Chicago Dermatological Society

June 2012
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
Case Presentations

Wednesday, June 13, 2012

Conference Host:
Division of Dermatology
Loyola University Medical Center
Maywood, Illinois

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Program

Conference Location

Stritch School of Medicine/Cuneo Center
Loyola University Medical Center
2160 South First Avenue, Maywood

Program Events

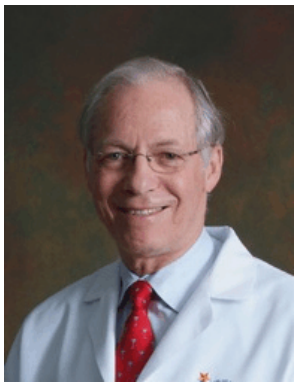
8:00 a.m.	Registration & Continental Breakfast *Main Lobby - Cuneo Center*
9:00 a.m. - 10:00 a.m.	**General Session – Resident Lecture** *Leischner Hall Room 390* Co-morbidities in Psoriasis with Emphasis on Cardiovacular Events" *ALAN MENTER, MD*
9:30 a.m. - 10:45 a.m.	**Clinical Rounds** • Patient & Poster Viewing - *Seminar Rooms 364, 396, 397, 431, 432, 463, 464, 496, 497 (signs will be posted)* • Slide Viewing - *Clinical Skills Center Room 398*
11:00 a.m. - 12:15 p.m.	**General Session – *Psoriasis Forum*** *Tobin Hall Room 190* Moderator: *KENNETH GORDON, MD* Panelists: *ALEXA KIMBALL, MD; CRAIG LEONARDI, MD; ALAN MENTER, MD*
12:15 p.m. - 12:45 p.m.	**Lunch Break** *Main Lobby - Cuneo Center; seating in Rooms 150 & 170*
12:45 p.m. - 1:00 p.m.	**CDS Business Meeting** *Tobin Hall Room 190*
1:00 p.m. - 2:30 p.m.	**General Session** – Case Discussions *Tobin Hall Room 190*
2:30 p.m.	**Meeting adjourns**

Mark the Date!

Next CDS monthly meeting – Wednesday, October 10, 2012 at the University of Illinois

Check for details on the CDS website: www.ChicagoDerm.org

Program Participants



Guest Speaker

ALAN MENTER, MD

Texas Dermatology Associates; Dallas, TX

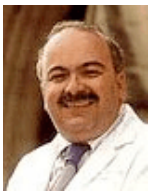
Dr. Alan Menter was born in England and received his dermatology residency training in South Africa. He subsequently undertook further postgraduate training and research at Guy's Hospital and St. John's Hospital for Diseases of the Skin in London, England. After moving to the United States, he completed a fellowship in Dermatology at Southwestern Medical School in Dallas, and was Board Certified in dermatology in 1977.

Dr. Menter has written more than 200 articles, two books, and 10 book chapters in peer reviewed medical publications, and has an international reputation as a clinician/researcher. In 2004, he spearheaded the formation of the International Psoriasis Council and currently serves as President. Recent lectures include Brasilia, Buenos Aires, Copenhagen, Florence, Istanbul, London, Madrid, and Tokyo, as well as talks in numerous US cities. He has presented at various American Academy of Dermatology conferences and at the World Congress of Dermatology in Buenos Aries in 2007

Panelists

Alexa Kimball, MD, MPH

Massachusetts General Hospital; Harvard Medical School
Boston, MA



Craig Leonardi, MD

Central Dermatology
St. Louis, MO

Panel Discussion Moderator

Kenneth Gordon, MD

Northwestern University
Chicago, IL

Continuing Education Credit

Chicago Dermatological Society

"Chicago Dermatological Society Monthly Conference"

June 13, 2012 *Maywood, IL*

Participants must attend entire session to receive all types of credit. CFMC hosts an online evaluation system, certificate and outcomes measurement process. Following the conference, you must link to CFMC's online site (link below) to complete an evaluation form, in order to receive your continuing education statement of hours (certificate). Once the evaluation form is complete, you will automatically be sent a copy of your certificate via email.

Continuing Education evaluation and request for certificates will be accepted up to 60 days post activity date. The Colorado Foundation of Medical Care (CFMC) will keep a record of attendance on file for 6 years. CFMC contact information: 303-695-3300, ext. 3139.

Link address to evaluation form:

www.yourcesource.com/eval?act=670!06132012

JOINT SPONSOR STATEMENT

This Continuing Educational activity is Joint-sponsored by the **Colorado Foundation for Medical Care, Office of Continuing Education** and the **Chicago Dermatological Society**. **CFMC is accredited by the ACCME to provide continuing medical education for physicians.**

GOAL / PURPOSE

To broaden the clinical knowledge of dermatologists with respect to diagnostic.

SESSION OBJECTIVES

Upon completion of sessions, participants will be able to apply new knowledge and skills in the area of physician learning.

1. Discuss the evaluation and treatment options for patients with refractory psoriasis.
2. Describe the association of psoriasis with cardiovascular co morbidities.

.CREDIT STATEMENTS

CME CREDIT

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 joint sponsorship of the Colorado Foundation for Medical Care, Office of Continuing Education (CFMC OCE) and Chicago Dermatological Society. CFMC is accredited by the ACCME to provide continuing medical education for physicians.

The Colorado Foundation for Medical Care designates this Live Activity for a maximum of 4.5 *AMA PRA Category 1 Credit(s) ™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

OTHER HEALTH CARE PROFESSIONALS

This educational activity has been planned and implemented following the administrative and educational design criteria required for certification of health care professions continuing education credits. Registrants attending this activity may submit their certificate along with a copy of the course content to their professional organizations or state licensing agencies for recognition for 4.5 hours.

DISCLOSURE STATEMENTS

Alan Menter:

Advisory Board - Abbott, Amgen, Centocor, Galderma, Wyeth
Consultant - Abbott, Amgen, Centocor, Eli Lilly, Galderma, Stiefel, Wyeth
Investigator – Abbott, Allergan, Amgen, Celgene, Centocor, Eli Lilly, Novartis, Novo Nordisk, Pfizer, Stiefel, Syntrix Biosystems, Wyeth
Speaker – Abbott, Amgen, Centocor, Galderma, Wyeth
Grant – Abbott, Allergan, Amgen, Celgene, Centocor, Eli Lilly, Novartis, Novo Nordisk, Pfizer, Stiefel, Syntrix Biosystems
Honoraria – Abbott, Amgen, Centocor, Galderma, Steifel, Wyeth

All other members of the faculty and planning team have nothing to disclose nor do they have any vested interests or affiliations. **It is the policy of the Chicago Dermatological Society and Colorado Foundation for Medical Care (CFMC) that the faculty discloses real or apparent conflicts of interest relating to the topics of the educational activity.**

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 1**

Presented by Ricardo Berrios, MD, Julia Kamalpour, MD, Vanessa Lichon MD, Anita Shetty, MD, and Rebecca Tung, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 67 year-old Caucasian male presented to our clinic for evaluation of fourteen, new, hyperkeratotic lesions on face, trunk and extremities. Eighteen months prior to presentation, he had been diagnosed with superficial spreading melanoma (Breslow depth 1.8 millimeters, T2aN0M0) treated with wide local excision at an outside institution. Six week prior to presentation, he developed cutaneous (left thigh) and pulmonary metastasis. B-RAF analysis revealed the V600E mutation, and he was enrolled in a vemurafenib trial where he was given the active agent at 600 milligrams (mg) twice daily. At presentation, all lesions were biopsied and were confirmed to be invasive squamous cell carcinomas (SCCs).

PAST MEDICAL HISTORY

Metastatic melanoma – as detailed above

MEDICATION

Vemurafenib 600 mg BID

FAMILY HISTORY

Brother, sister – basal cell carcinoma

SOCIAL HISTORY

Occupation – banker, retired
Tobacco – 10 pack-year history; quit 40 years ago

PHYSICAL EXAM

Numerous, hyperkeratotic, thin and thick papules and nodules, some tender to palpation, were noted over the face, trunk and extremities.

HISTOPATHOLOGY

A representative example of a shave biopsy performed on the right upper thigh revealed a crateriform proliferation of well-differentiated, squamous cells with glassy, pink cytoplasm extending into the superficial dermis.

DIAGNOSIS

Eruptive squamous cell carcinomas in the setting of vemurafenib

TREATMENT AND COURSE

Upon initial evaluation, systemic chemoprevention with acitretin was considered but not permitted per study protocol. Given that the patient had expressed preference for surgical management only for the larger, more painful lesions, excision with Mohs micrographic surgery was completed on five of the initial lesions. At three weeks follow-up post-excision, twelve additional lesions suspicious for SCCs were identified on the face, trunk, and extremities. Having elected to pursue a non-surgical approach, a combination of photodynamic therapy (PDT), pulsed dye laser (PDL) and 5-fluorouracil (5-FU) 5% cream was initiated. PDT was performed on the extremities using 5-aminolevulinic acid; it was allowed to incubate for three hours followed by exposure to a 610-nm light source for sixteen minutes.

PDL settings were as follows: 595 nm, triple pulsing, 7 mm spot size, 7 joules, 7 msec pulse duration. 5-FU cream was applied nightly to all lesions for two weeks. Nine weeks later, the modified laser-PDT regimen was repeated to lesion with residual, clinical disease. Fifteen weeks later, lesions identified to have any remaining, residual disease were surgically excised (13 of 26).

Melanoma metastases to the brain were confirmed shortly thereafter, and vemurafenib was discontinued after seventeen weeks of therapy. The patient was started on a regimen of whole-brain radiation, stereotactic radiosurgery, and four cycles of ipilimumab. No additional skin lesions suspicious for non-melanoma skin cancers (NMSCs) developed during this period. Following completion of the above regimen, follow-up MRI scans revealed resolution of the metastatic foci, and he was restarted on vemurafenib 960 mg BID. One month after resuming therapy, he returned to our clinic with fourteen, new SCCs. Surgical excisions were performed on the larger, more painful lesions while smaller ones were treated with a combination of PDL and PDT; topical 5-FU was also re-started.

At the most recent follow-up, he continues to develop new NMSCs. In total, to date, he has developed 58 SCCs and five basal cell carcinomas (BCCs). Despite this, he maintains a good quality of life and high functional status.

DISCUSSION

The mitogen activated protein kinase (MAPK) pathway functions to promote cell survival, differentiation, and proliferation. The canonical signaling cascade consists of RAS, RAF, MEK, and ERK, which sequentially relay activating signals (mainly through phosphorylation events) beginning with mitogen, hormone, or neurotransmitters binding on the cell surface on through to nuclear activation via translocation of ERK.

Mutations in all of these proteins have been observed in melanoma, but over sixty percent harbor mutations in B-RAF, a member of the RAF family (A-RAF and C-RAF are the other two). Specifically, the V600E mutation converts valine to glutamic acid at codon 600; this renders mutant B-RAF 10.7 fold more active that wild-type protein and frees it of necessary, up-stream RAS activation.

Approved in 2011 for the treatment of metastatic melanoma, vemurafenib is a small molecule that is reported to specifically inhibit ^{V600E}B-RAF. In the landmark Phase 3 trial published in June 2011, vemurafenib was shown to reduce the relative risk of death in patients with metastatic melanoma by 63% at month six when compared to dacarbazine. This translated into an increase in median survival of approximately four months.

Several cutaneous side effects have been observed in patients treated with vemurafenib, reported in the original, clinical trials and in several case reports since: keratosis pilaris-like eruptions with facial erythema, seborrheic dermatitis-like rashes, hyperkeratotic, tender, plantar papules, and squamous cell carcinomas.

The association between vemurafenib exposure and the development of NMSCs is particularly concerning, and the mechanism behind this phenomenon is thought to lie in mutations in other parts of the MAPK pathway. In cells containing wild-type B-RAF but oncogenic mutations in RAS, changes in RAS activity promote dimerization of other RAF isoforms – B-RAF:C-RAF, B-RAF:B-RAF, and C-RAF:C-RAF. Dimerization of these isoforms and subsequent transactivation (of C-RAF, in particular) allows for continued MAPK signaling despite inhibition of B-RAF by vemurafenib. In a recent article by Su et al., mutations in H-RAS were found in sixty percent of SCCs from patients treated with vemurafenib. The authors

suggest that vemurafenib may be acting to promote the rate of SCC development by uncovering mutations in lesions that would otherwise have remained quiescent – what has now been termed paradoxical MAPK-pathway activation.

Photodynamic therapy is an approved treatment for actinic keratoses, superficial BCC and SCC-in-situ, and its utility in the setting of multiple eruptive keratoacanthomas with vemurafenib has recently been reported. While blue light illumination is typical, recent studies have also shown that PDL (595 nm) is an effective light source for PDT due to an absorption peak of protoporphyrin IX near 585 nm. Laser-assisted PDT is safe, effective, and tolerable. In our patient, all SCCs that were openly excised were immediately treated with laser-PDT with significant response. Potentially, increased absorption of 5-ALA at the open surgical sites may lead to enhanced clinical results. Moreover, PDT may have also elicited an immune response against the development of further SCCs; Pierre et al reported successful treatment of cutaneous metastatic melanoma with a combination therapy of imiquimod followed by intralesional injection of a photosensitizing dye (indocyanine green) and irradiation with 810-nm diode laser. Tumor cells killed by this method may serve as an antigenic source for a local immune response, heightening surveillance against recurrence. Similar immune up-regulation may have been induced in our patient.

Interestingly, our patient has exceeded expected time of survival with metastatic melanoma. Modified PDT may have served as an adjuvant treatment to our patient's oral regimen by enhancing immune surveillance. He has been pleased with the lifestyle maintenance afforded by his individualized treatment plan. We present this case not only to highlight a dramatic presentation of an emerging secondary effect, but also to introduce the concept of combination therapy (surgery with modified PDT and 5-FU) for treatment of extensive SCCs in patients with metastatic melanoma receiving vemurafenib.

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Special thanks to Murad Alam MD, Kelli Hutchens MD, Anita Shetty MD, Bryan Gammon MD, Ramin Fathi, MS4, Meghan Dubina, MD, and Meredith Hancock, MD for their assistances in this case.

Presented by Allison Goddard, MD, and Laura S. Winterfield, MD
Division of Dermatology, Loyola University Medical Center

UNKNOWN

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 3**

Presented by Loebat Julia Kamalpour, MD, and Anthony Peterson, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 23 year-old African American female presented to the emergency room with a six-month history of fatigue, progressive dyspnea on exertion, and decreased appetite resulting in a 25-pound weight loss. She also reported a 12-month history of thick, crusted scale over her entire scalp along with new pink, pruritic, and painful papules that had developed within her tattoos over the preceding two weeks. A prior piercing site over her upper cutaneous lip had also recently become inflamed. She had been seen by multiple outside physicians for the extensive scaling in her scalp and had undergone three unsuccessful trials of oral griseofulvin in addition to frequent (up to two to three times daily) use of ketoconazole 2% shampoo and over-the-counter anti-dandruff medications.

PAST MEDICAL HISTORY

Iron deficiency anemia

MEDICATION

Ferrous sulfate 325 mg po tablet TID

ALLERGIES

No known drug allergies

FAMILY HISTORY

Noncontributory

SOCIAL HISTORY

The patient denied tobacco or illicit drug use. She reported occasional alcohol use.

PHYSICAL EXAM

Physical exam was notable for four indurated erythematous discrete papules within a tattoo over the left upper extremity. One hyperpigmented thin slightly scaly macule was seen over a left anterior thigh tattoo. An indurated, violaceous papule was noted at a prior piercing site over the patient's right upper cutaneous lip. Thick, verrucous plaques without associated alopecia were present diffusely throughout the patient's scalp.

HISTOPATHOLOGY

Punch biopsy of the left upper extremity tattoo showed marked granulomatous inflammation with zones of suppurative inflammation extending from the papillary dermis into the subcutis. Transbronchial biopsy of the lung showed replacement of the alveolar architectures with epithelioid granulomas with scant foci of necrosis. Gram, AFB and PAS stains were negative for bacterial or fungal organisms. Fine needle aspiration (FNA) of an enlarged paratracheal node was negative for malignancy. Punch biopsy from the scalp showed papillomatosis and acanthosis of the epidermis with spires of parakaratotic scale. Dense fibroblasia of the papillary and reticular dermis was noted, but sarcoidal granulomas were absent.

LABORATORY RESULTS

The following laboratory tests were within normal limits:

BMP
p-ANCA, c-ANCA
Blood cultures x 2
Aerobe anaerobe, fungal, and AFB cultures of bronchoalveolar lavage, and tissue biopsies from skin and lung
PPD, Hepatitis panel, and HIV
Blastomycosis and Histoplasmosis urine antigens

The following laboratory tests were abnormal:

Angiotensin Converting Enzyme: 253 high (9-67 normal)
CBC: microcytic anemia with wbc 4.4, hgb 8.9, hct 28, plt 222
Iron: 22 low (35 – 140 normal)

RADIOLOGY

CT Chest/abdomen/pelvis with contrast was compared to CT chest from outside hospital that was done 3 weeks prior to admission and showed progression of numerous pulmonary nodules, nonspecific ground glass opacities with stable mediastinal and hilar lymphadenopathy. A new right lower lobe nodular opacity was seen with suggestion of central cavitation.

DIAGNOSIS

Verrucous cutaneous sarcoidosis

TREATMENT AND COURSE

Due to the presence of granulomatous and suppurative inflammation on tissue biopsy, there was significant clinical suspicion for a possible infectious etiology. Once tissue cultures returned and were found to be negative for bacteria, fungal or atypical mycobacteria infection, the patient was discharged home on 40 mg of oral prednisone daily. Fluocinolone acetonide 0.01% topical oil was prescribed for her scalp lesions and triamcinolone ointment was recommended to treat the granulomas within her tattoo. At one-week follow-up exam, all of the patient's cutaneous lesions were seen to have resolved, including complete clearance of the verrucous plaques over her scalp.

DISCUSSION

Cutaneous sarcoidosis may present a diagnostic challenge to physicians due to its protean manifestations. The diagnosis of sarcoidosis remains one of exclusion, established by the histological finding of noncaseating granulomas after ruling out other possible causes of such lesions, including infectious etiologies or foreign bodies.

Only eight cases of verrucous sarcoidosis have been reported in the English literature. All reported cases have occurred in African American patients between the ages of 16 and 34. Verrucous sarcoidosis has been found either as the sole manifestation of the disease or in combination with other cutaneous forms including papules, plaques, ulcerative papules or atrophic plaques. Work-up for a possible infectious etiology has been negative in all reported cases. Improvement in cutaneous lesions has been described with the use of both systemic and topical steroids.

Verrucous plaques of sarcoidosis have been described over the forehead, trunk, bilateral upper extremities, lower extremities, groin, and perianal regions. There have been no previously reported cases of verrucous sarcoidosis with scalp involvement. Most affected patients have been found to have significant pulmonary involvement of their sarcoidosis.

Histopathologic examination of verrucous sarcoidosis typically reveals an acanthotic epidermis with raised papillomatous areas in which tissue is seen to extend upward in a digitate fashion. Thick, hyperkeratotic scales with foci of parakeratosis are seen to overlie the epidermis. Dermal involvement varies from the more typical discrete sarcoid granulomas to those showing central fibrinoid necrosis surrounded by an inflammatory cell infiltrate.

While histopathologic exam of this patient's verrucous lesions did not reveal dermal granulomas, the changes seen within the epidermis were similar to those described in previously reported cases of verrucous sarcoidosis. Furthermore, the rapid and complete clearance of her previously recalcitrant scalp lesions with systemic steroid use provides further circumstantial evidence for a diagnosis of verrucous sarcoidosis, particularly in the context of concomitant lung and skin granulomas. In the appropriate clinical context, sarcoidosis should remain in the differential diagnosis for verrucous plaques presenting in African American patients, especially in the setting of systemic involvement with pulmonary disease.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 4**

Presented by Anita Shetty, MD, and David Eilers, MD
Section of Dermatology, Edward J. Hines Veteran's Administration Hospital

HISTORY OF PRESENT ILLNESS

A 67 year-old African-American male presented to the dermatology clinic in April 2010 for evaluation of a pruritic rash and oral ulcerations present for approximately three months. He had no treatment for the cutaneous lesions, and was using over-the-counter Biotene wash for the oral ulcerations. The patient had a history of metastatic melanoma diagnosed and treated at outside hospitals. The primary lesion was of the acral lentiginous subtype, 7mm in Breslow depth, and located on the right great toe; he was status-post amputation of the first metatarsal ray in 2004. At that time, the patient elected against a sentinel lymph node biopsy because he was unsure whether he would want adjuvant therapy in case of locally metastatic disease. In February 2009, due to clinically apparent lymphadenopathy, he had a right inguinal lymph node dissection with 13 out of 14 positive nodes. After presenting to an outside hospital in status epilepticus in April 2009, an MRI was suspicious for right frontal lobe metastatic disease. However, a follow-up MRI in June 2009 did not show evidence of metastatic disease. The patient had not pursued any further medical therapy prior to our clinical evaluation.

PAST MEDICAL HISTORY

Post-traumatic stress disorder

MEDICATION

Acetaminophen
Amlodipine
Docusate
Levetiracetam
Magnesium oxide
Metformin
Phenobarbital
Potassium chloride
Sertraline
Simvastatin
Warfarin

ALLERGIES

No known drug allergies

FAMILY HISTORY

No family history of melanoma or autoimmune disorders

SOCIAL HISTORY

The patient served in the military and was stationed in Vietnam; he reports Agent Orange exposure. He had a history of alcohol use; he denied use of tobacco, intravenous, and illicit drugs.

PHYSICAL EXAM

Physical exam revealed symmetrically distributed, violaceous, pink and depigmented, scaly, flat-topped papules on periorbital skin, ears, preauricular region, perinasal region, and vermillion lips. Lesions on the lips also had a white reticulated appearance. Superficial ulcerations were seen on the bilateral buccal mucosa. Violaceous, flat-topped, scaly papules were also present on the sternal chest, back, and at a previous tracheostomy site.

HISTOPATHOLOGY

Punch biopsies of the left preauricular cheek and the sternal chest revealed a moderately dense interface, perivascular, and periadnexal lymphohistiocytic inflammatory infiltrate. A Mart-1 immunostain showed a complete absence of melanocytes. A few follicles showed follicular plugging.

LABORATORY RESULTS

The following laboratory tests were within normal limits: Hepatitis B and C, liver transaminases, lipid panel

RADIOLOGY

A computed tomography scan done in April 2010 revealed metastatic lesions in the liver and the lung.

DIAGNOSIS

Inflammatory vitiligo and cutaneous lupus erythematosus overlap in the setting of metastatic melanoma

TREATMENT AND COURSE

Due to an initial clinical suspicious of lichen planus, the patient was started on acitretin 10mg daily, as well as hydrocortisone valerate 0.2% cream twice daily to facial lesions, betamethasone 0.05% ointment twice daily to body lesions, and triamcinolone 0.1% paste twice daily and viscous lidocaine 2% swish and spit three times daily for oral ulcerations. At one month follow-up, the oral ulcerations had improved, and speckled repigmentation and flattening were seen in the facial lesions, as well as relief of pruritus. Lesions on the chest were flattened but still depigmented. Therapy for the facial lesions was switched to tacrolimus 0.1% ointment twice daily. All lesions continued to improve at five month follow-up, and acitretin was discontinued. Due to the patient's unwillingness to pursue systemic therapy in the event of an autoimmune disorder, serologic tests for lupus erythematosus were not performed. The patient succumbed to complications of metastatic melanoma six months after initial clinical evaluation.

DISCUSSION

Vitiligo is a result of the autoimmune destruction of melanocytes. It may be seen primarily or secondary to a malignancy, frequently malignant melanoma. The development of vitiligo in the setting of melanoma is often correlated with a better prognosis, as it is indicative of an immune response to the malignancy. Similarly, other autoimmune conditions can develop subsequent to malignancy due to an upregulated immune response induced by the cancer.

Lesions of inflammatory vitiligo may be erythematous or elevated, with lesions generally presenting at the margin of the more typical depigmented macular lesions. Lymphohistiocytic inflammation is seen on histopathologic examination, generally in a lichenoid pattern. However, the degree and pattern of inflammation seen in our patient's vitiligo lesions was more than normally seen in inflammatory vitiligo, suggesting a concomitant secondary autoimmune process, such as lupus erythematosus. It is possible that the patient's metastatic melanoma triggered both autoinflammatory conditions, or that one condition triggered the other through the Koebner phenomenon. Koebnerization of vitiligo is common, and has also been described in lesions of both systemic and discoid lupus erythematosus.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 5A**

Presented by Ricardo Berrios, MD, Shraddha Desai, and Edward Keuer, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 3 year-old Asian male presented to our clinic for evaluation of dyspigmentation and blistering. Per the mother, the child, at 1-3 months of age, began developing tense blisters at sites of rubbing or scratching. When he started crawling and walking, similar blisters would form on the knees, palms, and soles. At initial evaluation by an outside dermatologist in 2008, several, intact vesicles were noted, and Darier's sign was elicited. At that time, loratidine was started, and the mother was given an epinephrine pen. He continued to experience itching and blistering despite being on both topical and oral steroids, topical antibiotics and oral antihistamines. Presently, he continues to develop new blisters and scarring although the frequency has diminished.

PAST MEDICAL HISTORY

Normal gestation and delivery
Normal development to date

MEDICATION

Hydroxyzine

ALLERGIES

None

FAMILY HISTORY

None pertinent

PHYSICAL EXAM

Hypopigmented macules and thin, confluent, plaques were noted on the face, trunk, and extremities; some were atrophic and annular (left thumb) while others were circinate (extremities) and linear (trunk). No bullae or vesicles were appreciated, but dermatographism was elicited on non-lesional skin. Mild, periorbtial edema was noted.

HISTOPATHOLOGY

A punch biopsy from a representative lesion on the left scapular back revealed an increased number of mast cells in the superficial dermis.

DIAGNOSIS

Bullous mastocytosis

TREATMENT AND COURSE

Upon initial evaluation, the patient was started on cetirizine 2.5 mg daily, hydroxyzine 10 mg nightly, and Cerave cream. At subsequent visit, the mother noted mild but persistent itching and fewer blisters; daily fluticasone 0.005% ointment to pruritic areas was started. As of the most recent follow-up, his level of pruritus has significantly improved but continues to develop new blisters with diminished frequency.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 5B**

Presented by Ricardo Berrios, MD, Edward Keuer, MD, and James Swan, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 7 year-old Hispanic male presented to our clinic with his mother who complained of itchy, dark bumps over the patient's entire body. Per the mother, lesions began to appear shortly after birth, slowly increasing in numbers since then. The lesions are often pruritic and sometimes raised; a few of them have blistered repeatedly producing clear fluid. The number of lesions and the degree of itching are not associated with particular foods, time of year, temperature, or personal care products. Review of systems was notable for joint pains brought on by mild exercise.

PAST MEDICAL HISTORY

Normal gestation and delivery
Normal development to date

MEDICATION

None

ALLERGIES

None

FAMILY HISTORY

Father had a similar, pruritic rash present shortly after birth that cleared following removal of a gastric tumor in Mexico while in his 30's.

PHYSICAL EXAM

On the face, neck, trunk, and extremities, there were numerous, small to medium, discrete, brown macules and papules, some with overlying excoriations and hypopigmented scars. Hyperpigmented patches were noted over the distal, dorsal fingertips as well as larger, confluent ones over the posterior thighs and buttocks. Dermatographism was absent, and Darier's sign was negative.

HISTOPATHOLOGY

A punch biopsy from a representative lesion on the left mid-chest revealed an increased number of mast cells in the superficial dermis.

LABORATORY RESULTS

The following laboratory tests were within normal limits: CMP, CBC with differential, ANA, RF, ESR, CRP, and tryptase.

DIAGNOSIS

Urticaria pigmentosa in the setting of familial mastocytosis.

TREATMENT AND COURSE

After initial evaluation, the patient was started on loratidine and diphenhydramine, but, at subsequent follow-up, continued to experience significant pruritus. He was switched to hydroxyzine at bedtime, and, at last visit, had achieved good relief.

DISCUSSION

Childhood cutaneous mastocytosis (CCM), defined as skin mast cell hyperplasia having onset before puberty, encompasses a wide variety of clinical presentations including mastocytoma, urticaria pigmentosa (UP), diffuse cutaneous mastocytosis, telangiectasia macularis eruptiva perstans (TMEP), and bullous mastocytosis (BM). Fifty-five percent of patients present by the age of 2 years, and up to 10% present later; 25% of cases are congenital. While generally sporadic, familial cases have been reported – some 70 to date.

CCM differs from the adult type (ACM) in several, important ways. First, the frequency of TMEP is much lower than in adults. Secondly, CCM has a tendency to resolve spontaneously before puberty, and, thirdly, cases of CCM are rarely associated with other hematologic disorders and infiltration of other organs.

Both adult and childhood types of mastocytosis have been shown to harbor mutations in the *c-kit* gene, however, distinct mutations been documented between groups. Moreover, children with spontaneous disease are much less likely to have a known mutation in *c-kit* at all. Even in cases of familial mastocytosis, mutations in *c-kit* have proven difficult to find. A rare exception to this is cases of gastrointestinal stromal tumor (GIST) associated with familial mastocytosis, where several activating mutations have been reported.

The *c-kit* gene, located on chromosome 4q12, encodes the protein product KIT, a tyrosine kinase receptor that, when activated, is both mitogenic and anti-apoptotic in mast cells. The ligand for KIT is stem cell factor (SCF), which exists in both membrane-bound and circulating forms. The most well known mutation in *c-kit* is the 816 mutation. Found much more frequently in ACM than CCM, it imparts a constitutive activation of KIT that drives mast cell proliferation and prevents apoptosis.

Once in the skin, mast cells have the potential to induce vesiculation and bullae formation via the release of serine proteases, histamine, and other mediators of vascular leak. While most blisters resolve without scarring, intense mast cell activity can result in tissue destruction severe enough to leave scarring. This frequency of vesiculation diminishes as the child ages, and is found only rarely once they reach 2 years.

While many children with CCM have little to no symptoms, management is targeted largely at treating what symptoms there may be. Oral histamine type 1 receptor antagonists, alone of in combination with H2 receptor antagonists, are very helpful in controlling not only itch but skin whealing, flushing, dizziness, and abdominal complaints. Other effect oral options include the tricyclic antidepressant doxepin and the mast cell stabilizer cromolyn sodium. Psoralen plus UVA (PUVA) therapy has been shown to effectively treat the pruritus and whealing but not other symptoms associated with internal involvement. Short courses of oral steroids are useful, and extended courses of topical steroids under occlusion have been shown to induce remission of symptoms for up to 12 months following therapy. Importantly, patients and their families should be educated in avoidance of known mast cell degranulators – alcohol, anticholinergic agents, aspirin, NSAIDs, heat, friction, narcotics, and polymyxin B sulfate. Interestingly, while administration of general anesthesia is traditionally thought of as potentially dangerous, children with isolated cutaneous disease are at fairly low risk for complications related to their mastocytosis.

We present these two cases of mastocytosis to highlight both the scarring potential of this entity and its inheritability.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 6**

Presented by Krisanne Sisto, MD, and Laura Winterfield, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

On day one of life, a full term male infant was transferred to the neonatal intensive care unit at Loyola University Center Medical Center for evaluation and treatment of a large congenital mass on the right thigh. The infant was born by vaginal delivery to a healthy 32 year-old primigravid with good prenatal care. No anomalies were noted on routine 20 week ultrasound. Apgar scores were 9/9/9 at one, five and ten minutes.

PAST MEDICAL HISTORY

None

MEDICATION

None

ALLERGIES

NKDA

FAMILY HISTORY

None

SOCIAL HISTORY

No known maternal use of alcohol, tobacco or illicit drugs. No known exposure to teratogens.

PHYSICAL EXAM

Birth Weight: 2.897 kg (6 lb 6 oz)
Temp 98.1F, HR 160, RR 56, BP 57/37, SaO2 97% on room air
The patient was a well-developed newborn male. On the right thigh there was a 9x16 cm well defined red-purple vascular mass with central ulceration. The mass had a palpable thrill and audible bruit. Cardiac examination by the primary team revealed a iii/vi systolic murmur best heard at the left sternal border.

LABORATORY RESULTS

The following laboratory tests were within normal limits:
WBC, electrolytes

The following laboratory tests were abnormal:
Hemoglobin 13.7 gm/dl (ref: 15-24 gm/dl)
Platelets 123 k/ul (ref: 150-400 k/ul)
PTT 60.1 sec (ref: 21.4-31.5 sec)
PT 14.7 sec (ref: 9.8-11.9 sec)
D-dimer 4600 ng/ml (ref: <581 ng/ml)
Fibrinogen 130 mg% (ref: 181-456 mg%)

RADIOLOGY

Chest x-ray: Cardiomegaly with mild pulmonary vascular congestion.
Echocardiogram: Mitral and tricuspid regurgitation with reasonable cardiac function.

Abdominal ultrasound: Unremarkable abdomen. The right pelvis demonstrated a dilated right iliac artery and vein which extend into a dilated right femoral artery and vein. These then extend into a high flow vascular mass of the right thigh.
Magnetic resonance imaging right leg, with and without contrast: Large subcutaneous heterogeneous mass of the anterior and medial thigh. Low T1 and high T2 signal compared to muscle. Multiple dilated and tortuous vessels within the mass which connect proximally with two dilated vessels likely representing the femoral artery and vein. No abnormalities of muscle or bone.

DIAGNOSIS
Rapidly involuting congenital hemangioma

TREATMENT AND COURSE
The patient was closely monitored in the neonatal intensive care unit for nine days. He was treated with minimal supportive care for mild high output cardiac failure and remained stable throughout his hospitalization. His initial tachycardia resolved and repeat echocardiogram prior to discharge showed stable and reasonable cardiac function. His hemangioma was dressed with white petroleum and a loose, non-adhesive dressing. The lesion was noted to be lighter in color at discharge as compared to initial presentation. Since leaving the hospital, the infant has thrived, and his hemangioma has continued to show signs of involution. At his three and a half month follow up visit, the hemangioma was soft and nearly flesh colored, and the central ulceration had completely healed.

DISCUSSION
Hemangiomas are common vascular tumors of infancy. The majority of these lesions are common infantile hemangiomas, with a reported incidence of 4.3 to 10%. Common infantile hemangiomas develop during the post-natal period, undergo a rapid proliferative phase and then slowly regress during the first few years of life. Congenital hemangiomas are a much rarer type of vascular tumor, with a reported incidence of 0.3%. They develop in utero, and are fully formed at the time of birth. Two forms of congenital hemangioma are recognized: the rapidly involuting congenital hemangioma (RICH) and the non-involuting congenital hemangioma (NICH). The two are clinically indistinguishable at the time of birth, but follow vastly different clinical courses. RICH begin to involute almost immediately, and the majority have undergone complete involution by 12-18 months of age. NICH, the rarer of the two, never involute. They grow in proportion with the child and eventually require excision.

Clinically, congenital hemangiomas present as purplish vascular tumors, often with a pale halo. Central ulceration may be present. They are typically solitary lesions that occur on either the head or limbs. There is an equal gender distribution. Complications of congenital hemangiomas include bleeding, high output cardiac failure and a mild thrombocytopenia secondary to localized intravascular coagulation. Profound thrombocytopenia, as seen in Kasabach-Merritt phenomenon, is not normally encountered.

The diagnosis of congenital hemangioma is based on clinical presentation, imaging, and if indicated, biopsy. On ultrasound, congenital hemangiomas demonstrate fast flow, are typically heterogeneous, and may have areas of calcification. MRI reveals a vascular tumor with flow voids. T2-weighted images are hyperintense (increased water content) and T1 images are isointense (soft tissue). Histology demonstrates small capillary lobules with plump endothelial cells surrounded by abundant fibrous collagen. Congenital hemangiomas are glucose transporter-1 protein (GLUT-1) and Lewis Y antigen negative but insulin like growth factor 2 (IGF-2) and vascular endothelial growth factor (VEGF) positive.

The most relevant differential diagnoses in this case are congenital fibrosarcoma and arteriovascular malformation (AVM). Congenital fibrosarcoma presents as a purplish tumor, which may have a vascular appearance, ulceration, or hemorrhage, but is firmer than a hemangioma. Imaging reveals a solid mass. Biopsy shows sheets of densely packed spindle shaped cells with abundant mitosis and many vessels. Arteriovascular malformations present as warm vascular plaques or masses, often with a palpable thrill or throbbing. As in congenital hemangioma, AVMs demonstrate high flow on ultrasound, however a connection between the arterial and venous systems can usually be visualized. Biopsy reveals irregularly thickened vessels and communication between vessels with different elastic properties.

Once the diagnosis of RICH has been established, observation and conservative management are the standard of care for uncomplicated cases.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 7**

Presented by Anjali Shah, MD, and Anthony Peterson, MD
Division of Dermatology, Loyola University Medical Center

UNKNOWN

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 8**

Presented by Krisanne Sisto, MD, and Edward Keuer, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 16 year-old male with moderate inflammatory acne presented to our dermatology department with a complaint of facial swelling of one year's duration. The swelling was persistent throughout the day but was worse upon waking. He had seen several outside specialists, including a dermatologist and otolaryngologist, without elucidation as to the cause of the swelling. Previous work-up had included computed tomography and magnetic resonance imaging which showed soft tissue swelling. At the time of presentation he was taking doxycycline 100 mg BID, which had led to a limited improvement in his acne but had not had any impact on his facial edema.

PAST MEDICAL HISTORY

None

MEDICATION

Doxycycline 100 mg BID

ALLERGIES

NKDA

FAMILY HISTORY

None pertinent

SOCIAL HISTORY

No history of tobacco, alcohol or illicit drug use.

PHYSICAL EXAM

Weight 58 kg.
On exam the patient was noted to have well demarcated soft tissue swelling of the lower forehead, glabella, nasal saddle and lower eyelids. Erythematous papules and pustules were noted on the forehead, cheeks, chin and upper back.

LABORATORY RESULTS

The following laboratory tests were within normal limits:
CBC, LFTs, lipid profile

DIAGNOSIS

Solid facial edema in a patient with moderate inflammatory acne

TREATMENT AND COURSE

Doxycycline was discontinued, and the patient was started on isotretinoin 40 mg daily (0.69 mg/kg/day). Improvement in both his acne and facial edema were noted after two months and no side effects were observed. Isotretinoin was subsequently increased to 30 mg BID (1mg/kg/day) and he completed an additional three months of therapy at this dose. At the conclusion of treatment there was marked improvement of his acne and resolution of his facial edema.

DISCUSSION

Solid facial edema, or Morbihan's disease, is a rare condition most often seen in association with acne vulgaris. Young males are most commonly affected. The clinical presentation is a non-pitting, non-painful edema of the upper face, particularly the forehead, glabella, nasal saddle and eyelids. The edema tends to be most prominent in the morning and improves as the day goes on. A similar swelling of the face may be seen in association with rosacea or Melkersson-Rosenthal syndrome.

The etiology of solid facial edema is not certain but the most widely held hypothesis is that the inflammation associated with acne (or rosacea) causes obstruction of dermal lymphatic channels. Alternatively, it has been theorized that the inflammation leads to loss of blood vessel wall integrity and the subsequent leakage of fluid from the vessels. In chronic cases mast cells may induce fibrosis of the dermis resulting in a permanent induration of the skin, a process akin to the fibrosis seen in chronic lymphedema involving the lower extremities.

Histological examination typically reveals a normal epidermis, interstitial edema and a perivascular and periadnexal lymphohistiocytic infiltrate. An increased number of mast cells and dermal fibrosis have been noted in some biopsy specimens.

Treatment of solid facial edema can be a challenge, and not all cases respond to therapy. Isotretinoin is the most often cited successful therapy, sometimes used in combination with ketotifen (2 mg/day), an H1 antihistamine and mast cell stabilizer. Both low dose isotretinoin (0.2 - 0.5 mg/kg/day) and standard dose (1 mg/kg/day) isotretinoin have been used successfully. The sebostatic as well as the anti-inflammatory properties of isotretinoin likely contribute it its efficacy. Oral corticosteroids have been used with varying success. Oral antibiotics do not appear to be beneficial in most cases.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 9**

Presented by Allison Goddard MD, and David Eilers, MD
Section of Dermatology, Edward J. Hines Veteran's Administration Hospital

HISTORY OF PRESENT ILLNESS

This is a 47 year-old male who presented to our clinic with a diffuse rash for 2 years. He reported a similar rash in 2001 that started on the bilateral inguinal folds and axilla that initially cleared with topical triamcinolone. Nine years later the rash returned in the same location but eventually spread to involve the trunk and all extremities. The scalp, face, palms, soles, and genitals were spared. The patient reported significant associated pruritus. Prior to presentation in our clinic the patient had been treated with topical clobetasol and topical tacrolimus with minimal improvement. The patient noted that lesions on the arms had improved with natural sunlight.

PAST MEDICAL HISTORY

Osteoarthritis of the knees, right shoulder impingement syndrome, sleep apnea, central serous retinopathy

MEDICATION

Ibuprofen prn
Benadryl prn
Vitamins B12, D, C
Hydroxyzine prn
Clobetasol 0.05% ointment
Tacrolimus 0.1% ointment

ALLERGIES

Possible latex/elastic waistband material (TRUE patch testing negative)
Levofloxacin
Meperidine HCL

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Denies tobacco or recreational drugs. Drinks 4-5 alcoholic beverages per week

PHYSICAL EXAM

Over the trunk and extremities were hundreds of 2-3 mm erythematous to violaceous macules and thin papules with areas coalescing into patches and plaques around the waist and hips. No lymphadenopathy was appreciated.

HISTOPATHOLOGY

Sections showed an atypical lymphoid infiltrate present in a band-like pattern in the upper epidermis. Epidermotropism in the form of Pautrier's microabscesses was noted. The atypical lymphocytes were CD4 positive and CD8 negative. CD30 stained rare cells.

Prior biopsies from outside institutions
11/2011: Psoriasiform dermatitis with epidermotropism of lymphocytes and intraepidermal nests of lymphocytes

9/2011: Superficial perivascular lymphocytic inflammation with red blood cell extravasation and mild epidermal spongiosis. The epidermis showed some acanthosis and a focus of lymphocyte exocytosis. The changes seen were consistent with the clinical impression of a benign pigmenting purpura
1/2011: Mild spongiotic dermatitis with chronic inflammatory infiltrate

LABORATORY RESULTS
The following laboratory tests were within normal limits: LDH, peripheral blood flow cytometry, AST, ALT, total bilirubin, alkaline phosphatase, BUN, creatinine, WBC, Hgb, HCT, platelet count

The following laboratory tests were abnormal: None

RADIOLOGY
None

DIAGNOSIS
Cutaneous T-cell lymphoma, pigmented purpuric variant. Stage IB

TREATMENT AND COURSE
Prior to presenting in our clinic the patient had been treated with various topical steroids, topical calcineurin inhibitors to flexures and groin, as well as short courses of oral prednisone. He was also advised avoidance of rubber or latex waistbands in his clothing. Due to the widespread distribution we have stopped topical steroids and started narrowband ultraviolet-B therapy three times per week.

DISCUSSION
Mycosis fungoides (MF) is a rare cutaneous T-cell lymphoma. Clinical presentation is variable with the most common being erythematous scaly patches or plaques in a bathing suit distribution. Other less common presentations include poikilodermatous patches, hypopigmented patches, lymphomatoid papulosis-like lesions, indurated alopecic plaques, erythematous or ulcerating tumor nodules, and pigmented purpura-like patches or plaques. Our patient has mycosis fungoides presenting as diffuse pigmented purpuric eruption.

In 1988 Barnhill and Braverman reported that eruptions closely resembling pigmented purpuric dermatitis (PPD) could be associated with a cutaneous T-cell lymphoma (CTCL). Persistent pigmented purpuric dermatitides (PPPD) are a group of capillaritides of unknown etiology, manifested as localized or generalized pigmented, petechial eruptions and can be seen in both the pediatric and adult population. There are rare reports of a PPPD progressing to MF. The association of PPPD with MF is variable and can also be the presenting sign of MF Even more rare is the concomitant existence of simultaneous MF and PPPD.

Histopathologic differentiation of PPPD from patch or plaque stage MF can be challenging. A number of authors have suggested criteria for differentiating the two entities although to date there is no standardized or universal protocol. Suggested cytoarchitectural features that support the diagnosis of pigmented purpuric MF include: lymphocytes with highly convoluted, medium to large size nuclei clustered in the epidermis and in small sheets in the dermis, a greater degree of epidermotropism of mononuclear cells, a relative paucity of epidermal spongiosis, and absence of significant papillary dermal fibrosis. Unfortunately gene rearrangement studies, especially gamma chain probes and PCR cannot be used to differentiate MF and PPD because both conditions can demonstrate clonality.

Pigmented purpuric lesions are uncommon, but are an established characteristic of MF. In patients with PPPD, long-term clinical and histopathological follow-up is recommended.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 10**

Presented by Anjali Shah, MD, and Anthony Peterson, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 36 year-old male patient presented to the emergency department with a rash on his face, chest, and back. He reported a two-year history of an intermittent pruritic dermatitis on his back. He noted a flare last month while he was traveling to Alabama where the weather was hot and sunny. A few weeks prior to admission, the rash spread to his face and chest. He complained of intense itching, stinging, and burning. The pain on his face was rated 10/10 in severity. He also experienced fevers, chills, malaise, muscle pain and fatigue for three days. He denied oral or genital lesions.

Prior to this admission, the patient had been seen at multiple outside emergency departments and prescribed cefadroxil, clotrimazole, clindamycin, and hydrocodone/acetaminophen. He denied any improvement with this regimen and the rash continued to worsen.

There was no history of this rash as a child; patient reported normal skin until two years prior. No family history of any skin disease.

PAST MEDICAL HISTORY

Alcohol abuse

MEDICATIONS/ALLERGIES

None/NKDA

SOCIAL HISTORY

Tobacco, alcohol abuse

PHYSICAL EXAM

On the back and chest in a seborrheic distribution were numerous erythematous crusted and eroded papules. The face had numerous eroded and crusted papules, and the lateral neck with small vesicles. Examination of the nails revealed few nails with distal V-shaped notches. The oropharynx was clear.

HISTOPATHOLOGY

Shave biopsy of the right upper back revealed suprabasal acantholysis with corp ronds consistent with Darier's disease. Multiple multinucleated giant cells and smaller cells with viral cytopathic changes suspicious for herpes simplex virus were also noted.

LABORATORY RESULTS

The following laboratory tests were within normal limits: HIV, CBC, CMP

The following laboratory tests were abnormal: Direct fluorescent antibody: Positive for herpes simplex virus. Aerobic culture: Positive for a few colonies of MRSA

DIAGNOSIS

Adult-onset Darier's disease complicated by Kaposi's varicelliform eruption

TREATMENT AND COURSE

The patient was admitted and treated with intravenous fluids, oral acyclovir 800mg TID, oral sulfamethoxazole and trimethoprim DS BID, as well as benadryl and hydrocodone/acetominophen as needed for itch and pain, respectively. His symptoms drastically improved over the subsequent two days. His fever resolved, and the pain and pruritus significantly improved. After reviewing the new diagnosis of Darier's disease and triggers, he was discharged home on acyclovir and sulfamethoxazole and trimethoprim with dermatology follow up. Unfortunately, the patient was lost to follow up after discharge and we have not been able to reach him.

DISCUSSION

Darier's disease (Darier-White disease, keratosis follicularis), is a rare-autosomal-dominant genodermatosis. It is caused by mutations in the ATP2a2 gene on chromosome 12q23-24 that encodes for a sarco/endoplasmic reticulum calcium ATPase (SERCA 2). This gene defect leads to an abnormality in desmosome attachment and a breakdown in cell adhesion and disordered keratinization. The histopathology classically shows suprabasilar acantholysis with corp ronds and grains.

Clinically, the disease is characterized by pruritic, warty, flesh-colored to yellow or brown papules most often found in a seborrheic distribution. The nails classically have distal V-shaped notches and can show alternating red and white longitudinal bands. Palmoplantar pits and keratotic papules are frequently seen. Oral involvement occurs in 15-50%, and ranges from a fine granular to a coarse pebbly appearance of the palate. The disease typically presents between the ages of six and 20 years but may develop later in life, as was the case in this patient.

Management of Darier's disease includes avoiding exacerbating factors such as sunlight, heat, perspiration, and mechanical trauma. Topical steroids, oral and/or topical retinoids, and urea of lactic acid containing emollients are important mainstays of treatment.

The most common complication of Darier's disease is superinfection. This is secondary to the defective epidermal barrier, and also postulated to be due to defects in cell-mediated immunity. Oral antibiotics are often used when indicated as patients frequently become infected with *staphylococcus aureus*. Patients are also more susceptible to widespread viral infections such as eczema vaccinatum and, as evidenced by this patient, Kaposi's varicelliform eruption. This complication is most commonly caused by herpes simplex virus and can be life-threatening, thus requiring prompt detection and treatment with antiviral therapy.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 11**

Presented by Loebat Julia Kamalpour, MD, and Anthony Peterson, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

This 60 year-old South Asian male presented to dermatology clinic with a 15-year history of pigmented lesions over the scalp, axillae, trunk, groin and buttocks. He reported that the lesions appeared intermittently, with many of them fading slowly over time and others leaving behind areas of blue, grey or brown pigment. The patient denied any potential medication exposures at the time the lesions initially started. He had recently begun using an over-the-counter skin lightening lotion without much success.

PAST MEDICAL HISTORY

Diabetes
Gastroesophageal reflux disease
Migraine headaches
Hypertension
Hyperlipidemia

MEDICATION

Aspirin 81 mg tablet daily
Atorvastatin 20 mg tablet daily
Glipizide 20 mg tablet daily
Lisinopril 10 mg tablet daily
Metformin 500 mg tablet twice daily
Insulin glargine 15 units subcutaneous injection
Fish Oil
Sumatriptan 50 mg tablet prn migraine

ALLERGIES

No known drug allergies

FAMILY HISTORY

Mother with history of similar skin lesions (unknown diagnosis)

SOCIAL HISTORY

The patient denied tobacco, alcohol or illicit drug use.

PHYSICAL EXAM

Physical exam was notable for a slate-grey patch over the frontal scalp, and violaceous to brown linear patches over the left axilla and left antecubital fossa. Oval hyperpigmented patches were seen over the patient's back and sacrum, with several larger lesions appearing to follow the lines of cleavage. Thin violaceous plaques with slight scale were seen over the bilateral flanks and depressed hyperpigmented papules and plaques were seen over the patients palms. Pterygium of the right first nail was also noted.

HISTOPATHOLOGY

Punch biopsy of the midback showed orthokeratosis, epidermal atrophy, and a lichenoid band of inflammation. Sawtoothing of the rete ridges and squamatization of the basal layer were

seen. Numerous melanin-containing macrophages were seen in the papillary dermis. Punch biopsy from the right palm showed similar histologic features.

DIAGNOSIS

Lichen Planus Pigmentosus

TREATMENT

The patient was treated with tacrolimus ointment 0.1% ointment twice daily to the affected areas.

DISCUSSION

Lichen planus pigmentosus-inversus (LPP-inversus) is a recently described rare variant of lichen planus presenting with asymptomatic to mildly pruritic hyperpigmented macules and patches with tropism for intertriginous skin. Only 20 cases have been described to date, largely in the European literature, with only one case report from the United States. Lesions are primarily seen in flexural areas, especially the axilla and groin. Cutaneous lesions clinically and histopathologically consistent with classic lichen planus may be found in non-intertriginous areas in a small percentage of patients. Larger lesions may appear in a linear configuration following lines of cleavage. Scalp, nail or oral lesions are usually absent.

The first case series of 7 affected patients was from the Czech Republic. Subsequent reported cases have all described patients of Asian descent. In all reported cases, LPP-inversus shows predilection for intertriginous and non-sun exposed sites, as well as lack of nail, scalp or oral involvement. Hepatitis C viral infection is only rarely associated. LPP-inversus follows a variable course with some lesions resolving spontaneously while others are chronic and recalcitrant to therapy with topical steroids.

Histologically, LPP-inversus lesions demonstrate a variably dense lichenoid infiltrate of lymphocytes and histiocytes, epidermal atrophy, and prominent pigmentary incontinence in the superficial dermis. LPP-inversus cannot be distinguished from LPP based on histopathologic findings.

Our patient had features of classic lichen planus, lichen planus pigmentosus and lichen planus pigmentosus-inversus. All of these conditions likely lie along a continuum and strict division between them is therefore difficult and unlikely to affect management. This case is illustrative of the protean manifestations of lichenoid eruptions in pigmented individuals. Unfortunately treatment remains challenging and further studies are needed.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 12**

Presented by Shraddha Desai, MD, Vanessa Lichon, MD, and Anthony Peterson, MD
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 57 year-old African American female presented to our clinic for evaluation of lesions on her tongue present for fourteen months. The patient described the lesions as persistent, white dots that were slowly enlarging and associated with excruciating pain, especially with the consumption of hot or spicy foods and beverages. She had two previous biopsies (one from an outside dermatologist and another from an otolaryngologist), both of which were negative for malignancy but showed inflammation and ulceration. She was using dexamethasone swish and spit four times daily with some improvement over the two weeks prior to presentation. She denied other rashes or lesions elsewhere on the body including the genital area.

PAST MEDICAL HISTORY

Depression, Osteoarthritis

MEDICATION

Aripiprazole
Calcium plus Vitamin D
Escitalopram
Nabumetone
Tramadol
Sertraline

ALLERGIES

No known drug allergies

FAMILY HISTORY

No family history of similar lesions

SOCIAL HISTORY

No alcohol, tobacco, or illicit drug use

REVIEW OF SYSTEMS

Pertinent positives include a 30-40 pound weight loss attributed to pain with eating and fatigue

PHYSICAL EXAM

On the right dorsal tongue, there were two 5mm ulcers with shaggy borders on a brightly erythematous base. On the right ventral tip of the tongue, a similar-appearing, 6mm, cribriform erosion was found. The buccal and gingival mucosa as well as the remaining skin exam was normal.

HISTOPATHOLOGY

Punch biopsy from the tongue revealed an area of erosion with an underlying lichenoid interface dermatitis without parakeratosis or eosinophils.
Direct Immunofluorescence studies revealed diffuse fibrinogen deposition along the dermo-epidermal junction with focal IgG and C3, but no IgM or IgA, kappa or lambda.

LABORATORY RESULTS
The following laboratory tests were within normal limits:
CBC with differential, CMP, HIV, RPR, Hepatitis panel

DIAGNOSIS
Erosive oral lichen planus

TREATMENT AND COURSE
The patient was initially started on a trial of metronidazole 500mg orally twice daily in addition to the dexamethasone swish and spit four times daily while her previous slides were reviewed. The patient did well on this regimen, but ultimately had a recurrence of pain. As a result, a repeat punch biopsy was performed and sent for Hematoxylin and Eosin staining as well as for direct immunofluorescence. Her biopsy and immunofluorescence results were consistent with erosive oral lichen planus. After a detailed discussion and baseline laboratory and vital signs, the patient was started on sirolimus 2mg by mouth daily. The patient completed a three-month course with monthly laboratory and vitals monitoring and had complete resolution of pain quickly after initiation of treatment. However, healing of the ulcers was delayed by a few months. She did note decreased tongue flexibility (unable to roll her "r's") during treatment, but this resolved. The patient continued to do well and remained clear for up to twelve months after completion of therapy.

DISCUSSION
Lichen planus is a T-cell mediated, chronic, inflammatory, mucocutaneous condition most often characterized by a papular skin eruption and is associated with a higher prevalence of hepatitis C infection than the general population. Oral lesions occur in 50 to 70% of the patients with lichen planus and may be exclusive in 20 to 30%. Oral lichen planus may present as reticular, atrophic, papular, erosive, bullous and erythematous forms and is characterized by its chronic nature, persistence, and resistance to therapy.

Erosive lichen planus consists of bright red, well-demarcated erosions often found on the gingival and buccal mucosa, but also involves the tongue. Pain is usually intense with a profound effect on the patient's quality of life. There is also an increased risk for the development of squamous cell carcinoma in these lesions.

First line therapy consists of potent topical corticosteroids (oral suspensions, ointment or orabase paste), but due to resistance with erosive lesions, steroid-sparing agents, such as topical calcineurin inhibitors (tacrolimus and pimecrolimus) may be necessary. In severe or recalcitrant cases, immunosuppressive therapies such as cyclosporine, methotrexate, azathioprine, and mycophenolate mofetil have been reported.

Sirolimus (rapamycin, Rapamune®) is a macrolide that was FDA-approved in 1999 for the prevention of renal transplant rejection. It works by binding and inhibiting the mTOR complex with subsequent inhibition of a response to interleukin-2 (IL-2) and prevention of T and B cell activation. Blocking this pathway directly impedes tumor cell proliferation. It can also restrain vascular endothelial growth factor (VEGF)–mediated angiogenesis in established tumors. This antiproliferative effect has also been used in conjunction with coronary stents to prevent restenosis after angioplasty. Current research is focused on its use as an anti-cancer agent, especially in Kaposi's sarcoma.

Side effects include increased risk of infections, hypertension, hyperlipidemia, renal toxicity, diabetic-like symptoms, potential liver toxicity (due to metabolism by the cytochrome p450 pathway), and lung toxicity (more so in lung transplant patients). Because of this, close

monitoring of CBC, CMP, lipid profile, and blood pressure is required during the treatment course.

Given the immunosuppressive and antitumor effects of sirolimus, the therapeutic effects were investigated for chronic erosive oral lichen planus (CEOLP) in a study by Soria et al. Seven women applied topical sirolimus (rapamycin 1mg/ml) twice daily for three months to both oral and genital lesions. Four women had complete remission and two had partial remission (surface of erosion decreased by more than 50%), while one stopped treatment due to local discomfort. All women had tingling and burning after application of the medication.

Due to the extent and duration of our patient's lesions, morbidity, and subsequent risk of oral squamous cell carcinoma, a trial of oral sirolimus was performed. The patient successfully completed a three-month course of sirolimus 2mg by mouth daily with complete and persistent resolution of her lesions at 12 months and minimal side effects.

To our knowledge, treatment with oral sirolimus has not yet been reported for erosive lichen planus. We present this case as a novel treatment for this condition.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 13**

Presented by Vanessa Lichon, MD, Krisanne Sisto, MD, Alexander Means, MD, Diana Monaghan PA-C, Paul O'Keefe, MD and Rebecca Tung, MD
Divisions of Dermatology and Infectious Disease, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 48 year-old Caucasian male presented to our clinic complaining of tender scabs on the side of his head. He stated he was recently incarcerated for 40 days prior to his appointment. Over the last few weeks, he had noticed the growths on his scalp which were somewhat pruritic and tender. He mentioned that there was a cat at home with scabs, but he described minimal contact with the animal. Otherwise he was feeling well and had no systemic complaints. He denied fevers, chills, sweats, weight loss. There were no other cutaneous concerns

PAST MEDICAL HISTORY

Epilepsy

MEDICATION

Acetaminophen
Divalproex sodium

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

The patient was recently incarcerated for 40 days.

PHYSICAL EXAM

Right parietal scalp demonstrated thick, crusted yellow to brown plaques.

HISTOPATHOLOGY

Punch biopsy from the right parietal scalp demonstrated mild epidermal acanthosis, focal parakeratosis, superficial, deep perivascular, and interstitial lymphohistiocytic inflammation. Periodic acid Schiff (PAS) was negative for fungal organisms.

LABORATORY RESULTS

Fungal culture grew *Rhodotorula*. HIV 1 and 2 antibodies were negative.

DIAGNOSIS

Cutaneous *Rhodotorula* treated with photodynamic therapy (PDT)

TREATMENT AND COURSE

After cultures grew *Rhodotorula*, the patient was diagnosed with a cutaneous fungal infection and initially prescribed itraconazole; however, he was subsequently started on fluconazole with twice daily dilute vinegar soaks due to insurance issues. After a month without improvement, he was referred to infectious disease for further evaluation and management. Flucytosine was recommended but not covered by his insurance. As an alternative, he was treated with courses of oral itraconazole and voriconazole in conjunction with ketoconazole

2% shampoo and 6% salicylic acid over the course of several months still without clinical improvement.

A repeat biopsy was performed two and a half months after presentation with similar findings on hematoxylin and eosin and no evidence of fungal organisms on PAS or Grocott's methenamine silver stain despite examination of deeper levels. Given the recalcitrant nature of the patient's illness and the prohibitive expense of alternative antifungal medications, we devised an in-office treatment plan which incorporated the use of a superficial chemical peel and a modified PDT session.

Prior to PDT, the patient's head was shaved and all crusted areas were treated with 30% salicylic acid and manually debrided. Topical 5-aminolevulinic acid (ALA) 20% was applied to the entire scalp and incubated under occlusion with plastic wrap for one hour. The whole scalp was then exposed to BLU-U® for fifteen minutes. Focal hyperkeratotic areas were additionally illuminated with the 595-nm pulsed dye laser (VBeam®, Candela Corporation, Wayland, MA at settings of 10-ms pulse duration, 7-mm spot size, 7.00 J/cm^2, and dynamic cooling device of 30/20). Following the procedure, the patient was instructed to continue taking voriconazole for an additional thirty days as well as to continue cleansing with topical 2% ketoconazole shampoo and application of 6% salicylic acid gel. Complete resolution of the cutaneous fungal infection was appreciated at the patient's one month and three month follow-up appointments. He reported no complications after treatment.

DISCUSSION

Rhodotorula is a basidiomycetous yeast like *Cryptococcus*. It has been isolated from common environmental sources such as soil, water, and air and is also capable of colonizing human respiratory and gastrointestinal tracts. In the largest case series of *Rhodotorula* reported in the literature, Tuon and Costa report that 87% of *Rhodotorula* infections were shown to be associated with underlying immunosuppression or malignancy, with the use of central venous catheters being the most important risk factor for disease. Fungemia was the most common manifestation, followed by eye infections, catheter-associated peritonitis, and meningitis. Amphotericin is considered the treatment of choice as susceptibility to triazoles is variable and resistance to echinocandins has been reported, but flucytosine has also been shown to be efficacious in vitro.

We report the first use of modified PDT, an effective and minimally invasive treatment modality that has previously been employed with success in treating actinic keratoses, non-melanoma skin cancers, acne, photo-damaged skin, and some skin infections—including cutaneous mycoses due to *Candida*, *Malassezia,* and *Trichophyton*—against recalcitrant *Rhodotorula.* ALA-based PDT involves application of the solution to the skin, followed by an incubation period to allow drug penetration into target cells. In fungi, this process is thought to be mediated via a membrane transporter that allows for internalization of the prodrug through facilitated diffusion, with intracellular metabolism to protoporphyrinogen IX (PPIX), a photosensitizer. The area is then exposed to a light source (either laser or non-coherent) causing activation of PPIX and generation of reactive oxygen species and other free radicals, which induce local cell death through damage to the plasma membrane, mitochondria, and cellular DNA.

While the application of the concentrated salicylic acid peel prior to PDT may have only served to promote keratinolysis and penetration of the ALA, it may have also directly contributed to the resolution of the patient's fungal infection via pharmacologic interactions with *Rhodotorula*. Prostaglandin production from exogenous arachidonic acid has been demonstrated to be important for fungal metabolism and viability in pathogenic *Cryptococcus*

species. Studies have also shown that this prostaglandin cascade can be inhibited by topical salicylic acid. *Rhodotorula* is capable of producing arachidonic acid endogenously. It is possible that the effect of the concentrated salicylic acid peel may have been adjunctive, with resulting antifungal activity similar to the mechanism observed in *Cryptococcus*. We did not find any documented use of salicylic acid prior to PDT in the literature, but we hypothesize that its utilization as a (chemical exfoliant), like reported cases of microdermabrasion (physical exfoliation) prior to PDT, does enhance the penetration of ALA by interrupting the barrier function of the stratum corneum, therefore increasing the efficacy of PDT.

Our success in treating this patient's cutaneous fungal infection with a unique combination of salicylic acid, PDT, and pulsed dye laser provides a well-tolerated treatment option for recalcitrant cases.

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Presented by Anita Shetty, MD, Anthony Peterson, MD, and James Swan, MD
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HISTORY OF PRESENT ILLNESS

This 69 year-old Caucasian male has a greater than 50-year history of psoriasis and psoriatic arthritis and often experiences pruritus in his lesions. Previous treatments include methotrexate (1980-2006, stopped due to liver transaminitis), etanercept (2002-2005, stopped as disease was no longer responsive to medication), adalimumab (6 months in 2005, stopped due to development of dyspnea with exertion), cyclosporine (9/2009-4/2010, stopped due to liver transaminitis), acitretin (9/2009-5/2010, stopped due to liver transaminitis). He was referred by dermatology to liver clinic for transaminitis and was diagnosed with cirrhosis in 7/2011; cirrhosis was thought to be secondary to alcohol and non-alcoholic steatohepatitis. He has also been treated with narrow-band UVB (multiple courses, most recently 4/2011-8/2011), as well as various topical steroids, topical vitamin D analogs, and oral antihistamines. Clinically, it is unclear whether treatment with adalimumab was responsible for the patient's dyspnea, as the patient had a 80-lb weight gain in the year previous to starting the medication and had known left ventricular hypertrophy. The dyspnea did improve after stopping adalimumab. The patient's hematologist has recommended against ustekinumab due to his anemia. The patient was cautiously restarted on etanercept in 11/2011 and has had improvement in his cutaneous lesions, but is now experiencing mild dyspnea.

PAST MEDICAL HISTORY

Liver cirrhosis, hypertension, asthma, left ventricular hypertrophy, iron deficiency anemia, peripheral neuropathy, obesity, osteoarthritis, nonmelanoma skin cancer, metabolic syndrome, benign prostatic hyperplasia, depression

MEDICATION

Amitriptyline
Aspirin
Etanercept
Citalopram
Clonazepam
Diltiazem
Ferrous sulfate
Folic acid
Furosemide
Gabapentin
Glucosamine
Hydromorphone
Multivitamin
Omeprazole
Sildosin
Spironolactone
Valsartan

ALLERGIES

Bee venom

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

The patient has a history of alcohol use (stopped in 2010). He denies tobacco or illicit drug use.

PHYSICAL EXAM

Physical exam reveals extensive, well-defined, erythematous plaques with silvery scale on the chest, abdomen, lower back, buttocks, and bilateral upper and lower extremities involving approximately 30% of the patient's body surface area.

LABORATORY RESULTS

The following laboratory tests were within normal limits: Hepatitis A, B, C panel, HIV, white blood count, platelet count, complete metabolic panel (with exceptions noted below)

The following laboratory tests were abnormal: Hgb (11.1), HCT (33.1), RDW (23.8), ALT (229), AST (149), glucose (185)

DIAGNOSIS

Psoriasis, plaque-type

DISCUSSION POINTS

1. What is the best treatment option for psoriasis in patients with:
    a. Known liver cirrhosis or steatohepatitis?
    b. Metabolic syndrome?
2. Can TNF-alpha inhibitors be considered for use in patients at high risk for cardiac conditions or mild heart failure?
3. Should ustekinumab be avoided in this patient due to his anemia?