An excisional biopsy of the lesion was performed.

PAST MEDICAL HISTORY

Lung adenocarcinoma (diagnosed in 2009, now with omentum metastasis detected in February 2014); Basal cell carcinoma status post ED&C prior to the initiation of LGX818.

FAMILY HISTORY

No history of melanoma

PHYSICAL EXAM

Left abdomen: 8mm brown and black irregularly pigmented macule with asymmetric dark globules and blue-white structures centrally.

LABs/Imaging

Abnormal: Hgb12.1. CT scan-C/A/P: tumor shrinkage in the lungs and omental/peritoneal carcinomatosis are stable. New interval bronchopleural fistula

Normal: WBC and platelets, BMP, LFTs and LDH

HISTOPATHOLOGY

There was an irregular proliferation of nests and fascicles of atypical melanocytes with pleomorphic nuclear detail and hyperchromasia along the dermal epidermal junction with pagetoid spread of melanocytes into the upper epidermis. Nests of atypical epithelioid melanocytes were also seen invading the dermis to a Breslow depth of 0.55mm and Clark's level III. An associated dermal nevus component was also noted. Epidermal ulceration, perineural, or angioinvasion were not identified and the dermal component mitotic count was <1 mitosis/mm^2. The margins were free of involvement by the melanoma and nevus components. The melanoma cells were negative for BRAF^{V600E} immunohistochemical staining.

DIAGNOSIS

Primary cutaneous wild-type *BRAF* melanoma induced by treatment with BRAF inhibitor

TREATMENT AND COURSE

He underwent 1cm wide local excision of the melanoma biopsy scar and tumor bed revealing scar without residual melanoma. During that visit he was also found to have two clinically atypical appearing nevi on the right shoulder and abdomen. Biopsies revealed compound lentiginous nevi without atypia. He also subsequently developed Grade III hand foot syndrome, as well as a bronchopleural fistula. He was then taken off the clinical study.

DISCUSSION:

Advances in molecular diagnostics have led to the discovery of *BRAF* oncogenes in solid tumors (melanoma, lung and thyroid carcinoma). This has paved the way for important developments in targeted RAF inhibitor drug therapy. The second-generation RAF inhibitors vemurafenib, dabrafenib and LGX818 were developed specifically to inhibit the RAF–MEK–ERK signaling pathway in cells expressing the mutant *BRAF*^{V600E} oncogene. These drugs potently inhibit MEK phosphorylation and growth of *BRAF*^{V600E}-mutated tumor cells, therefore highly effective at inducing tumor regression.

Over the past several years, there has been growing utilization of RAF inhibitors for the treatment of metastatic melanoma as well as certain thyroid and lung carcinomas harboring the *BRAF*^{V600E} mutation. These medications have provided patients with metastatic disease with improved treatment response rates, progression-free survival and overall survival. Well recognized cutaneous adverse effects of BRAF inhibitor therapy include keratoacanthomas and squamous cell carcinomas. Patients exposed to BRAF inhibitors can also develop darkening of existing nevi, atypical melanocytic proliferations, or second primary cutaneous melanomas.

Recently, Dalle et al. reported their experience with 5 patients treated with vemurafenib for metastatic melanoma who developed atypical pigmented lesions after 4 to 12 weeks of therapy. Five of these lesions were BRAF wild-type melanomas. Chapman et al. also described 5 other cases of superficial spreading melanoma among the 464 patients treated during the phase 2 and 3 trials in patients taking vemurafenib. Gerami et al. reported for the first time a case of a patient with marked dermoscopic changes in a number of his nevi after 5 weeks of vemurafenib therapy. Five of these nevi underwent biopsy and revealed severe dysplasia.

It has been well demonstrated in vitro that vemurafenib and other selective BRAF inhibitors decrease activity of the MAP kinase pathway in cells with mutated BRAF. Conversely, cells with wild-type BRAF may be stimulated and paradoxically have increased MAP kinase activity and elevated levels of phosphorylated ERK. It has been previously shown that in the presence of active RAS, wild-type BRAF forms dimers. When vemurafenib binds to the kinase domain of one of the two proteins in the dimer, transactivation of the kinase domain of the other protein in the dimer occurs, resulting in increased activity of the MAP kinase pathway. Conversely, V600E-mutated BRAF cells have low levels of RAS and do not form dimers. It has been postulated that the changes in pre-existing nevi or the appearance of new pigmented lesions in patients treated with BRAF inhibitors may be the result of transactivation of wild-type BRAF. More studies to assess the risk of wild-type BRAF melanoma in patients treated with selective BRAF inhibitors and documentation of potential changes in nevi in these patients are needed.

Our cases highlight the need for very close dermatologic management of patients undergoing anti-BRAF treatment. The recent literature suggests total body skin examinations with dermatoscopic evaluation at intervals of 1, 2, and 3 months after treatment initiation followed by every three month skin examinations.

REFERENCES:

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2) Chu EY, et al. Diverse cutaneous side effects associated with BRAF inhibitor therapy: a clinicopathologic study. *JAAD*. 2012;67(6):1265-1272.
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CHICAGO DERMATOLOGICAL SOCIETY **Case #3**

Presented by Katherine Mercy, MD and Anthony J. Mancini, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

This is an 8-year-old male who presented with blue discoloration of the skin for 1 month.

Unknown

Presented by Ainah U. Tan, MD, Bethanee J. Schlosser, MD, PhD and Joaquin C. Brieva, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

CASE A

HISTORY OF PRESENT ILLNESS

This 27-year-old African American female presented with a long-standing history of recurrent painful oral erosions and ulcers since age 7 as well as vulvar/vaginal ulcers, which began 2 months prior to presentation. She reported flares with crops of ulcers every 2 months, lasting up to 6 weeks. The painful oral ulcers interfered with eating and drinking. The patient identified no exacerbating or alleviating factors. She had previously been diagnosed by dermatology with oral erosive lichen planus and treated with tacrolimus 0.1% ointment. Following oral biopsy by ENT, she was prescribed lidocaine jelly, magic mouthwash (diphenhydramine/ lidocaine), and oral prednisone taper. Also prior to presentation, the patient had been evaluated by OB/GYN, diagnosed clinically with vulvar lichen planus and prescribed clobetasol 0.05% ointment, which the patient had not yet used at the time of initial presentation.

PAST MEDICAL HISTORY

Oral/vulvar ulcers (as per HPI)

MEDICATIONS

Iron sulfate, multivitamin, levonorgestrel-releasing IUD

FAMILY HISTORY

Diabetes mellitus

SOCIAL HISTORY

Married. Director of university student housing. Denies tobacco, alcohol or drug use.

PHYSICAL EXAM

Right extensor forearm: a 2.5 cm x 1.2 cm x 0.8 cm well-demarcated erythematous thin plaque with pink erythema at periphery with central dark brown hyperpigmentation and minimal scale.
Oral mucosa: bilateral buccal mucosa with light feathery white reticulation with overlying brown hyperpigmentation; buccal mucosa and gingivae with multiple erythematous erosions and superficial ulcers.
Vulva: Right medial inferior labium minus extending into introitus with indurated tender edematous nodule with overlying 2 cm x 1 cm ragged ulcer with overlying fibrous yellow exudate and surrounding erythema.
No intact vesicles or bullae on initial mucocutaneous examination.

LABS/IMAGING

Positive/abnormal: ELISA for IgG autoantibody to BP180: 24 (ref < 15); BP230: 25 (ref < 9)
Negative/normal: CBC, CMP, Lipid Panel, G6PD, Quantiferon Gold, Hepatitis B/C panel

HISTOPATHOLOGY

Right Oral Ulcer (performed by ENT): Squamous mucosa with ulceration and acute and chronic inflammation. Unable to determine nature of inflammatory process given absence of epithelium. Subepithelial split was clean. No suprabasalar split or acantholysis.
Right Extensor Forearm: Consistent with mild resolving interface dermatitis
Vulva Right Inferior Labium Minus/Introitus: Lichenoid dermatitis with eosinophils.
DIF (Vulva Right Inferior Labium Minus/Introitus): No evidence of immune deposits

DIAGNOSIS
Lichen Planus Pemphigoides

TREATMENT AND COURSE
The year following initial presentation, the patient continued to have oral and vulvar lesions along with ongoing elevated titers of autoantibodies to BP180 and BP230. She was started on rituximab (7 weekly infusions, then maintenance every 4 weeks); however this was eventually discontinued secondary to muscle and joint soreness. Patient transitioned to prednisone taper with no progression of oral or vulvar ulcers. She was put on azathioprine for ~ 1 year but continued to have breakthrough with significant oral ulcerations. She was then started on mycophenolate mofetil, however unexpectedly became pregnant (in the context of reported OCP use); mycophenolate mofetil was immediately discontinued, she carried the pregnancy to term and delivered with no complications. Patient was lost to follow-up for about one year and re-presented with flares of mucosal lesions shortly after the birth of her daughter. Patient again was placed on short-course prednisone tapers as needed for flares in conjunction with topical tacrolimus 0.1% ointment. She most recently had intralesional triamcinolone injections to acute painful oral ulcers and added clobetasol ointment with partial improvement.

CASE B
HISTORY OF PRESENT ILLNESS
This 50-year-old African American female presented with a skin eruption for 4 months. The eruption began shortly after being hospitalized for a COPD exacerbation, during which she was intubated for 9 days and received furosemide for diuresis. She first noticed blisters on her palms, which progressively worsened and generalized including her genital and oral mucosa. She described her skin as both itchy and tender. Furosemide was discontinued after the onset of the eruption. Biopsy during her hospitalization showed polymorphic infiltrate and dermal edema consistent with drug eruption. She was treated with topical triamcinolone and oral prednisone, however the patient discontinued both agents because she did not believe the triamcinolone helped and she reported soreness of her neck and body from the prednisone. Patient's cutaneous eruption flared shortly after discontinuation of prednisone and she was then prescribed mycophenolate mofetil, which she never took. A second set of biopsies was consistent with bullous pemphigoid, lichen planus pemphigoides variant.

PAST MEDICAL HISTORY
Hypertension, asthma, chronic obstructive pulmonary disease

MEDICATIONS
Hydrochlorothiazide, nifedipine, ranitidine, albuterol-ipratropium inhaler

ALLERGIES
Furosemide, penicillins, sulfa

FAMILY HISTORY
Asthma, eczema, hypertension

SOCIAL HISTORY
Married. Lives at home with her husband. Smokes ½ pack of cigarettes daily. Drinks 2-3 alcoholic beverages per week. Reported occasional marijuana and cocaine use.

PHYSICAL EXAM

The patient's mucocutaneous exam was notable for patchy alopecia of the scalp, disseminated ulcerations with clean base on the oral commissure, lower labial mucosa, soft palate, trunk, and bilateral legs. Exam was also notable for a solitary superficially eroded plaque on the right labium majus. No intact vesicles or bullae.

LABS/IMAGING

Positive/abnormal: CT chest/abdomen/pelvis: borderline sized to mildly enlarged lymph nodes.
Negative/normal: CBC, CMP, HIV, Hepatitis B/C panel, LDH, Quantiferon gold, desmoglein 1 and 3, HHV 8, lymph node biopsy showing benign reactive process

HISTOPATHOLOGY

H&E (Left Forearm): Subepidermal necrotic blister with neutrophilic infiltrate. Most suggestive of erythema multiforme or Stevens-Johnsons syndrome. Typical changes of paraneoplastic pemphigus not noted.
DIF (Left Forearm): Positive linear basement membrane deposits of C3 as well as intercellular (chicken wire like) deposits of C3; IgG deposits not identified.
DIF (NU): Weak intercellular immunoglobulin G antibodies compatible with paraneoplastic pemphigus.
IIF (University of Utah): Consistent with lichen planus pemphigoides mostly, no evidence of paraneoplastic pemphigus .

DIAGNOSIS

Lichen Planus Pemphigoides

TREATMENT AND COURSE

The patient was admitted to Northwestern for treatment and evaluation of her drug eruption. All studies for internal malignancy, including Castleman's and lymphomas, were negative. She was started on rituximab, topical clobetasol 0.05% ointment for the body and hydrocortisone 2.5% ointment for the face, axillae, and groin. The patient improved after 2 infusions of rituximab, however had to discontinue treatment due to insurance and social issues. The patient subsequently had a severe flare of mucocutaneous lesions and re-presented to the dermatology clinic. Patient was restarted on rituximab at increased frequency (once a week).

DISCUSSION

Lichen planus pemphigoides (LPP) is a rare disease usually affecting adults, with less than 100 cases of LPP reported in the literature over the past 50 years. It is thought to be a combination of lichen planus (LP) and bullous pemphigoid (BP), however its pathogenesis is incompletely elucidated. The diagnosis of LPP is made by a combination of clinical, histopathological, and immunologic features.

Clinically, LPP is characterized by the development of blisters on lichenoid lesions and/or on uninvolved skin. The mean age at diagnosis is 52 years, and most patients have no family history of blistering disorders. Clinically, bullae predominantly occur on the lower and upper extremities; involvement of palms and soles is more frequent in children. Oral mucosa may be involved, other mucosal lesions are rare (pharynx, esophagus, palate, vulvae, and conjunctiva), and nail involvement is rare. LPP is typically considered to be idiopathic, but there have been some case reports of drug-associated LPP (4 case reports associated with angiotensin converting enzyme antagonists). There have also been reports of association with internal malignancy, phototherapy, and hepatitis B virus infection. The differential diagnosis includes bullous LP or association of LP with erythema multiforme.

The BP180 ELISA for IgG autoantibodies against epitopes of the NC16a domain is positive for most patients with LPP. Biopsy from lesional skin of a bulla shows a subepidermal blister containing numerous eosinophils with perivascular inflammatory cell infiltrates of eosinophils, histiocytes, and lymphocytes in the dermis. Changes consistent with LP can also be seen with sawtooth acanthosis and a band-like lymphocytic inflammatory infiltrate in the upper dermis. Direct immunofluorescence (DIF) of perilesional skin reveals linear deposits of IgG and/or C3 along the basement membrane zone (BMZ).

Most patients with LPP are successfully treated with systemic corticosteroids. Patients are usually started on oral prednisolone (0.5-1 mg/kg/d) and gradually tapered. Other therapies such as dapsone, azathioprine, mycophenolate mofetil, methotrexate, rituximab, oral retinoids, hydroxychloroquine, and phototherapy have been used in addition to topical or systemic corticosteroids as steroid-sparing agents. The prognosis of LPP is thought to be good with a low rate of recurrence of the blisters (estimated about 20%).

It is thought that LPP is a variant of bullous pemphigoid (BP) or that there is a strong association between the two entities. Immunoelectron microscopic studies of LPP have shown immunoreactants in the lamina lucida or hemidesmosomes of the epidermal cells as is seen in BP. This insinuates that the antigen targeted by the LPP autoantibody is in the BMZ and its location is consistent with the antigen in BP. Zillikens et al. reported unique antibody reactivity against epitope region 4 of the NC16a domain of the BP180 antigen (as opposed to regions 2 and 3.5 which is seen in BP). This indicates that the immunologic pattern for LPP differs from BP and that LPP has a unique antigen; therefore LPP represents a distinct entity from BP.

An emerging hypothesis suggests that a primary inflammatory process such as LP or a drug eruption causes the release and exposure of a previously sequestered antigen, leading to a secondary autoimmune response against the newly released antigen. In the case of LPP, LP might cause BMZ damage and expose BP180 antigens, which allow the production of autoantibodies against the BMZ, through epitope spreading. Subsequent circulating autoantibodies then induce a secondary subepidermal bullous dermatosis. This is supported by a study by Sekiya et al. that demonstrated the presence of circulating autoantibodies to BP180 only after the appearance of bullae.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #5**

Presented by Sarah Adams, MD, Sarah Chamlin, MD and Annette Wagner, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
This 4-year-old Hispanic female was transferred to Lurie Children's Hospital for management of severe metabolic acidosis and leukocytosis of unknown etiology. Several days prior to admission, she developed URI symptoms and an erythematous eruption around her eyes and mouth, which progressed to involve her axillae and inguinal folds. She continued to deteriorate, developing abdominal pain, nausea and vomiting. On admission to an OSH, she was noted to be lethargic, tachycardic to the 150s and tachypneic with a Kussmaul breathing pattern. Laboratory evaluation revealed a profound hypoglycemia, acidosis and leukocytosis. She was pan-cultured and empirically started on broad-spectrum antibiotics. On transfer to Lurie Children's, she was found to have well-demarcated erythematous plaques in the intertriginous folds of the axillae and groin, as well as periorificial areas.

PAST MEDICAL HISTORY
Full term NSVD, uncomplicated pregnancy and delivery. Several episodes of similar, milder appearing eruptions when sick with pyelonephritis (3/2014) and URIs.

MEDICATIONS
None

FAMILY HISTORY
No family history of any skin diseases.

SOCIAL HISTORY
Lives at home with both parents, only child. No recent travel or foreign visitors. No pets. No dietary restrictions.

DEVELOPMENTAL HISTORY
Growing appropriately and meeting all developmental milestones.

PHYSICAL EXAM
General: Well-developed, well-nourished Hispanic female. Somnolent but awakens easily, responsive to voice, follows commands.
Skin: Well-demarcated, mildly scaly, brightly erythematous, non-tender thin plaques in the intertriginous folds of the axillae, inguinal creases, peri-oral and peri-ocular skin.

LABS/IMAGING:
WBC 55.7 K/uL (3.5-10.5 K/uL), glucose 44 mg/dL (70-110 mg/dL), HCO_3 2 mEq/L (21-31 mEq/L), lactate 18 mmol/L (0.5-2.2 mmol/L), pH 6.76 (7.35-7.45), UA 40+ ketones and 30+ protein
Respiratory virus panel: +Rhinovirus/enterovirus
Plasma carnitine: Total 29.2 umol/L (35-84 umol/L), free 3.5 umol/L (24-63 umol/L), acylcarnitine 25.7 umol/L (4-28 umol/L), acylcarnitine:free carnitine ratio 7.3 umol/L (0.1-0.8 umol/L)
Acylcarnitine profile: Proprionylcarnitine (C3) 4.44 nmol/mL (<1.78 nmol/mL), 3-hydroxyisovalerylcarnitine (C5-OH) 1.79 nmol/mL (<0.11 nmol/L)
Urinary organic acids**:** Markedly elevated lactate, 3-hydroxybutyric and acetoacetic acids; elevated 3-ketovalerate, proprionylglycine, 3-methylglutaconate, methylcitrate, isovalerylglycine and 3-methylcrotonylglycine

Holocarboxylase synthetase genotyping: Compound heterozygous mutations; Val550Met and deletion in at least exons 4-5

Normal/negative: Hgb/Hct, plt, LFT, ammonia, salicylates, acetaminophen, blood EtOH, rapid strep, biotinidase enzymatic activity
Cultures: Blood, urine, CSF and skin
Studies: Renal ultrasound, echocardiogram, EEG

DIAGNOSIS:
Multiple carboxylase deficiency due to holocarboxylase synthetase defect

TREATMENT AND COURSE:
On admission to the pediatric ICU, the patient was intubated for impending respiratory failure and underwent emergent hemodialysis for severe metabolic acidosis. Her complete infectious work-up was positive only for enterovirus/rhinovirus. Her skin eruption was suspicious for a nutritional deficiency and laboratory evaluation revealed elevated levels of proprionylcarnitine (C3) and 3-hydroxyisovalerylcarnitine (C5-OH) in addition to markedly elevated urinary organic acids indicative of multiple carboxylase deficiency. Given that her biotinidase enzyme activity was normal, she was presumed to have a mutation in holocarboxylase synthetase. She was also noted to have low levels of free carnitine. She was started on biotin and carnitine supplementation on day 2 of the hospitalization with subsequent improvement in her metabolic acidosis, mental status and skin findings. She was discharged on day 7 with genetics follow-up. At a 2-week visit, she was noted to be in her usual state of health. Holocarboxylase synthetase gene sequencing revealed compound heterozygous mutations in the enzyme. Repeat carnitine levels were within normal limits. Carnitine supplementation was therefore discontinued and she was maintained on biotin 10mg daily.

DISCUSSION:
Biotin is a water-soluble B vitamin that acts as a co-factor for several important mitochondrial and cytosolic carboxylase enzymes involved in energy metabolism. Dietary deficiency in biotin is rare given its abundance in many foods and its synthesis by intestinal bacteria. The most common cause of dietary biotin insufficiency is high consumption of raw eggs, which contain the protein avidin, a biotin scavenger. Other less common etiologies include iatrogenic cases from failure to supplement TPN, long-term therapy with anti-convulsants and chronic hemodialysis.

More commonly, biotin deficiency is the result of inborn errors of metabolism leading to multiple carboxylase deficiency. This can result from mutations in two separate enzymes; holocarboxylase synthetase (HLCS) and biotinidase. HLCS is the enzyme that converts biologically inactive apocarboxylases to their active forms by catalyzing the covalent linkage of biotin. Carboxylases are enzymes that fix carbon dioxide and are involved in energy metabolism. HLCS is required for the activation of four distinct carboxylases including mitochondrial enzymes 1- pyruvate carboxylase, essential for gluconeogenesis, 2- propionyl coA carboxylase required for the catabolism of isoleucine and valine, 3- 3-methylcrotonyl coA carboxylase which functions in the degradation of leucine and 4- cytosolic acetyl-coA carboxylase, which is necessary for fatty acid biosynthesis and chain elongation in lipogenesis. Biotinidase, on the other hand, is involved in the recovery and recycling of biotin after proteolytic degradation of carboxylases and also functions in the intestinal absorption of biotin from dietary food sources.

HLCS deficiency is an autosomal recessive disorder caused by mutations on chromosome 21q22.1. It classically presents in neonates with a constellation of neurologic, respiratory and

dermatologic findings, which can lead to fatal illness early in life. Typically, these infants present with recurrent episodes of metabolic acidosis and ketosis with a distinct pattern of organic aciduria characterized by the accumulation of lactate, 3-hydroxyisovalerate, methylcitrate and 3-methylcrotonylglycine in the urine. Neonates often have failure to thrive, respiratory distress and neurologic impairment, which can progress from lethargy and hypotonia to seizures, ketotic coma and ultimately death. Dermatologic manifestations include an erythematous, scaling, sharply demarcated rash, which can be more generalized or take on the distribution pattern reminiscent of acrodermatitis enteropathica with prominence in the intertriginous folds of the axillae and groin and the peri-orificial skin of the face. There can also be profound alopecia. Biotinidase deficiency presents similarly to HLCS deficiency though typically is associated with a later onset in infancy and a milder clinical phenotype. However, the presentation of HLCS deficiency is highly variable and the only way to reliably distinguish between these two disorders is through the use of bio-enzymatic assays.

Most patients with HLCS deficiency exhibit the classic neonatal presentation of the disease. However, as in this case, late onset occurrences have been described in the literature with variability in the disease severity. Mutational profiling in HLCS deficiency has revealed more than 35 unique mutations. Most of these are single nucleotide polymorphisms that arise in the putative biotin-binding domain of the gene. These mutations have been shown to alter enzyme kinetics causing a decreased affinity of HLCS for biotin at physiologic levels of the vitamin. Thus patients tend to respond well to dietary supplementation. Mutations arising in other parts of the HLCS gene have less predictable outcomes and can be associated with either a milder phenotype or a more severe and less biotin-responsive phenotype. This patient's late onset presentation that was likely precipitated by the catabolic stresses of a respiratory infection suggests the former. She has an excellent long-term prognosis with continued low-dose supplementation of biotin.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #6**

Presented by Melanie Clark, MD and Simon Yoo, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS AND PHYSICAL EXAMINATION
This is a 73-year-old Caucasian female who presented with multiple large squamous cell carcinomas (SCCs) of the bilateral lower extremities and underwent wide local excision (WLE) of three SCCs on the right leg and one SCC of the left leg in November 2013. All excision sites were repaired with a split-thickness skin graft (STSG) from a right proximal thigh donor site. The STSG donor site on the right anterior thigh and the SCC excision site/STSG recipient site on the right shin subsequently developed numerous erythematous firm papules.

PAST MEDICAL HISTORY
Multiple SCC of the skin, multiple basal cell carcinomas of the skin, hypertension, hyperlipidemia. No history of exposure to chemical carcinogens.

FAMILY HISTORY
No family members with a history of multiple SCC or keratoacanthomas.

MEDICATIONS
Hydrochlorothiazide, telmisartan

PHYSICAL EXAM
December 2013: Right anterior thigh STSG donor site with twenty-five erythematous firm 2-6 mm tender dome-shaped papules (resolved on acitretin)
January 2014: Right shin SCC excision site/STSG recipient site with five 2-8 mm erythematous firm crusted tender papules (persistent on acitretin – required repeat excision)
May 2014: Repeat WLE site of right shin for multiple SCCs repaired with STSG from left thigh donor site, well healed
June 2014: Left anterior thigh STSG donor site with two erythematous firm 5 mm domed papules
July 2014: Right shin WLE/STSG recipient site with fifteen 2-6 mm firm erythematous dome-shaped papules

LABS/IMAGING
Abnormal: AST/ALT (on acitretin): 246/134
Tissue culture right thigh: rare *staphylococcus aureus* (oxacillin resistant)
Normal/negative: CBC, BMP, peripheral blood flow cytometry, urine arsenic, lipid panel, LDH, alkaline phosphatase, direct and indirect bilirubin, Hep A, Hep B, Hep C, tissue fungal culture, tissue mycobacterial culture

HISTOPATHOLOGY
Right anterior thigh (2 papules): Epidermal hyperkeratosis, infiltration into the upper dermis by irregular strands of large cells with abundant eosinophilic cytoplasm and pleomorphic nuclei
Right shin (2 papules): Irregular strands and lobules of large cells with eosinophilic cytoplasm and pleomorphic nuclei, squamous eddies and keratinous microcysts present
Left anterior thigh (2 papules): Keratin-filled plug with epithelial collaretes, epithelium with large and glassy appearing keratinocytes without significant atypia

DIAGNOSIS
Eruptive SCCs and keratoacanthomas (KAs) arising in both STSG donor site and recipient site

TREATMENT AND COURSE

The patient was treated with doxycycline for *staphylococcus aureus* superinfection and started on acitretin with resolution of SCCs on the right thigh STSG donor site. Acitretin therapy was complicated by transaminitis and subsequently discontinued without recurrence of lesions on the right thigh. The patient required repeat WLE of the right shin for multiple SCCs (persistent despite acitretin) with repair by STSG from a left anterior thigh donor site. This STSG donor site again developed multiple KAs, which resolved with repeat acitretin course (discontinued due to transaminitis). Both STSG donor sites continue to be clear of KAs and SCCs. However she developed recurrent firm erythematous papules on the right shin despite topical 5-fluorouracil treatment. Radiation therapy is currently being considered.

DISCUSSION

KAs are rapidly proliferating epidermal tumors that are considered a variant of SCC and are thought to be follicular in origin. KAs and SCCs most-commonly occur on sun-exposed areas of light-skinned, middle-aged and older individuals as single lesions. Multiple KAs have been described in the Ferguson-Smith, Grzybowski, Witten and Zak subtypes, as well as in genetic syndromes with defects in DNA repair systems such as Muir-Torre and xeroderma pigmentosum. The pathogenesis of KAs and SCCs is not fully understood but these entities have been associated with chemical carcinogen exposure, immunosuppression, viruses, and trauma.

The presentation of multiple eruptive KAs and SCCs occurring within a surgical site and STSG donor site is rare. Few case reports describe a similar presentation to our patient in which multiple KAs or SCCs developed at a surgical wound after SCC excision. Approximately ten cases of a single KA or well-differentiated SCC arising within a STSG donor site have been reported since this entity was first described in 1948. However, only one case of numerous KAs occurring in a STSG donor and recipient site has been published to date. Eruptive KAs within a site of diffuse trauma, in one case after a medium depth chemical peel and another after fractional laser ablation, have been reported suggesting a role of pathergy triggering these neoplasms. Pathergy also has been described as a precipitant of KAs in the Grzybowski subtype. It is unclear to what degree pathergy may have triggered KA and SCC development in our patient or if trauma may have caused a local immunosuppression that promoted the growth of these neoplasms within vulnerable sites in an already predisposed individual.

The clinical presentation of eruptive KAs and SCCs presents a therapeutic challenge. Surgical options include excision, Mohs micrographic surgery, and cryosurgery. When lesions are multiple, large, or surgery is contraindicated, treatment with an oral retinoid may be successful, however systemic toxicity may limit the use of these agents as was the case in our patient. Topical and intralesional therapies that have anecdotally been reported as beneficial include topical 5-fluorouracil, intralesional 5-fluorouracil, intralesional methotrexate, intralesional bleomycin, intralesional interferon alpha-2b, and intralesional corticosteroids. Radiation therapy may also be considered to control localized disease.

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Fast Break 7A

Presented by Lauren Guggina, MD, Jonathan Cotliar, MD, Joan Guitart, MD.
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This is a 50-year-old male who presented with fever, night sweats, and a rash on his arms, legs, and trunk. The patient subsequently developed scattered bullae and crusted plaques on his arms and legs.

What is the etiology of this patient's symptoms?

Fast Break 7B

Presented by Lauren Guggina, MD, Jonathan Cotliar, MD, Joan Guitart, MD.
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS

This is a 67-year-old male who presented with a rash that has persisted for five months. Upon presentation, he noted associated fever, malaise, shortness of breath and a twenty-pound weight loss.

What diagnosis should be suspected in this case?

CHICAGO DERMATOLOGICAL SOCIETY **Case #8**

Presented by Michael Pelster, MD, Alba Posligua, MD, Monica Rani, MD, Joaquin C. Brieva, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
This 50-year-old Caucasian female was referred to our clinic with a two-month history of a new disfiguring facial eruption consisting of large erythematous crusted plaques on the face, as well as painful and pruritic erosions on the oral mucosa. She denied systemic symptoms. Two years earlier, she had been diagnosed with discoid lupus erythematosus and was started on hydroxychloroquine. When her facial rash initially appeared, she was evaluated at an outside dermatology clinic and was empirically treated for an acute DLE flare with oral methotrexate, intralesional triamcinolone, and high-dose oral prednisone. Despite the treatment, the lesions had progressively worsened by the time of the referral.

PAST MEDICAL HISTORY
Crohn's disease, DLE

MEDICATIONS
Infliximab, hydroxychloroquine, prednisone, methotrexate

FAMILY HISTORY
Hypertension, heart disease, diabetes mellitus, rheumatoid arthritis

PHYSICAL EXAM
The forehead and perioral skin had large infiltrated erythematous plaques with thin overlying yellow crust. There were erosions of the right buccal mucosa. There was no lymphadenopathy.

LABS/CULTURE
Abnormal: Tissue culture: *Candida albicans* (pan-susceptible), MSSA

Normal/Negative: CBC with differential, T-cell panel, quantitative immunoglobulins, HIV, CMP, urinalysis, mycobacterial tissue culture

HISTOPATHOLOGY
The epidermis revealed irregular acanthosis with pseudoepitheliomatous hyperplasia. There was a superficial crust with neutrophils and debris. Within the epithelial strands there were neutrophilic aggregates, plasma cells, histiocytes, and some eosinophils. Spores and pseudohyphae were also noted. DPAS was positive, and Gram stain showed numerous clusters of Gram-positive cocci at the surface. AFB and Giemsa were negative.

DIAGNOSIS
Facial *Candida* granuloma associated with immunosuppressant therapy

TREATMENT AND COURSE
Methotrexate and prednisone were discontinued, and infliximab was temporarily held. Fluconazole 200 mg/day was initiated and later increased to 400 mg/day with near-complete resolution of the lesions after 12 weeks of treatment.

DISCUSSION
Mucocutaneous *Candida* infections most frequently present either as thrush or as erythematous patches or thin plaques with satellite papules and pustules typically affecting the intertriginous

regions of the body. These classic presentations often are easily treated with topical antifungal agents. In contrast, granulomatous lesions secondary to *Candida* infection are significantly less common. Granulomatous candidal infection is most frequently described as a late manifestation of chronic mucocutaneous candidiasis (CMC), which is a heterogeneous group of disorders characterized by impaired cellular immunity that lead to chronic, recalcitrant candidal infections of the integument. Multiple genetic mutations have been associated with CMC, most of which cause defective maturation of dendritic cells and impaired Th17 responses.

Candidal granulomas most often affect the scalp, face, and chest. They have been reported specifically in some of the subtypes of CMC. In chronic localized candidiasis, patients develop lesions on the face and scalp in association with thrush. Similarly, candidal granulomas have also been reported in patients with autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy syndrome, which is caused by mutations in the AIRE gene leading to a wide variety of autoimmune pathology and high susceptibility to *Candida*. Histopathologically, lesions show marked acanthosis with hyperkeratosis and parakeratosis, branching hyphae and spores in the stratum corneum, and a brisk inflammatory infiltrate comprised of lymphocytes, plasma cells, and histiocytes in the papillary dermis. Notably, fungal structures are only occasionally identified in the dermis. Patients with CMC often require long courses of oral azole antifungal agents.

We present the challenging case of a patient with intestinal Crohn's disease that developed extensive granulomatous facial lesions after years of continuous immunosuppressant therapy. Given the patient's medical history, one of the other entities on the differential diagnosis was metastatic Crohn's disease (MCD). MCD presents as granulomatous skin lesions that occur remote from the active inflammation in the GI tract. The mechanism by which MCD occurs has not been clearly elucidated. Interestingly, most studies have not found an association between GI disease activity and the presence of skin lesions. MCD most often presents as erythematous plaques and nodules that sometimes ulcerate. Scale and crust are often present. Importantly, extragenital MCD most commonly affects the trunk and lower extremities, although facial involvement (including cheilitis granulomatosa-like lesions) has been reported. Histopathologic examination of these lesions reveals noncaseating granulomatous inflammation involving the entirety of the dermis with a predominantly lymphocytic infiltrate, although plasma cells and eosinophils may also be present. MCD often responds briskly to both topical and systemic glucocorticosteroids. In treatment-refractory MCD, success has been described with both methotrexate and the TNF-alpha inhibitors.

Although clinically and histopathologically granulomatous candidal infection and metastatic Crohn's disease are hard to distinguish, the patient's disease progression after the initiation of glucocorticosteroids and methotrexate strongly argues against metastatic Crohn's disease. Although the isolation of *Candida* from the epidermis could theoretically represent incidental fungal superinfection of another primary dermatosis, the near-total resolution of the patient's plaques with 12 weeks of fluconazole and cessation of her immunosuppressant regimen strongly supports the diagnosis of *Candida* granuloma. To the best of our knowledge, this is the first case report of this variety of candidiasis in a Crohn's disease patient on infliximab therapy.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #9**

Presented by Lauren Guggina, MD, Joaquin C. Brieva, MD and Emily Keimig, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
This 44-year-old Caucasian female presented with a one-year history of painful oral and vulvar erosions, a new mild cutaneous eruption, and severe shortness of breath. The oral lesion was biopsied and diagnosed as consistent with lichen planus at an outside hospital. She was subsequently treated with Magic Mouth wash without improvement. She then received multiple courses of high-dose systemic corticosteroids with temporary relief and recurrent flares upon discontinuation of the treatment. Six months prior to her presentation, she developed a persistent cough and severe shortness of breath. Pulmonary function tests revealed an obstructive defect and diffusion restriction. . CT scan revealed a large mediastinal mass and scattered ground glass opacities. Excisional biopsy of the mass was consistent with benign lymph node with prominent vasculature. Despite standard treatment for COPD exacerbation versus severe asthma, her respiratory function continued to decline at the time of her initial visit.

PAST MEDICAL HISTORY
Polycystic ovarian syndrome, Asthma, recurrent orolabial HSV

MEDICATIONS
Aclidinium bromide, cholecalciferol, famotidine, Magic mouthwash (hydrocortisone 500 mg, tetracycline 200 mg, nystatin 60 ml, xylocaine viscous 20 ml), lorazepam, loratidine, metformin, multi-vitamin, oxyocodone, fluticasone-salmeterol, prednisone

FAMILY HISTORY
HTN, diabetes mellitus, CHF, CAD, breast cancer.

SOCIAL HISTORY
Married, two children, former paralegal, no tobacco use, alcohol use, or illicit drug use

PHYSCIAL EXAM
Fitzpatrick phototype I, cushingoid habitus with facial hypertrichosis.
Oral mucosa: extensive yellow-based punched out ulcers at right ventral tongue, bilateral maxillary and mandibular attached gingival, and lower mucosal lip. Bilateral buccal mucosa had confluent hyperemic erosions with erythematous borders. Oral commissures had subtle whitish lacy patches extending into the mucosa. Vermillion lip with re-epithelialized erythematous patches.
External genitalia: a 3 mm ulcer with surrounding erythema at left posterior labia majora
Bilateral flanks: multiple erythematous oval flat-topped shiny papules with mild scale

LABS/IMAGING:
Abnormal: Rheumatoid factor 24 (0-14 IU/ml); ESR 30 (2-25 mm/hr); HSV IgG seropositive.
CT chest: enlarged pulmonary artery, bronchiectasis, patchy bilateral pulmonary ground glass opacities, a 6.2 x 3.4-cm mediastinal mass and a pericardial effusion
PET CT: with abnormal uptake in the mediastinum, numerous pulmonary abnormalities

Normal/Negative: CBC, CMP, UA, ANA, dsDNA, Sm IgG, Scl-70 IgG, SS-A IgG, SS-B IgG, C3, C4, cardiolipin IgA, cardiolipin IgG, cardiolipin IgM, anti-CCP, cANCA, pANCA, CRP, ESR, CCP, CPEP/UPEP, a1trypsin, hepatitis panel, HSV culture, SPEP, quantitative Jo-1 antibody, mammogram, upper and lower GI endoscopy, chest X-ray, Pap smear, bone marrow biopsy,

thyroid biopsy, lymph node biopsy, mediastinal mass excision, pericardium biopsy, lung middle lobe wedge resection, CT abdomen/pelvis, bronchoscopy, MRI brain, Lumbar puncture

HISTOPATHOLOGY

Skin lesion, abdomen: lichenoid reaction with minimal and focal acantholysis.
Tongue erosion: lichenoid reaction, with acanthotic epithelium with overlying parakeratosis and a superficial band-like lymphohistiocytic infiltrate with focal squamatization of the basal cell layer and occasional necrotic keratinocytes
Lower lip vesicle: lichenoid reaction.
Direct immunofluorescence, lower lip vesicle: no evidence of immune deposits.
Indirect immunofluorescence on simple rat bladder epithelium substrate: strong intercellular staining of IgG at lower epithelium, consistent with paraneoplastic pemphigus.

DIAGNOSIS

Paraneoplastic Pemphigus (PNP) with bronchiolitis obliterans

DISCUSSION

Paraneoplastic Pemphigus (PNP) is a polymorphic autoimmune blistering disorder associated with the concurrent presence of neoplasm, most commonly a lymphoproliferative neoplasm. It is frequently accompanied by systemic involvement, and therefore the term paraneoplastic autoimmune multiorgan syndrome (PAMS) has been suggested as an alternative, more accurate term for the disease.

Clinically, PNP is characterized by both mucosal and cutaneous involvement. Mucosal involvement usually occurs first, with extensive painful erosions and ulcerations, often involving the lateral tongue and vermillion lip. These lesions are classically refractory to treatment. Cutaneous lesions are often polymorphic, and may resemble a wide range of diagnoses, including lichen planus, pemphigus vulgaris, pemphigus foliaceus, graft versus host disease, erythema multiforme, and Stevens-Johnson Syndrome.

Histopathologically, PNP is characterized by intraepidermal and/or subepidermal blistering. With a spectrum of disease presentations, histopathology can also vary, although lichenoid interface dermatitis is commonly seen. Direct Immunofluorescence typically shows IgG and complement C3 deposits in an intercellular and/or linear pattern, and has been reported to have a 41% sensitivity and an 87% specificity. Indirect Immunofluorescence typically shows IgG and complement C3 deposits in an intercellular or linear pattern on stratified squamous epithelium, but also binds rat bladder and cardiac muscle, with an 86% sensitivity and 98% specificity rates. PNP serum recognizes multiple targets, including desmoplakin I, bullous pemphigoid antigen I, desmoplakin II, envoplakin, desmoglein 3 and desmoglein 1.

PNP has been associated with a mortality rate of up to 90% usually due to sepsis, the underlying neoplasm, or pulmonary involvement. The lymphoproliferative disorders and neoplasms most commonly associated with PNP include Castleman's tumor, non-Hodgkin's lymphoma, thymoma, follicular dendritic cell sarcoma, and chronic lymphocytic leukemia. PNP has been reported to be associated with respiratory inflammatory disease, and more specifically, bronchiolitis obliterans, as seen in our patient. Also termed constrictive bronchiolitis, bronchiolitis obliterans is characterized by progressive airway obstruction that does not respond well to immunosuppressive therapy, and is often the cause of significant morbidity and mortality. Our case exemplified the importance to have a low threshold for evaluation of obstructive airway disease in patients with PNP.

Treatment of PNP starts with the identification and treatment of the underlying neoplasm or lymphoproliferative disorder. This is usually followed by immunosuppression, immunomodulation, or removal of pathogenic autoantibodies. Our patient was initially managed with corticosteroids. Mycophenolate mofetil was added for treatment of her lung disease, but patient had progression of her hypoxia and was transitioned to cyclosporine. Throughout the course of her disease she has been on varying doses of oral steroids. Currently, her mucocutaneous lesions are managed with tacrolimus ointment and the oral agents used to treat her lung disease (oral steroids and cyclosporine). While her mucocutaneous lesions have improved, her lung disease has not responded to treatment and she is currently on the waiting list for a lung transplantation

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #10**

Presented by Luzheng Lisa Liu, MD PhD, Monica Rani, MD, and Joaquin C. Brieva, MD
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HISTORY OF PRESENT ILLNESS
This 76-year-old African American male presented in November 2013 with numerous cutaneous warts throughout body that progressively developed since 2003. These lesions have been asymptomatic, and refractory to multiple sessions of cryosurgery prior to his presentation.

PAST MEDICAL HISTORY
AIDs (diagnosed in 1990's); squamous cell carcinomas on palate and skin; CAD, HTN, dyslipidemia, benign prostate hyperplasia

MEDICATIONS
Darunavir, ritonavir, raltegravir, sulfamethoxazole-trimethoprim, triamterene-hydrochlorothiazide, metoprolol, irbesartan, potassium, atorvastatin, aspirin, tamsulosin, oxybutynin, latanoprost.

FAMILY HISTORY
No family history of similar lesions.

SOCIAL HISTORY
Single, retired. Denied tobacco and illicit drug use; occasional social alcohol.

PHYSICAL EXAM
Numerous hypopigmented to pink thin papules coalescing into plaques with intervening hyperkeratotic furrows on the cheeks, neck, trunk, buttocks, groin, penis and scrotum.

LABS
Abnormal: Absolute CD4 cell count 62/μl (340-1568 /μl), HIV viral load <117 copies/ml (<= 20 copies/ml), Hgb10.5 g/dl (11.6-15.4 g/dL), Hct 32.5% (38-50%), Plt 104 K/ml (140-390 K/ml),
Negative/normal: WBC, ALT, basic metabolic panel, quantitative immunoglobulins

HISTOPATHOLOGY
Compact orthokeratosis, coarse hypergranulosis with "Bird's eye" cells, consistent with verruca plana. No atypia was identified.

DIAGNOSIS
Acquired epidermodysplasia verruciformis in the setting of AIDS

TREATMENT AND COURSE
The patient was initially treated with imiquimod 3.75% cream daily with cimetidine 800 mg TID. No clinical improved was appreciated after 2 months of treatment. He was subsequently started on acitretin 10 mg daily on July 3rd. He tolerated the treatment well.

DISCUSSION
Epidermodysplasia verruciformis (EV) is a rare autosomal recessive genodermatosis caused by homozygous mutations in EVER1 and EVER2 on chromosome 17q25. It is characterized with an increased susceptibility to specific human papilloma virus (HPV) genotypes, resulting in both benign and malignant skin lesions. EV skin lesions are frequently described as pityriasis versicolor-like macules, flat wart-like papules, or verrucous and seborrheic keratosis-like papules and plaques. The term "acquired EV" was recently introduced to the literature and describes EV

occurring in patients with impaired cell-mediated immunity leading to increased susceptibility to infections by beta-HPV. Acquired EV primarily occurs in patients with human immunodeficiency virus (HIV) infection, and transplant recipients on long-term immune suppressants. In the HIV-positive population, acquired EV seems to be more frequent in young and vertically HIV-infected patients compared to adults infected by HIV later in life. This may be explained by the lack of well-developed immunity in the vertically infected patients at the time of primary (first-time exposure) HPV infection. On the contrary, older patients infected with HIV via non-vertical mechanisms as well as transplant recipients are likely already exposed to this ubiquitous pathogen and acquired protective immune memory to HPV prior to the development of immunocompromised state. The same hypothesis may also explain the observations that malignant transformation of EV lesions to SCC were primarily seen in vertically transmitted cases in the HIV setting.

The most frequent HPV strains implicated in skin eruptions of the EV patients are HPV 5 and 8, although co-infection with a wide range of other HPV types has also been documented. In a non-blinded case series of 37 skin biopsies from 17 patients with acquired EV, oncogenic HPV types are detected in approximately one-half of skin biopsies and the relative risk for epidermal dysplasia in such lesions is much higher than in the genetic type of EV. Currently, there is no evidence to support efficacy of Gardasil vaccination in treating existing infections or prevention of malignant transformation by the HPV types not covered by the vaccine. However, vaccination can prevent new infections by vaccine strain HPV. Vaccines targeting broadly cross-neutralizing epitopes are under investigation.

There are no randomized controlled therapeutic trials in patients with either genetic or acquired form of EV. Literatures suggest that the progression of cutaneous lesions of acquired EV is not influenced by the immunological status of the patients and response to anti-retroviral therapy in HIV infected patients is poor. A number of anecdotal treatment regimens have been reported in case reports or case series. Cryosurgery, topical retinoic acid, or imiquimod alone is ineffective. Oral cimetidine has been reported to have limited benefit. Monotherapy with systemic retinoic acid, interferon alpha, or photodynamic therapy have all been used with limited and variable success. Combination therapy with systemic retinoic acid and concurrent topical imiquimod appear to have the better and more sustainable response in a few case reports. In addition, infection by oncogenic HPV strains and the immunocompromised state warrant diligent skin exam and low threshold for skin biopsy in the management of patients with acquired EV.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #11**

Presented by Melanie Clark, MD and Joaquin C. Brieva, MD
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This is an 18-year-old Asian female who presented with a two-month history of blistering eroded pruritic plaques on the arms.

Unknown

CHICAGO DERMATOLOGICAL SOCIETY **Case #12**

Presented by Victoria Godinez-Puig, MD and Joan Guitart, MD
Department of Dermatology, Feinberg School of Medicine, Northwestern University

HISTORY OF PRESENT ILLNESS
This 76-year-old Hispanic male presented with a 10-year history of evolving pruritic facial papules and nodules. He denied fever, chills, night sweats, weight loss, malaise, or photosensitivity. Five years prior to his presentation, the patient was diagnosed with cutaneous plasmacytosis with polyclonal plasma cell infiltrate, and received bortezomib and systemic glucocorticosteroids with limited improvement. He was subsequently lost to follow-up.

PAST MEDICAL HISTORY
Adult-onset asthma, CAD, diabetes mellitus type II, HTN, glaucoma.

MEDICATIONS
Hydralazine, prednisone taper, doxepin, metformin, albuterol inhaler.

PHYSICAL EXAM
Multiple facial erythematous nodules and plaques, with resultant leonine facies. A large, indurated erythematous plaque was noted on the left cheek. Erythematous nodules were present on the left pre-auricular area. Bilateral palpable parotid enlargement and cervical lymphadenopathy were also noted.

LABS/IMAGING
Abnormal: WBC 16.1 (3.5-10.5 K/UL), absolute neutrophil count 13.8 (1.5-8 K/UL), absolute eosinophil count 1.3 (0.0-0.6 K/UL), IgG 1710 (700-1600 mg/dL), IgG4 197 (4-86 mg/dL), IgE 4195 (<114 IU/mL), IgG anti H. pylori reactive.
SPEP: hypergammaglobulinemia, accentuated beta band, and restricted band in gamma region.
Immunoglobulin gene rearrangement skin: suspicious for clonal B cell rearrangement.
CT head, neck, larynx: Diffuse nodular thickening along the skin surface of the face and neck. Multiple enlarged intraparotid and cervical lymph nodes.
CT chest, a/p: Left inguinal and right paratracheal enlarged lymph nodes.

Normal/negative: Basic chemistry panel, ALT, AST, ALP, LDH, IgA, IgM, serum immunofixation, TCR rearrangement PCR, hepatitis panel, TCR rearrangement PCR, Lyme disease antibodies, TSH, uric acid, ANA, dsDNA, C3, C4,
c-ANCA, p-ANCA.
Serum immunofixation: no monoclonal bands seen.

HISTOPATHOLOGY
Facial lesion biopsy: Atypical plasma cell infiltrate with eosinophils. *In situ* hybridization and immunohistochemistry revealed a κ:λ ratio of less than 6:1 (upper range of normal limits).
Left intraparotid lymph node biopsy: Reactive lymphadenopathy of IgG4-related disease.
Parotid excision: Lymphocyte and plasma cell infiltrates suggestive of IgG4-related disease.

DIAGNOSIS
IgG4-related disease of the skin and parotid

TREATMENT AND COURSE

The patient completed 12 cycles of rituximab with minimal improvement in his skin lesions. He was then switched to azathioprine, which he did not tolerate well. He subsequently started mycophenolate mofetil, after which he was lost to follow-up.

DISCUSSION

IgG4-related disease (IgG4-RD) is an increasingly recognized immune-mediated entity characterized by tissue infiltration by IgG4 plasma cells and distinct fibro-inflammatory changes that manifest with tumefactive lesions. IgG4-RD affects the pancreas and other organs such as the salivary and lacrimal glands, orbit, kidney, aorta and retroperitoneum. Single organ presentations, although rare, have also been described. It has been postulated that high levels of circulating IgG4 could represent a marker of systemic disease.

IgG4-RD of the skin is a rare entity. Different presentations sharing features with several entities such as cutaneous plasmacytosis, pseudolymphoma and angiolymphoid hyperplasia with eosinophilia have been described. Interestingly, it has recently come to light that a considerable number of patients historically diagnosed with cutaneous plasmacytosis also meet criteria for IgG4-RD of the skin, as was the case in our patient.

Although no definitive criteria for diagnosis have been established, characteristics of this entity include (1) distinct cutaneous lesions characterized by erythematous papulo-nodules and infiltrated plaques, and (2) lymphoplasmacytic infiltrates with IgG4+/IgG+ plasma cells >40% and >10 IgG4+ plasma cells per field. Circulating IgG4 levels > 135 mg/dL are thought to be associated with systemic disease. Patients with IgG4-RD of the skin may also have manifestations from other involved organs. Although lymphadenopathy is common, most patients lack fever or B symptoms. Allergic symptoms also prevail. As in our patient, blood and tissue eosinophilia are frequently detected, and are thought to be the result of elevated Th2 cytokine levels.

Treatment modalities for IgG4-RD include systemic glucocorticosteroids, and in refractory cases, B-cell depletion with rituximab, which leads to targeted reductions in IgG4 levels. Azathioprine and mycophenolate mofetil have also been suggested as reasonable second line therapies. Finally, thalidomide has been reported to be effective in patients presenting with pseudolymphoma.

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CHICAGO DERMATOLOGICAL SOCIETY **Case #13**

Presented by Lara E. Rosenbaum, MD, and Simon Yoo, MD
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HISTORY OF PRESENT ILLNESS

This 52-year-old male initially presented in December 2004 with a red, pruritic lesion on the left scrotum. A biopsy revealed infiltrative basal cell carcinoma (BCC) and he underwent excision. In June 2007, recurrence was noted in the scrotal flap, which was unable to be cleared after six excisions and was subsequently treated with radiation. In June 2008, a PET/CT revealed hypermetabolic left iliac and right inguinal lymph nodes. Surgical excision was offered but the patient chose to enroll in a clinical trial with vismodegib. In May 2010 vismodegib was discontinued due to disease progression. He underwent four cycles of cisplatin and docetaxel with good response and remained progression-free until February 2013 when a CT scan revealed an enlarged left groin mass. He then received cisplatin and docetaxel for two cycles and in June 2013 restarted vismodegib. His disease remained stable until May 2014 when disease progression was detected by his oncologist, who referred him back to dermatology.

PAST MEDICAL HISTORY

BCC on nose and scalp (excised); Post-radiation sarcoma on left thigh (excised); HTN

MEDICATIONS

Vismodegib, lisinopril, furosemide, morphine sulfate ER, hydrocodone-acetaminophen, lorazepam, multivitamin, iron, solifenacin succinate, melatonin, gabapentin, duloxetine

FAMILY HISTORY

Mother and two sisters: BCC; Father: laryngeal carcinoma

PHYSICAL EXAM

On the right proximal thigh, bilateral inguinal folds, penis, and scrotum were numerous deep thick plaques with rolled pearly borders. There is a deep ulcer circumferentially at the base of the penis and in the left inguinal crease, along with scattered ulcers on the shaft. There is bulky right inguinal lymphadenopathy.

IMAGING

CT Chest/Abdomen/Pelvis – May 2014: Two new pulmonary nodules, suggestive of intrapulmonary lymph nodes (cannot exclude metastasis). Enlargement of soft tissue in left groin (5.4 cm x 2.8 cm, previously 5.0 cm x 2.5 cm). Stable nodular skin thickening extending to right of midline and stable right inguinal lymph node.

HISTOPATHOLOGY

2005-2010: Multiple specimens from the groin revealed BCC, infiltrating type

May 2014: Right thigh, right groin and ventral shaft of penis: Poorly differentiated basaloid tumor most consistent with recurrent BCC. Tumor cells were positive for p63, p16, CK5, vimentin, cytokeratin (AE1/3), Cam 5.2 and partially positive for BER-EP4; negative for epithelial membrane antigen, S-100, CD31, chromogranin, CK20 and HPV. Bcl2 showed no nuclear staining but weak and focal cytoplasmic staining.

DIAGNOSIS

Metastatic BCC, failing vismodegib and systemic chemotherapy

TREATMENT AND COURSE

In May 2014 due to the bulky skin lesions, disease progression and increasing voiding difficulty, the now 62-year-old patient was urgently referred to urology and plastic surgery. He underwent radical resection of this metastatic inguinal and penoscrotal BCC (total size 21 cm x 16 cm) along with right radical inguinal lymphadenectomy, total scrotectomy, right radical inguinal orchiectomy, partial urethrectomy with perineal urethrostomy, partial penectomy and left inguinal mass excision. There were no complications post-operatively.

Two weeks later he presented to the hospital for planned split-thickness skin graft and was found to have an oxygen saturation of 88% along with dyspnea at rest and orthopnea. Evaluation revealed large bilateral pleural effusions. Both effusions were drained and analysis revealed no evidence of metastatic or infectious etiology. The patient was discharged after 6 days, breathing comfortably on room air.

Four days later the patient returned with increased shortness of breath. Video-assisted thoracoscopic surgery with pleural biopsy revealed metastatic BCC. Unfortunately, his hospital course was complicated by hypercapnic respiratory failure and progressive agitation. He was made DNR/DNI with comfort measures only and expired on August 18, 2014.

An autopsy revealed widespread metastatic BCC in the lungs, extending into the diaphragm, pericardium and pleura, as well as in the heart, liver and bone marrow. He was also noted to have an organized thromboembolism occluding the lumen of the right main pulmonary artery.

DISCUSSION

Although BCC is the most common cancer worldwide, it only very rarely metastasizes at a rate estimated to be 0.0028% to 0.55%. While typically occurring in sun-exposed areas, BCCs may also develop on sun-protected areas. BCCs of the genitalia represent less than 1% of cases. Multiple case reports and small case series have been previously published describing metastases of BCCs arising on the scrotum. Of these, 7/53 developed metastases (13%) with the majority treated with surgery (in the case of regional metastases) and few with chemotherapy (in the case of distant metastases). The majority of patients showed complete clearance with no evidence of recurrence.

New understanding of the genetic changes in BCC has led to the development of vismodegib, a hedgehog pathway inhibitor that is FDA approved for metastatic BCC. From the phase II trial, the estimated response rate of metastatic BCC to vismodegib is 30%.

This gentleman initially presented with a BCC on an unusual location, emphasizing the need for thorough examinations of our patients and prompt surgical management. The patient also developed a superficial post-radiation sarcoma, successfully treated with excision. A multi-disciplinary approach was critical in the care of this patient, requiring dermatology (including dermatologic surgery and dermatopathology), hematology/oncology, radiation oncology, urology, plastic surgery, vascular surgery and thoracic surgery. He failed both vismodegib and systemic chemotherapy. The patient died from widely metastatic disease. This case illustrates that, while exceedingly rare, BCCs can metastasize and cause significant morbidity and mortality in a very few unfortunate individuals.

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