Chicago Dermatological Society

May 2011
Monthly Educational Conference
and Awards Luncheon

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, May 11, 2011
Stephens Convention Center - Rosemont

Conference Host:
Department of Dermatology
Rush University Medical Center
Chicago, Illinois

Program

Conference Location

Stephens Convention Center – Level 2 of the Conference Center
5555 N. River Road, Rosemont

Registration – beginning at 8:00 a.m.
Foyer outside Ballroom 26, Level 2

Program Events

8:00 a.m.	Registration Opens for All Attendees *Outside Ballroom 26, Level 2 of the Conference Center*
9:00 a.m. - 10:00 a.m.	**Resident Lecture** – "Learning to Clinically Control the Principal Pivot Point of the Immune System" RICHARD L. EDELSON, MD *Level 2 - Ballroom 27*
9:45 a.m. - 11:00 a.m.	**Clinical Rounds** Slide & Poster Viewing; Refreshments *Level 2 - Ballroom 26*
11:00 a.m. - 12:00 p.m.	**General Session** - *MALKINSON LECTURE* "Cellular Eavesdropping to Outflank Cutaneous T Cell Lymphoma (CTCL)" RICHARD L. EDELSON, MD *Level 2 - Ballroom 27*
12:15 p.m. - 1:00 p.m.	Awards Luncheon *Level 2 - Ballroom 26*
1:00 p.m. - 2:30 p.m.	**General Session** President's Presentation and Case Discussions *Level 2 - Ballroom 27*
2:30 p.m.	**Meeting adjourns**

Mark the Date!

Next CDS monthly meeting – Wednesday, June 8, 2011 at Loyola University Medical Center
Featuring Harold Rabinovitz, MD

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

Guest Speaker

RICHARD EDELSON, MD

Chairman, Department of Dermatology
Yale School of Medicine,
New Haven, CT

Delivering the Frederick Malkinson Lecture

Richard L. Edelson, MD is the chairman of the Department of Dermatology and is the Aaron B. and Marguerite Lerner Professor of Dermatology at the Yale School of Medicine. He holds a BA from Hamilton College in New York and earned his MD in 1970 at the Yale School of Medicine. Dr. Edelson was a dermatology resident at Massachusetts General Hospital, Boston, from 1971-72, and he was senior resident at Columbia-Presbyterian Hospital from 1975-1976. He also completed a fellowship in immunology at the National Institute of Health. Before coming to Yale in 1986, he was head of the Immunobiology Group in Columbia University's Comprehensive Cancer Center and associate director of that institution's General Clinical Research Center. While on the Yale faculty, he has served continuously as chairman of the department of dermatology and, at various times, as director of the cancer center, deputy dean for clinical affairs, director of the Cancer Center's Lymphoma Research Program, and a member of both the Yale-New Haven Hospital Board of Trustees and the Yale Medical Group Board of Governors. He is a member of the American Society for Clinical Investigation and the Association of American Physicians, and an honorary member of several international medical associations.

CME Financial Disclosure: Dr. Edelson has no significant financial relationships to disclose.

Continuing Education Credit

Chicago Dermatological Society

"Chicago Dermatological Society Monthly Conference"

May 11, 2011 *Rosemont, 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:
http://www.yourcesource.com/eval/?act=518!05112011

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.

After participating in this program, physicians should be able to:

- Describe the dependency of CTCL clonal expansion on epidermal Langerhans cells.
- Discuss the natural evolution of CTCL to an invasive and dangerous malignancy.
- Explain how intelligent interruption of CTCL cell-Langerhans Cell communication can prevent the natural progression of the cancer.

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 ***5.5 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 5.5 hours.

DISCLOSURE STATEMENTS

All 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, and also discloses discussions of off-label uses of drugs and devices before their presentation(s).**

TABLE OF CONTENTS

CHICAGO DERMATOLOGIC SOCIETY **CASE #1**

Presented by Mark Romanelli, MD, Warren Piette, MD, and Michael Tharp, MD
Department of Dermatology, Rush University Medical Center

HISTORY OF PRESENT ILLNESS

The patient is a 61 year old white male with an eight year history of pruritic patches, papules, and plaques distributed over his face, head, neck, bilateral upper extremities, and trunk. The first lesion appeared on the patient's waist and subsequently the back, axillae, and abdomen developed papules. In 2003 another physician diagnosed him with urticaria. Subsequently, the patient self-treated with short courses of prednisone, antihistamines, and over the counter moisturizers with little relief. His main concern was intractable pruritus interfering with daily activities as well as sleep. The patient presented to our clinic in January of 2006.

PAST MEDICAL HISTORY

Myocardial infarction

MEDICATIONS

None

ALLERGIES

No known drug allergies

FAMILY HISTORY

Stroke, Coronary Artery Disease, Hypertension: Father
Diabetes: Mother

PHYSICAL EXAM

Scalp, neck, axillae, thighs, legs, arms, and forearms with isolated pink scaly indurated plaques varying from 1-4 cm with intermixed erythematous papules. Approximately 5% of total body surface area involvement. Total mucocutaneous exam showing benign nevi pattern. No neck, axillary, or groin lymphadenopathy. No hepatosplenomegaly.

REVIEW OF SYSTEMS

Negative (The patient denied weakness, fatigue, weight loss, fevers, chills, night sweats, difficulty breathing, chronic cough, abdominal pain, nausea, vomiting, diarrhea, constipation, chest pain, palpitations, headache, paresthesias, joint pain or swelling, and bone pain.)

HISTOPATHOLOGY

Lichenoid infiltrate consisting of atypical lymphocytes and lymphocyte exocytosis. Large cells with dark hyperchromatic nuclei were visualized in the dermis and epidermis. A CD 3 stain was positive in approximately 90% of the infiltrate. CD 20 and CD30 stains were negative.

LABORATORY RESULTS

None

RADIOLOGY

Chest X ray: No lymphadenopathy, no osseous abnormalities.
CT Chest, Abdomen, & Pelvis: Scattered small retroperitoneal and inguinal lymph nodes not suspicious for lymphadenopathy.

DIAGNOSIS

Cutaneous T Cell Lymphoma: Mycosis Fungoides subtype

TREATMENT AND COURSE

The patient was prescribed Triamcinolone 0.1% ointment and hydroxyzine with minimal change in his condition. PUVA twice per week and topical nitrogen mustard to the head lesions were administered for 2 months with some improvement. At follow up, nodules were detected in the axillae. Bexarotene was added and titrated up to a dose of 525 mg daily with improvement in pruritus and flattening of lesions. Hypertriglyceridemia and hypothyroidism were detected after initiation of this medication, leading to the addition of fenofibrate and levothyroxine. Labs were monitored periodically. The patient's triglyceride level continued to increase despite treatment while on bexarotene, leading to its discontinuation. He was enrolled into a trial of zanolimumab in 2007 and presented at the Chicago Dermatologic Society that same year after a favorable initial response. However, the patient withdrew due to concerns of possible side effects and the development of new lesions. Next, he was enrolled in a Phase II trial of vorinostat at 400 mg daily in addition to PUVA and nitrogen mustard therapy. After 9 months on this regimen, the patient developed flu like symptoms and erythroderma, with a Sézary count of 40%. Vorinostat was held and the patient admitted for management with hydration and prednisone, initially 60 mg daily. Prednisone was tapered to 20 mg daily and Interferon-α. Narrow band UVB, topical steroids, and extracorporeal photopheresis every 2 weeks were initiated. His peripheral WBC count returned to normal with few Sézary cells being detected. However, his skin remained active and flared with attempts to reduce his corticosteroids below 20 mg/day. The patient developed steroid induced diabetes and was started in insulin. He also developed a foot ulcer growing MSSA and was placed on antibiotics. Due to the patient's intolerance of the adverse effects of interferon treatment, it was discontinued. Because his tumor burden appeared to be mostly in the skin, total body electron beam treatment was given. The patient completed 33/35 treatments before developing significant leg and scrotal edema and blisters. Radiation was discontinued. He developed a leg ulcer growing MRSA which was treated and is slowly resolving. Currently, the patient is stable on 20 mg prednisone daily, wound care to his leg ulcer, gabapentin, and narcotics.

DISCUSSION

Cutaneous T cell lymphomas (CTCLs) include various types of non Hodgkin lymphomas that represent T cell lymphocytes that infiltrate the skin. The most common subtype is mycosis fungoides (MF) and its leukemic variant, Sézary Syndrome (SS). In early stages, MF typically is languid, variably progressing over years from patches to plaques on the extremities and buttocks to tumors, erythroderma, and potential involvement of viscera. Skin complications may include exfoliation, fissures, and ulceration. SS involves blood, lymph nodes, and skin and is considered a more aggressive from of CTCL with approximately a 30% 5 year survival.

Diagnosis of MF and SS are based on the identification of highly characteristic abnormal T cells with cerebriform or multiply folded nuclear borders in the blood, or in the dermis and epidermis, sometimes forming collections known as Pautrier microabscesses. The paucity of histologic findings in early disease can be supplemented with immunophenotyping showing loss of the normal antigens of benign T cells such as CD2, CD3, and CD5. A T cell receptor gene rearrangement is not necessary for diagnosis.

Appropriate staging of CTCL is useful for prognostic and therapeutic considerations, with significantly decreased survival at later stages. Typically, death eventuates not from the lymphoma, but from the impaired immunity caused by both the loss of normal T cells, Th1 cytokines as well as the adverse effects of medical therapy.

MF and SS traditionally have been considered components of a single disease spectrum. However, Sézary Syndrome can arise de novo, presenting with erythroderma and lymphadenopathy in the absence of antecedent patches, plaques or tumors. In addition, surface marker analyses of patients with MF compared to SS show distinct molecular profiles. T cells isolated from MF skin demonstrate the consistently high skin homing markers CLA (cutaneous lymphocyte associated antigen), CCR6 (chemokine receptor 6), and CCR10. These markers also are found in a normal skin homing T cell subset known as T effector memory (T_{em}) cells. These cells are long lived in the skin and have the ability to recruit inflammatory cells, producing the chronic and localized lesions of MF. T cells from SS peripheral blood, on the other hand, have variable expression of these markers, but consistently high expression of lymph node homing markers CCR7, L-selectin, and CD27. This marker profile also is observed in a normal lymph node homing subset of T cells known as T central memory (T_{cm}) cells.

Treatment of MF/SS varies according to stage, with earlier stages receiving skin targeted therapy alone and subsequent stages or aggressive disease receiving the addition of biologic agents or chemotherapeutic agents. The potentially curative treatment of allogeneic hematopoietic stem cell transplant is reserved for a highly limited group of patients, namely young and healthy patients with aggressive disease that have not be treated with numerous therapies.

Skin directed treatments for CTCL include topical corticosteroids, topical nitrogen mustard, topical retinoids, phototherapy (UVB for thin plaques, PUVA for thick plaques), and electron beam radiation (local or total body). Biological therapies include Interferon α, retinoids, extracorporeal photopheresis, and alemtuzumab (anti CD-52: Campath). Other monotherapies that may be also be used in combination include methotrexate, denileukin difitox, vorinostat, and chemotherapeutic drugs. We chose to treat this patient most recently with electron beam because it appeared that most of his disease was localized to his skin. While his skin is much improved after radiation, there is still evidence of residual disease.

The differences in cell markers, clinical behavior, and response to treatment of both Mycosis Fungoides and Sézary Syndrome suggest that they may be distinct disease entities rather than clinical variants of the same disease. The implications of such differences impact the appropriate counseling, prognosis, treatment of each disease.

REFERENCES

1. Lansigan, Frederick and F Foss. Current and emerging treatment strategies for cutaneous T-cell lymphoma. Drugs 2010; 70: 273-286.
2. Galper, Shira, BD Smith, and LD Wilson. Diagnosis and management of mycosis fungoides. Oncology 2010; 24: 491-501.
3. Lech-Marand, Ewa, E Robak, and T Robak. Novel systemic drugs for cutaneous T-cell lymphoma. Recent Patents on Anti-Cancer Drug Discovery 2011; 6: 70-93.
4. Campbell, James, RA Clark, R Watanabe, and TS Kupper. Sézary Syndrome and mycosis fungoides arise from distinct T-cell subsets: a biologic rationale for their distinct clinical behaviors. Blood 2010; 116: 767-771.
5. Jiang, Liuyan, CM Yuan, J Hubacheck,, JE Janik, W Wilson, JC Morris, GA Jasper, and M Stetler-Stevenson. Variable CD52 expression in mature T cell and NK cell malignancies: implications for alemtuzumab therapy. British Journal of Haematology 2009; 145: 173-179.

6. Querfeld, Christiane, N Mehta, ST Rosen, J Guitart, A Rademaker, P Gerami, and TM Kuzel. Alemtuzumab for relapsed and refractory cutaneous T-cell lymphoma: a single institution experience from the Robert H. Lurie Comprehensive Cancer Center. Leukemia & Lymphoma 2009; 50: 1969-1976.
7. Pothiawala, Salma, BT Baldwin, BS Cherpelis, MH Lien, NA Fenske. The role of phototherapy in cutaneous T-cell lymphoma. Journal of Drugs in Dermatology 2010; 9: 764-772.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 2**

Presented by Hina Ahmad, MD, Amanda Kleinman, MD, and Michael Tharp, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 58 year old Hispanic female initially presented to the Dermatology clinic with a 6 week history of perianal and perineal ulcerations. She had a previous diagnosis of lichen sclerosus et atrophicus which had been quiescent for the preceding 2 years. Her ulcerations had been slowly growing in size and were associated with burning pain and constant "drainage." She denied any history of sexually transmitted diseases or sexual partners other than her husband, with whom she was last sexually active 10 years ago. She also denied any oral ulcerations, eye symptoms, gastrointestinal problems, cough, fevers, chills, or night sweats. No new topical or oral medications had been started and she denied any recent travel outside of Chicago. She did however mention that she had a habit of "picking." The patient was applying lidocaine cream as well as over the counter Vagisil to the ulcers with minimal relief of her symptoms.

PAST MEDICAL HISTORY

Hyperlipidemia
Osteopenia
Vaginal lichen sclerosus et atrophicus

MEDICATIONS

Alendronate
Simvastatin
Rabeprazole
Calcium
Fish oil

ALLERGIES

Metronidazole
Neomycin
Hydrogen peroxide

FAMILY HISTORY

No history of autoimmune disease or irritable bowel disease.

SOCIAL HISTORY

Smokes ½ -1 pack of cigarettes per day.
The patient reports a lot of distress at home due to her husband, who is an alcohol and drug abuser.

PHYSICAL EXAM

On the labia majora, perineum, and inguinal folds, there were numerous shallow ulcerations, some of which had a linear orientation when present in skin folds. Perianally, there were numerous, large, perfectly round, and shallow ulcerations, extending from the anal verge out onto the buttock skin. All of the ulcers had a clean base with pink to yellow granulation tissue. Surrounding these ulcers, there was intense, ill-defined erythema.
On the distal lower legs there were numerous depressed, round, skin colored scars.
No inguinal lymphadenopathy was present.
No oral or conjunctival lesions were present.

HISTOPATHOLOGY

Throughout the course of the disease, numerous biopsies were performed.
A 4mm punch biopsy of a small ulcerated lesion obtained at initial presentation revealed an epidermal erosion with superficial and deep, dense mixed, perivascular infiltrate with abundant neutrophils and few eosinophils. Periodic Acid-Schiff stain as well as herpes simplex 1 and 2 immunostains were negative.
Numerous repeat biopsies revealed focal areas of epidermal erosion with scant underlying infiltrate and were essentially inconclusive.

LABORATORY RESULTS

Bacterial swab culture: light growth of pan-susceptible *Staphylococcus aureus* and moderate growth of pan-susceptible *Enterococcus*.

Tissue culture: moderate growth of pan-susceptible *Enterococcus faecalis* and rare *Staphylococcus aureus*. No growth of fungal or mycobacterial organisms.

HSV1, HSV2, and VZV PCR results negative.
HIV and RPR negative.
ANA <1:40
Complete blood count, comprehensive metabolic panel, C3/C4 and ESR all within normal limits.

Tissue wet drop preparation: negative for amoeba.
Stool for ova and parasites: negative.

IMAGING STUDIES

Colonoscopy: normal ileum and colon with some internal hemorrhoids. No evidence of inflammatory bowel disease. Rectal mucosa biopsies were also unremarkable.

MRI lumbar spine: diffuse bulging disc at L1/L2 with mild left foraminal narrowing. Mild disc bulging also noted at L2/L3 and L4/L5.

TREATMENT AND COURSE

Because the patient's initial biopsy revealed epidermal erosion, dense neutrophilic infiltrate, and no organisms with special stains, a diagnosis of atypical pyoderma gangrenosum was made. The patient was started on topical clobetasol 0.05% ointment twice daily to the ulcers, and was advised to apply pramoxine/hydrocortisone ointment to the perianal skin for symptom relief. At follow up, the patient reported worsening of her ulcerations with no relief in symptoms. She continued to complain of constant pain and "drainage" from the lesions, which often brought the patient to tears, however was never noted on our physical examination. At this point, she was started on colchicine 0.6mg twice daily, prednisone 20mg daily, as well as gabapentin 300mg nightly, and reported no relief after 3 weeks of continuous therapy. A gastroenterology consult was obtained to rule out underlying inflammatory bowel disease and empiric treatment with valacyclovir was also started. Her gabapentin was changed to pregabalin and ibuprofen was started in attempts to provide more symptom relief. The ulcerations continued to progress despite therapy, therefore her prednisone dose was increased to 40mg and then 60 mg daily. She was also started on dapsone while maintaining therapy with colchicine. On this regimen, the ulcerations stabilized, however she reported no healing after 1 month of therapy. The decision was made to stop her dapsone and colchicine, maintain her prednisone at a dose of 60mg daily, and start cyclosporine at a dose of 3mg/kg/day, which was eventually titrated up to 5mg/kg/day as her prednisone was titrated down. Because cultures at this point were growing *Enterococcus* and *Staphylococcus aureus*, cephalexin 500mg every six hours was prescribed for a total of 2 weeks.

Despite this intense regimen, there was no improvement in the patient's ulcerations. The patient's affect also raised some concerns of underlying depression and anxiety, therefore she was referred to our dermato-psychiatrist for evaluation. Given the patient's home life and destructive relationship with her husband, she was diagnosed with depression, and started on fluoxetine and valproic acid. Despite continued aggressive therapy, no clinical or symptomatic improvement was noted. Repeat biopsies were also unrevealing. Because the patient had no clinical improvement and the initial diagnosis was in question, the decision was made to admit the patient to the Dermatology inpatient service for monitoring and infliximab infusion. Further consultations were obtained from wound care and the pain service. The only additional recommendation was to obtain a colorectal surgery consultation for a possible diverting ileostomy to help promote wound healing of the perianal skin. During the patient's hospital stay, much of the support staff also noted her unusual affect and the odd relationship between her and her husband; however, no one witnessed the patient traumatizing her skin. After discharge, the patient continued to follow up in the Dermatology clinic every two weeks, with no clinical improvement despite an exhaustive treatment regimen, and worsening psychiatric distress. In the interim however, the patient self-discontinued all psychiatric medications and declined further psychiatric follow-up. Meanwhile, she frequently contacted our department to file disability papers on her behalf, using guilt and vague threats to hasten the process. The patient claimed disability was necessary because she was "too sick to sit for more than 15 minutes at a time." She only re-contacted Psychiatry when we informed her that these papers could not be completed until she followed up with her psychiatrist. At her Psychiatry follow up, the patient claimed to be "fine", "doing better", and "thinking about going back to work." When discussing the case with her psychiatrist, it was reported that the patient was pleasant, in no apparent distress, and was noted to sit for the entire 60 minute visit without complaint. This was noted to be in clear discordance with her prior claims which were made during her Dermatology visits. The patient was never confronted about this; however, during repeat discussions with her, she did admit to a history of picking the skin on her legs secondary to stress. Given lack of improvement, biopsies that were non-specific, and the patient's overall affect, a diagnosis of factitious disorder with components of malingering was made. We proceeded to titrate down all of her medications and eventually discontinue them. She was advised to apply topical gentamicin and silvadene to the ulcerated lesions daily, and within two months of discontinuing her oral medications 90% of the ulcerations had re-epithelialized.

DIAGNOSIS

Presumed factitial perianal ulcers

DISCUSSION

Anogenital ulcerations can have a vast number of etiologies, the most common being infectious in origin. These include sexually transmitted infections such as herpes simplex virus, syphilis, and less often chancroid, lymphogranuloma venereum, and granuloma inguinale. Other infectious causes of anogenital ulcers include cytomegalovirus, typical and atypical mycobacterial infections, histoplasmosis, and amebiasis cutis; however, these are almost exclusively seen in immunocompromised patients. Non-infectious etiologies in the differential diagnosis include Behcet's disease, cutaneous Crohn's disease, and rarely atypical pyoderma gangrenosum, ulcerative lichen planus, and autoimmune blistering diseases such as cicatricial pemphigoid and localized linear IgA disease. Lesions may also be iatrogenic as described in numerous case reports of nicorandil induced perianal ulcerations. If an exhaustive workup fails to reveal a diagnosis, trauma and factitial dermatitis must always be a consideration.

Factitial dermatitis, or dermatitis artefacta, is a very difficult diagnosis to make and often becomes a diagnosis of exclusion. Patients rarely admit to self-inflicting their skin lesions; therefore, they frequently undergo extensive and costly workups that are inconclusive.

The incidence and prevalence of dermatitis artefacta are unknown, and estimates often fall within a broad range. One study performed in 1987 estimated that dermatitis artefacta occurred in about 0.3% of dermatology patients, and was found to me more common in females. Patients typically present with a new and acute dermatosis; however, they may also present with an exaggeration of a pre-existing dermatosis. Presenting lesions can range from simple excoriations to more extensive blisters and ulcers. Patients also employ various techniques to create their skin lesions including suction, cutting, and the application of caustic substances or heat. Patients may even go as far as to inject foreign or infectious substances into their skin, including blood or feces. These actions are the ultimate outward manifestations of an underlying psychiatric condition, whether conscious or subconscious on the patient's part. The DSM-IV criteria for diagnosis of factitious disorder, or Munchausen's syndrome, includes the intentional production or feigning of physical or psychological signs or symptoms, having the sick role as being the main driving force for the symptoms, and the lack of external incentives for these behaviors. Factitious disorder should not be confused with malingering which requires an alternative external incentive such as financial gain, or with somatoform disorders in which both unconscious symptom production and motivations are present. Although factitious disorder and malingering are seen as two separate entities, the distinction can sometimes be blurred. Our patient initially presented with classic signs of factitious disorder, with the sick role being the main driving factor for her clinical disease. However, later in her disease course she began to portray features of malingering when she sought out secondary gain by trying to obtain disability income. Quite often, patients will present with components of both disorders. Underlying depression and anxiety can also be an element of these disorders. Patients with factitious disorder typically manifest physical signs when they experience emotional life stressors. It has been shown that the incidence of depression in patients with factitious disorder can be as high as 46%. Given these underlying findings, it is imperative to appropriately diagnose and treat these patients.

Unfortunately, there is a lack of studies in the literature regarding the management of factitious disorder; therefore, the majority of the data is extrapolated from case reports and case series. In a review article written by Eastwood et al, there was no significant difference in patient outcomes when a confrontational versus a non-confrontational approach was used to arrive at a diagnosis. They also found no significant differences between treatment with or without psychotherapy or psychiatric medication. Treatments were often individualized based on presenting symptoms and history of underlying psychiatric conditions. Because treatment may require a multidisciplinary approach, the most important role of the dermatologist is to arrive at the correct diagnosis and help guide patients to the appropriate medical professionals.

REFERENCES

1. Abe M, Sawamura D, Ito S, Nishio H, Yoshida H, Shimizu H. Perianal cytomegalovirus ulcer following herpes simplex virus in a patient with idiopathic thrombocytopenic purpura treated with immunosuppressants. Clin Exp Dermatol. 2005 Sep;30(5):596-8.
2. Akay N, Boyvat A, Heper AO, Soykan I, Arica IE, Bektas M, Ensari A, Cokca F. Behçet's disease-like presentation of bullous pyoderma gangrenosum associated with Crohn's disease. Clin Exp Dermatol. 2006 May;31(3):384-6.
3. Centers for Disease Control and Prevention (2010). Diseases characterized by genital, anal, or perianal ulcers. Retreived from http://www.cdc.gov/std/treatment/2010/genital-ulcers.htm.
4. Eastwood S, Bisson JI. Management of factitious disorders: a systematic review. Psychother Psychosom. 2008;77(4):209-18.

5. Gupta MA, Gupta AK, Haberman HF. The self-inflicted dermatoses: a critical review. Gen Hosp Psychiatry. 1987 Jan;9(1):45-52.
6. LaFrance WC Jr. Somatoform disorders. Semin Neurol. 2009 Jul;29(3):234-46.
7. Meis JF, van Goor H, Verweij PE. Perianal ulcer. Lancet. 1999 May 29;353(9167):1881.
8. Payne CM, McPartlin JF, Hawley PR. Ulcerative perianal lichen planus. Br J Dermatol. 1997 Mar;136(3):479.
9. Shimizu S, Natsuga K, Shinkuma S, Yasui C, Tsuchiya K, Shimizu H. Localized linear IgA/IgG bullous dermatosis. Acta Derm Venereol. 2010 Nov;90(6):621-4.
10. Van Joost T, Faber WR, Manuel HR. Drug-induced anogenital cicatricial pemphigoid. Br J Dermatol. 1980 Jun;102(6):715-8.
11. Verma GK, Sharma NL, Shanker V, Mahajan VK, Kaushik R, Verma S, Jindal N. Amoebiasis cutis: clinical suspicion is the key to early diagnosis.Australas J Dermatol. 2010 Feb;51(1):52-5.
12. Williams C, Tamuno P, Smith AJ, Walker SL, Lyon CC. Perianal ulceration and other cutaneous ulcerations complicating nicorandil therapy. J Am Acad Dermatol. 2007 May;56(5 Suppl):S116-7.
13. Yueh LH, Loo LY, Hoon TS, Hee TH. Persistent perianal ulcers. Tuberculosis cutis orificialis (TCO). Arch Dermatol. 2009 Aug;145(8):931-6.

CHICAGO DERMATOLOGICAL SOCIETY **CASE #3**

Presented by Jason Litak, MD, and Michael D. Tharp, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This is a 44-year-old woman who presented with a six-week history of bilateral leg ulcers. The lesions had begun as crusted erosions with surrounding erythema which rapidly progressed into large ulcerations. The ulcers were exquisitely painful requiring hydromorphone patient-controlled anesthesia and intravenous fentanyl in the operating room during dressing changes. Prior to presentation she had been hospitalized for two weeks and treated with debridement, ciprofloxacin and linezolid without improvement.

PAST MEDICAL HISTORY

Hypertension
Type 2 diabetes mellitus
Ascites
Hypergammaglobulinemia

MEDICATIONS

Insulin

PHYSICAL EXAM

BP: 172/90 mmHg
General: Well-developed, well-nourished woman in no acute distress.
Bilateral legs: Extensive circumferential irregularly-shaped superficial necrotic ulcerations with exquisite tenderness. Minimal surrounding erythema and branching purpura.

Pulse Exam:
Right Femoral 2+, Right Dorsalis Pedis 2+, Right Posterior Tibial Doppler
Left Femoral 2+, Left Dorsalis Pedis Doppler, Left Posterior Tibial Doppler

LABORATORY RESULTS

The following laboratory results were obtained and were normal:
BUN 15 mg/dl, creatinine 0.78 mg/dl, calcium 8.5 mg/dl, ionized calcium 1.05 mmol/l, phosphorus 3.4 mg/dl, white blood count 8 th/ul, INR 1.14, cardiolipin IgG, lupus anticoagulant, protein C, protein S, antinuclear antibody, ANCA titer, cryoglobulins, C3, C4, liver function tests, bone marrow biopsy, CEA, glucagon, homocysteine.

The following laboratory results were obtained and were abnormal:
albumin 2 g/dl (3.5-5.0), hemoglobin 10 th/ul (12-16), glucose 199 mg/dl (60-99), rheumatoid factor 66 (0-22), PTT 34.6 secs (23-33), CA-125 41 (0-31), serum protein electrophoresis/immunofixation: diffuse hypergammaglobulinemia, no paraprotein.

Leg, tissue culture (bacterial, fungal, AFB): moderate growth of *Acinetobacter baumanii*, heavy growth of coagulase-negative *Staphlococcus aureus*.

STUDIES

Ankle-Brachial Index (3 months prior to presentation): Right 0.75, Left 1.36 (normal 0.9-1.3)

MRI and CT, with IR-CT biopsy (abdomen, pelvis): Extensive fat stranding and fibrotic changes throughout the peritoneum representing nonspecific fibrous tissue with inflammatory cells and mild calcification without evidence of malignancy, moderate-advanced splenomegaly, moderate atherosclerotic calcifications throughout the aortoiliac system.

Technetium-99m bone scan, total body: No soft tissue calcification in the lower extremities. There is suggestion of bone marrow expansion.

HISTOPATHOLOGY

Leg, multiple incisional biopsies: Ischemic epidermal necrosis and ulceration with arteriolosclerosis as well as fibrin thrombi and focal calcification.

DIAGNOSIS

Martorell Hypertensive Ischemic Leg Ulcer

TREATMENT AND COURSE

The patient was initially treated with cinacalcet and sodium thiosulfate for presumed calciphylaxis with a moderate improvement in her pain. Supportive measures included aggressive pain control and empiric antibiotics. The ulcers were surgically debrided with subsequent split-thickness skin grafting by the plastic surgery team. At seven-week follow up most of the grafting remained successful, with approximately 100% coverage on the left leg, and 60% coverage on the right leg. The plan is for repeat grafting of the right leg.

DISCUSSION

The Martorell hypertensive ischemic leg ulcer is clinically defined by an extremely painful ulcer with an escharotic necrotic base that occurs over the anterolateral or posterolateral side of the lower legs. Bilateral and symmetric lesions are common. The ulcers may be rapidly progressive and varying episodes of enlargement or satellite lesions may occur. Rest or elevation does not relieve the extreme pain, which is out of proportion to the lesions, and is an important clinical sign of these ulcers.

The Martorell hypertensive ischemic leg ulcer represents the distal pattern of non-uremic calciphylaxis and is one of the four manifestations of ischemic arteriolosclerosis.

Table 1. Four Manifestations of Ischemic Arteriolosclerosis

Disease	Distal	Proximal
ESRD	Calciphylaxis, distal pattern *Synonym:* calcific uremic arteriolopathy *Distal:* legs and forearms, toes and fingers, penis *Mortality:* approximately 10%	Calciphylaxis, proximal pattern *Synonym:* calcific uremic arteriolopathy *Proximal:* trunk, thighs, upper arms *Mortality:* approximately 50%-70%
Non-ESRD	Martorell HYTILU *Synonym:* angiodermite nécrotique *Distal:* laterodorsal leg or Achilles tendon *Mortality:* approximately 10%	Nonuremic calciphylaxis *Synonym:* calciphylaxis in normal renal and PTH function or eutrophication in morbid obesity *Proximal:* trunk, thighs, upper arms *Mortality:* approximately 50%-70%

Abbreviations: approx, approximately; ESRD, end-stage renal disease; HYTILU, hypertensive ischemic leg ulcer; PTH, parathyroid hormone.

Hafner, J. et al. Arch Dermatol 2010;146:961-968.

Long-standing arterial hypertension and histologically proven subcutaneous arteriolosclerosis (showing medial calcinosis in 70% of specimens) are mandatory to make this diagnosis. Type I diabetes mellitus is present in approximately 60 percent of cases. These ulcers arise predominantly in women between 50 and 70 years of age.

Hypertensive leg ulcers were first described by Fernandez Martorell in 1945. They were renamed hypertensive ischemic leg ulcers by Hines and Farber in 1946. French dermatologists use the term “necrotic angiodermatitis,” and it accounts for over 1% of all ulcers treated in France. At least 900 cases of these ulcers have been reported in the literature.

Since its first description the characteristic clinical appearance of these ulcers has not been disputed, but a unifying pathogenesis has been a matter of debate. The pathophysiology may be related to inward hypertrophic arteriolar remodeling and luminal narrowing leading to increased vascular resistance despite an often normal ankle-brachial pressure index.

The mainstay of treatment includes surgical debridement with subsequent split-thickness skin grafting, which often requires multiple attempts. Aggressive antihypertensive therapy aimed at reducing arteriolar vasoconstriction may help heal existing lesions and prevent new lesions from forming, but does not appear to be sufficient in the vast majority of patients. Supportive care includes pain management, antibiotics, and vacuum-assisted negative pressure local wound care.

REFERENCES

1. Hafner J, Nobbe S, Partsch H, Läuchli S, Mayer D, Amann-Vesti B, Speich R, Schmid C, Burg G, French LE. Martorell hypertensive ischemic leg ulcer: a model of ischemic subcutaneous arteriolosclerosis. Arch Dermatol. 2010 Sep;146(9):961-8.
2. Vuerstaek JD, Reeder SW, Henquet CJ, Neumann HA. Arteriolosclerotic ulcer of Martorell. J Eur Acad Dermatol Venereol. 2010 Aug;24(8):867-74.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 4**

Presented by Andrea Kassim, MD and Mark D. Hoffman, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

An 85-year-old white woman presented with a four-year history of lesions on the bilateral lower extremities and a two-year history of lesions on the face. Lesions present on the legs were tender and some would ulcerate and bleed.

Prior treatment had consisted of betamethasone and triamcinolone creams, ammonium lactate lotion, 12%, metronidazole cream, and daily dressing changes with weekly debridement by podiatry with no response per the patient and son.

PAST MEDICAL HISTORY

CHF
HTN
CVA
Hyperlipidemia
Glaucoma, cataracts, blepharitis, and macular degeneration.
Degenerative joint disease
Thyroid cancer (type unknown)
Hypothyroidism
Dementia

PHYSICAL EXAMINATION

Irregularly shaped shallow ulcers were present on the bilateral legs (lateral more than medial) extending to near the knees.

Depressed and somewhat waxy pink to yellow plaques were scattered over the thighs, lower legs and scalp, and singly on the chest, upper and lower back.

Annular and arciform waxy plaques with scale were present on the bilateral cheeks, temples, and periorbital areas.

Oral mucosa appears normal.

HISTOPATHOLOGY

A 4-mm punch biopsy of a right medial thigh lesion revealed a palisading granulomatous infiltrate consisting of histiocytes and occasional giant cells along with necrosis of collagen bundles extending from the dermis to the subcutis.

A shave biopsy of a lesion in the right pre-auricular area was significant for a dense granulomatous dermal infiltrate abutting the epidermis with abundant histiocytes and multinucleated histiocytic giant cells including Langhans giant cells in addition to scattered inflammatory cells.

LABORATORY RESULTS AND IMAGING STUDIES

The following laboratory studies were normal or unremarkable:
Complete blood count with differential; complete metabolic panel; angiotensin converting enzyme level; Quantiferon Gold level; serum protein electrophoresis and serum immunofixation electrophoresis; antinuclear antigen, rheumatoid factor, C3 and C4; cryoglobulins and erythrocyte sedimentation rate.

Serum free light chain assay: increases in kappa and lambda chains with normal ratio: kappa 2.56 (0.33-1.94), lambda 3.24 (0.57-2.63), K/L 0.790 (0.260-1.650)

Chest x-ray: moderate cardiomegaly; no adenopathy.

Ankle brachial pressure index: < 0.35 with monophasic waveforms where present.

Tissue cultures for bacteria, fungi and acid-fast bacilli: all negative.

DIAGNOSIS

Necrobiotic xanthogranuloma

TREATMENT AND COURSE

Treatment since presentation has consisted of pentoxifylline 400 mg PO TID and fluocinonide ointment, 0.05% BID. The ulcerative activity on the legs has markedly diminished on this regimen, although the lesions persist.

DISCUSSION

Necrobiotic xanthogranuloma (NXG) is a rare histiocytosis first described by Kossard and Winkelmann in 1980. Although it is a relatively recently discovered entity with distinctive clinical and histological features, reports of atypical necrobiosis lipoidica, atypical multicentric reticulohistiocytosis and disseminated xanthoma prior to Kossard and Winkelmann's original description likely represent misclassified cases of NXG. Fewer than 150 cases of NXG have been reported in the English literature, with equal incidence in men and women and most cases occurring in the sixth decade of life with a range of 17 to 85 years.

The early cutaneous lesions of NXG are characterized by indurated, red to violaceous papules or nodules which enlarge into infiltrative plaques with a yellow or red-orange color. Fully developed plaques often have a xanthomatous quality with overlying telangiectasis, which may progress to central clearing and ulceration followed by atrophy.

The most commonly affected area in NXG is the face, in particular the periorbital region, with periorbital involvement reported in approximately 85% of cases of NXG. In addition to the face, the trunk and extremities are also common areas of predilection.

Extracutaneous associations of NXG classically consist of a monoclonal gammopathy, most commonly IgG kappa type, in up to 80% of cases, over 10% have or develop lymphoproliferative malignancies such as multiple myeloma, chronic lymphocytic leukemia, Hodgkin disease and non-Hodgkin lymphoma. There is no direct correlation between the severity of the hematological disease and the presence or extent of skin lesions.

Eye involvement may lead to complications in up to 50% of cases and consist of granulomatous infiltrates of the eye, conjunctivitis, keratitis, scleritis, episcleritis, iritis, uveitis, glaucoma, ptosis, ectropion, cataracts and blindness.

Other systemic manifestations of NXG include inflammatory infiltrates of the oral mucosa, larynx, respiratory tract, heart, skeletal muscle, central and peripheral nervous systems, kidney, liver, spleen, intestines, pelvis and retroperitoneum.
Abnormal laboratory findings may consist of an elevated erythrocyte sedimentation rate, leukopenia, neutropenia, anemia, thrombocytopenia, cryoglobulinemia, macroglobulinemia, amyloidosis, positive antinuclear antibodies, positive rheumatoid factor and inconsistent lipid profile findings.

The etiology of NXG is not known. Hypotheses regarding the underlying etiology include deposition of immunoglobulins and lipid complexes leading to a foreign body giant-cell reaction with monocyte activation and intracellular lipid accumulation.

It is difficult to distinguish histologically between NXG and necrobiosis lipoidica diabeticorum (NLD), as the two entities have multiple histological features in common. Shared histological findings include necrobiosis, the presence of various types of histiocytes (including foreign-body, Touton, Langhans and atypical multinucleated giant cells), lymphoplasmacytic infiltrates, transepidermal elimination of degenerate collagen and cholesterol clefts. The presence and degree of involvement of any of the above histological features may be variable in both conditions. A confident distinction between NLD and NXG often cannot be made based on histology alone and clinical findings must be therefore taken into consideration. Nonetheless, diagnostic classification can be challenging and our patient could, alternatively, represent an unusual presentation of NLD, which may ulcerate and rarely present on the face.

NXG is typified by a chronic, progressive course characterized by disfiguring lesions, usually occurring on the faces, which are often unresponsive to conventional therapy. Most of the morbidity and mortality associated with NXG, however, are attributed to complications of the paraproteinemia. Unfortunately, as the underlying cause of NXG is not fully understood and relatively few studies have been reported in the literature, there is limited data available regarding the efficacy of various therapeutic approaches for NXG. Treatment options include systemic and intralesional corticosteroid therapy, alkylating agents, particularly in the setting of an underlying monoclonal gammopathy, radiation therapy, plasmapharesis and recombinant interferon alpha 2b. Physical interventions include surgical resection followed by skin grafting and carbon dioxide laser resurfacing. However, the post-operative period of NXG is often complicated by lesion recurrence in excess of 40% and may be typified by increased disease activity. NXG therefore remains a therapeutic challenge.

REFERENCES

1. Wood, A., Wagner, M., Abbott, J., Gibson, L., “Necrobiotic Xanthogranuloma,” *Archives of Dermatology*, 2009; 145(3): 279-284.
2. Elner, V., Mintz, R., Demirci, H., Hassan, A., “Local Corticosteroid Treatment of Eyelid and Orbital Xanthogranuloma,”, *Trans Am Ophthalmol Soc*., 2005; 103: 69–74.
3. Criton S, Asokan PU, Pailey S, Kuttappan SS; Remani, Rodriguez FP, “Necrobiotic xanthogranuloma with paraproteinaemia,” *Indian J Dermatol Venereol Leprol.*,1996 Nov-Dec;62(6):383-5.
4. Vieira, V., Del Pozo, J., Martínez, W., Veiga-Barreiro. J., Fonseca, E., “Necrobiotic xanthogranuloma associated with lymphoplasmacytic lymphoma. Palliative treatment with carbon dioxide laser,” *Eur J Dermatol*., 2005;15(3):182-5.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 5**

Presented by Hina Ahmad, MD, Michael Tharp, MD and Arthur Rhodes, MD
Department of Dermatology, RUSH University Medical Center

UNKNOWN 1

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 6**

Presented by Hina Ahmad, MD, and Michael Tharp, MD
Department of Dermatology, RUSH University Medical Center

UNKNOWN 2

CHICAGO DERMATOLOGICAL SOCIETY **CASE #7a**

Presented by Jason Litak, MD, and Mark D. Hoffman, MD, Michael D. Tharp, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This 58-year-old African American woman presented with a four-month history of a painful ulcer on her right leg. The patient had a history of twenty-two similar ulcers on her legs over the past twenty years, with four occurring within the last twelve months. Previous lesions responded to conservative management with minocycline, clobetasol ointment, wound care, and occasional courses of systemic corticosteroids. Treatment for her current ulcer had included two six-day tapers of methylprednisolone (24mg on day 1) and levofloxacin, which led to significant improvement in the pain of the ulcer. The patient also has a long history of hidradenitis suppurativa in the axillary and gluteal areas as well as an excision of a pilonidal cyst.

PAST MEDICAL HISTORY

Hidradenitis suppurativa
Pilonidal cyst (status post excision 1990)
Sjogren's syndrome
Hypothyroid
Anemia

MEDICATIONS

Hydroxychloroquine 200mg BID
Pilocarpine
Levothyroxine
Furosemide
Iron supplement

FAMILY HISTORY

Great aunt (grandmother's sister) with unknown leg ulcer, otherwise negative for pyoderma gangrenosum or hidradenitis

PHYSICAL EXAM

Right superior-lateral leg: 16cm by 11cm cribiform ulcer with beefy red base and scarring at periphery with surrounding hyperpigmentation but no apparent erythema.
Bilateral legs: Several scattered cribiform scars.
Gluteal cleft and axillae: Few non-indurated sinus tracts and scarring.

HISTOPATHOLOGY/MICROBIOLOGY

Pretibial (1999): Perivascular neutrophilic collections with surrounding fibrosis.
Swab culture, right leg (1/11): *Enterococcus spp.*

LABORATORY RESULTS

The following laboratory results were abnormal:
ANA- 1:80, speckled
SSA- greater than 4.5 times index value
Hemoglobin- 9.3 gm/dl, MCV- 63.7 fl

The following laboratory results were normal:
White blood count
Complete metabolic panel
CD2 binding protein 1: no identifiable mutation

RADIOLOGY/PROCEDURES

X-ray, sacro-iliac joints: normal
Colonoscopy (2006): normal

DIAGNOSIS

Pyoderma gangrenosum associated with hidradenitis suppurativa.

TREATMENT AND COURSE

Because of the history of many previous ulcers healing with conservative measures and the current ulcer improving with minimal intervention, together with the patient's comorbid chronic anemia, a conservative approach to treatment was continued. The patient was started on minocycline 100mg BID and clobetasol ointment under occlusion. Intralesional triamcinolone acetonide 20mg/ml, 1ml, was injected to a focal area of the ulcer without effect. Prednisone 10mg BID was started. The lesion showed rapid healing and improvement in pain with complete healing over the next seven weeks. The predisone is being tapered. Because of this patient's remarkable responsiveness to systemic corticosteroids, the plan is to maintain treatment with low dose prednisone to prevent her multiply recurrent pyoderma gangrenosum.

CHICAGO DERMATOLOGICAL SOCIETY **CASE #7b**

Presented by Jason Litak, MD, and Mark D. Hoffman, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This 38-year-old African American woman presented with a one-week history of a lesion on her left leg. The lesion started as a "pustule" and rapidly progressed into a large painful ulcer. The patient reports a history of ten similar leg ulcers over the past twenty years. She also reports a history of scarring acne during her teenage years as well as hidradenitis suppurativa and non-axial joint pain beginning in her third decade of life.

PAST MEDICAL HISTORY

Hidradenitis suppurativa
Undifferentiated spondyloarthropathy
Acne, scarring
Type I diabetes mellitus
Hyperlipidemia
Nonalcoholic steotohepatitis
Osteopenia
Adrenal insufficiency

MEDICATIONS

Prednisone 10mg BID
Gabapentin
Tramadol
Hydrocodone-acetaminophen
Ibuprofen

PREVIOUS MEDICATIONS

Methotrexate, per rheumatology: insufficient effect
Sulfasalazine, per rheumatology: insufficient effect
Leflunomide, per rheumatology: did not tolerate
Infliximab, per rheumatology: caused acute hepatitis

ALLERGIES

Doxycycline
Minocycline

FAMILY HISTORY

None

PHYSICAL EXAM

Left lateral leg: 13cm by 13cm shallow ulceration with fibrinous and necrotic base and cribiform periphery.
Bilateral legs: Many cribiform scars.
Axillae, breasts, inguinal: Diffuse cribiform scarring and few non-indurated sinuses.
Face: Diffuse vermicular scarring.

HISTOPATHOLOGY/MICROBIOLOGY

Left leg (2008): Dermal fibrosis with scattered perifollicular and perivascular mixed cell infiltrate with many neutrophils.
Tissue culture (2008) (bacterial, fungal, AFB): *Enterococcus faecalis*, otherwise negative.
Swab culture (2011): *Staphlococcus aureus*, *Enterococcus spp.*, Group B *Streptococcus*.

LABORATORY RESULTS

The following laboratory results were abnormal:
White blood count: 28 th/ul, Neutrophil count: 22 th/ul
Hemoglobin: 10.4 gm/dl
Alkaline phosphatase: 395 u/l

The following laboratory results were normal:
CD2 binding protein 1: no identifiable mutation
HLA B-27: negative
ANCA titer
Serum protein electrophoresis
Creatinine
AST, ALT

RADIOLOGY/PROCEDURES

MRI pelvis: chronic bilateral sacroiliitis
Colonoscopy with random biopsies: normal

DIAGNOSIS

Pyoderma Gangrenosum associated with a PAPA-like phenotype

TREATMENT AND COURSE

The patient was given a pulse of prednisone 40mg BID for three days and cefazolin which led to significant improvement in pain, erythema, and drainage from the ulcer. The plan was to start etanercept, but the patient was very hesitant because of her history of hepatitis from infliximab. Two months later the patient was admitted to an outside hospital with subsequent debridement and successful skin grafting. She continues to take prednisone 10mg twice daily as attempts at managing her inflammatory arthritis with steroid-sparing medication have been unsuccessful.

DISCUSSION

Pyoderma gangrenosum (PG) is a rare inflammatory skin condition with lesions most commonly appearing on the lower extremities. The classic ulcerative PG lesion presents as a painful nodule or pustule that breaks down and evolves into an enlarging ulcer with a raised, undermined border. Approximately 50% of patients with PG have associated systemic diseases, including inflammatory bowel disease, myeloproliferative disorders, and inflammatory arthritis.

Hidradenitis suppurativa (HS) typically presents in the axillae, perineum, and inframammary sites and is characterized by the presence of multiple abscesses, fibrosis, and sinus tracts. It is associated with acne, Crohn's disease, dissecting cellulitis of the scalp, obesity, pilonidal disease, and smoking.

The appearance of PG and HS lesions in the same patient is seldomly reported. Hsiao *et al.* reported a case series of eleven patients with concomitant HS and PG. Ten of the eleven patients were women, which may reflect the female predominance of HS.

Comorbidities among their cohort included obesity (9 patients), acne (3 patients), pilonidal cyst (3 patients), arthritis (1 patient), anemia (5), colitis (2), type 2 diabetes mellitus (5), acanthosis nigricans (4), coronary artery disease (1), hypertension (3), asthma (2), gastritis (1), depression (5), and anxiety (1). Two distinct groups were identified: patients with PG in sites where the patient had HS lesions (6 patients) and those with PG in sites distinct from HS lesions (5 patients).

Hsiao and colleagues also and gave an eloquent summary of the twenty other cases of concomitant HS and PG described in the literature to date. Among these twenty patients the reported comorbidities included acne (7 cases), arthritis (3 cases), SAPHO syndrome (3 cases), Crohn's disease (1), Behcet's disease (1), iron-deficiency anemia (1), lupus (1), glomerulonephritis (1), psoriasis (1).

The pathogenesis for both PG and HS is incompletely understood. Both diseases are characterized by an intense inflammatory response that is mediated by neutrophils, and both diseases are commonly seen with other inflammatory processes such as inflammatory bowel disease. Additionally, other autoinflammatory conditions, such as Behcet disease, are associated with PG, SAPHO syndrome is associated with HS, and PG and HS are both features of PAPA syndrome.

Given these numerous associations Hsiao and colleagues postulate that PG and HS may both be in part due to dysregulation of the innate immune system, and that these diseases may be considered to be within the spectrum of the cutaneous disorders seen with the recently described autoinflammatory syndromes.

PAPA syndrome (pyogenic arthritis, pyoderma gangrenosum, and acne) was first described in 1997 as an autosomal dominant condition manifesting as the triad of pyogenic sterile arthritis, PG, and acne conglobata. Five families with PAPA syndrome have been reported with a reported penetrance as high as 100%. Point mutations in the CD2 binding protein 1 (CD2BP1) gene have been confirmed in all of these families. There has been one previously reported patient with the triad of pyogenic sterile arthritis, PG, and acne conglobata but without a family history or identifiable mutation in the CD2BP1 gene who has been designated as an example of PAPA syndrome nonetheless; our case 7b bears similarities with this latter patient in manifesting a PAPA-like phenotype.

REFERENCES

1. Hsiao JL, Antaya RJ, Berger T, Maurer T, Shinkai K, Leslie KS. Hidradenitis suppurativa and concomitant pyoderma gangrenosum: a case series and literature review. Arch Dermatol. 2010 Nov;146(11):1265-70.
2. Ah-Weng A, Langtry JA, Velangi S, Evans CD, Douglas WS. Pyoderma gangrenosum associated with hidradenitis suppurativa. Clin Exp Dermatol. 2005;30(6):669-671.
3. Leybishkis B, Fasseas P, Ryan KF, Roy R. Hidradenitis suppurativa and acne conglobata associated with spondyloarthropathy. Am J Med Sci. 2001 Mar;321(3):195-7.
4. Hong JB, Su YN, Chiu HC. Pyogenic arthritis, pyoderma gangrenosum, and acne syndrome (PAPA syndrome): report of a sporadic case without an identifiable mutation in the CD2BP1 gene. J Am Acad Dermatol. 2009 Sep;61(3):533-5.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 8**

Presented by Hina Ahmad, MD, and Lady Dy, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 17 year old White male presented to our Dermatology clinic with a two year history of "hair thinning" and "shorter hairs" limited to certain areas of his scalp. He denied any associated symptoms of pruritus or tenderness, and did not report any noticeable hair loss when washing or combing. He also denied taking any new medications, having any preceding illnesses or hospitalizations, and experiencing any major emotional stressors. The patient had been intermittently applying minoxidil 5% solution for months; also, he had been prescribed finasteride 1 mg by his primary care physician and was taking it for one month prior to presentation, without notable improvement.

PAST MEDICAL HISTORY

Anxiety
Depression

MEDICATIONS

Sertraline
SlowFe
Finasteride 1mg
Minoxidil 5% solution intermittently

ALLERGIES

NKDA

FAMILY HISTORY

Positive for hair loss in maternal uncle.
Lupus and thyroid disease in distant relatives.

SOCIAL HISTORY

Non-contributory

PHYSICAL EXAM

On the frontal, temporal, and crown of the scalp there was a mild to moderate decrease in the total hair density, with some miniaturization of the hair follicles. The parietal and inferior occipital scalp also contained short, wavy hairs which were in sharp contrast with his normal long, fine, and straight hair.

HISTOPATHOLOGY

Two 4mm punch biopsies were obtained from the frontal and occipital scalp, both of which were revealed a non-scarring alopecia with minimal underlying inflammation and a velus to telogen hair ratio of 1:3. These histological findings were consistent with a diagnosis of androgenetic alopecia.

LABORATORY RESULTS

Ferritin 53
Comprehensive metabolic panel, TSH, and complete blood count were all within normal limits.

DIAGNOSIS

Acquired progressive kinking of the hair (APKH) with a background of androgenetic alopecia.

TREATMENT AND COURSE

The patient had a prostate specific antigen level drawn and was told to continue his finasteride 1mg daily along with minoxidil 5% solution twice daily. Given his ferritin level of 53, he was also advised to continue taking one tablet of SlowFe daily. The patient has yet to follow up.

DISCUSSION

Acquired progressive kinking of the hair (APKH) is a condition that has been reported only a handful of times in the literature, with the earliest case being described by Wise and Sulzberger in 1932. Since then, about 25 other cases have been reported, with males being affected slightly more often than females. Typically, the condition is thought to be acquired during adolescence, and as such the pathogenesis is considered to be on a continuum with androgenetic alopecia. This model is also supported by the finding that many patients who present with this condition also have concurrent, or subsequent, androgenetic alopecia. Patients often present with a rapid onset of localized curly, frizzy, and sometimes lusterless hair. These changes are most frequent on the frontal, temporal, or vertex of the scalp. The growth rate of the affected hairs may also be delayed, as was the case with our patient. To the best of our knowledge, APKH with a delayed growth rate has only been reported in 3 other patients within the literature. Our patient also had involvement of the occipital scalp, which has been reported in only 5 other patients.

The diagnosis of APKH is a clinical one, with scalp biopsy not showing any specific findings. Because many of these patients can have concurrent androgenetic alopecia, often the biopsy will be reflective of this. Balsa and Alvarez have suggested a methodological approach to the diagnosis of this condition which involves an overall clinical examination, observation of the hair shaft with the naked eye, microscopic examination of hair shafts, and sometimes scanning electron microscopy. Clinical examination should reveal hair that is dull and wooly in a circumscribed area only. More detailed examination of the hair shaft reveals hair that is tortuous with the first twist appearing 3-4 cm from the scalp. Further, microscopic examination reveals a sharp reduction in hair shaft diameter.

The course and clinical outcome of APKH is variable. Some patients have continued worsening of the hair kinking, others may convert to androgenetic alopecia, while few have shown complete resolution of the disease. In a long term follow up study performed by Tosti et al, 7 patients were followed for a mean of 4.5 years. Eventually, all of these patients evolved into androgenetic alopecia. Unfortunately, given the rarity of the condition, there are no clinical or historical clues that allow us to predict the outcome of the disease. Treatment options are also lacking. Some studies have reviewed the utility of topical minoxidil but have not found it to be effective in halting the progression to androgenetic alopecia.

REFERENCES

1. Balsa RE, Ingratta SM, Alvarez AG. Acquired kinking of the hair: a methodologic approach. J Am Acad Dermatol. 1986 Nov;15(5 Pt 2):1133-6.
2. Tosti A, Piraccini BM, Pazzaglia M, Misciali C. Acquired progressive kinking of the hair: clinical features, pathological study, and follow-up of 7 patients. Arch Dermatol. 1999 Oct;135(10):1223-6.
3. Tran JT, Lucky AW, Subramaniam S. What syndrome is this? Acquired progressive kinking of the hair. Pediatr Dermatol. 2004 May-Jun;21(3):265-8.

4. Wise F, Sulzberger MB. Acquired progressive kinking of the scalp hair accompanied by changes in its pigmentation. Arch Dermatol Syph 1932;25:99–110.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 9**

Presented by Jill C. Anderson, MD, and Warren Piette, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This 72-year-old female presented to our clinic with a three-month history of new forehead, back, and buttock lesions. The lesions were asymptomatic, and she had not used any treatments prior to presentation. Upon review of systems, she noted chronic headaches, but otherwise felt well, denying any fevers, chills, night sweats, weight loss, or fatigue. She reported a history of similar forehead lesions in 2003. She underwent biopsy at that time, which demonstrated "Follicular Large B-cell Lymphoma." Her initial work-up demonstrated a normal complete blood count and normal bone marrow biopsy. She completed four cycles of R-CHOP and had an excellent response with regression of her lesions. Since 2003, she was followed by hematology and had an unremarkable course until the appearance of her new skin lesions.

PAST MEDICAL HISTORY

Follicular Large B-cell Lymphoma
Diabetes Mellitus
Hyperlipidemia
Hypertension
Hypothyroidism
Migraines

Breast Fibroadenoma
Renal Cell Carcinoma s/p Nephrectomy
Cesarean Section
Total Abdominal Hysterectomy
Bilateral Total Knee Replacements
Bilateral Oophorectomy

MEDICATIONS

pioglitazone
atorvastatin
metoprolol
levothyroxine

sumatriptan
diphenhydramine
acetaminophen

ALLERGIES

No known drug allergies.

FAMILY HISTORY

Denies family history of hematologic malignancies.

SOCIAL HISTORY

Retired secretary. Former smoker, 1 pack per day for 30 years (quit in 2002). Denies illicit drug or alcohol use.

PHYSICAL EXAM

Multiple red to violaceous smooth nodules over scalp, forehead, right lower back, and right buttock.
No cervical, supraclavicular, axillary, or inguinal lymphadenopathy noted.
No hepatosplenomegaly noted.

Page 27 is blank to accommodate missing page number

No information or data has been omitted. Case continues on page 28.

HISTOPATHOLOGY
Punch biopsy, right buttock and left forehead (12/23/10): Atypical dermal lymphoid infiltrate arranged in a vaguely nodular pattern. The central nodules contain ill-defined cells. The central area of the nodules consists of intermediate and large B-lymphocytes that are CD20, bcl-6, and CD10 positive, but are bcl-2 negative. The rim of intermediate sized B-lymphocytes are CD20 and bcl-2 positive with rare focal CD10 positivity. CD30 highlights scattered intermediate and large B-cell lymphocytes at the periphery of the follicle. CD4 highlights scattered macrophages and small T-lymphocytes throughout the lesion.

LABORATORY RESULTS
The following were positive or abnormal:
Alkaline phosphatase (12/20/10): 259 (normal 30-125)

The following were negative or within normal limits:
CBC with differential, CMP, Uric Acid, Phosphorus

RADIOLOGY
CT Chest, Abdomen, and Pelvis with IV contrast (January 2011): No pathologic lymphadenopathy noted. No splenomegaly.

DIAGNOSIS
Recurrent Primary Cutaneous Follicle Center Lymphoma

TREATMENT AND COURSE
After diagnosis, patient received a four week course of systemic rituximab, which she tolerated well. She has had regression of her lesions.

DISCUSSION
Cutaneous B-cell lymphomas are generally low-grade malignancies. In the United States, they represent approximately 5% of cutaneous lymphomas. The vast majority of cutaneous lymphomas are T-cell lymphomas. Of all non-Hodgkin's lymphomas, approximately 25% will present at an extranodal site with no systemic involvement. The most common primary extranodal site is the gastrointestinal system, with skin representing the second most common extranodal site. Our patient represents a case of cutaneous B-cell lymphoma with no systemic involvement. The pathogenesis is unknown.

The WHO-EORTC classification of cutaneous B-cell lymphomas include: primary cutaneous marginal zone B-cell lymphoma, primary cutaneous follicle center lymphoma, primary cutaneous diffuse large B-cell lymphoma (including leg type and other), and intravascular large B-cell lymphoma. Primary cutaneous marginal zone B-cell lymphoma and primary cutaneous follicle center lymphoma usually have an indolent course with a 5-year survival of more than 95%. Primary cutaneous diffuse large B-cell lymphoma, leg type has a worse prognosis with a 5-year survival of 55%. In patients with primary cutaneous diffuse large B-cell lymphoma, leg type, increasing numbers of lesions predict an even worse prognosis.

Patients with primary cutaneous B-cell lymphoma usually present with red-brown to violaeous papules, nodules, and plaques. The lesions typically present on the head and neck, but may also be present on the trunk or extremities. Lesions are usually asymptomatic. Rare ulceration may occur. Systemic symptoms (fevers, chills, night sweats, weight loss) are usually not present.

Histopathology aids in the differentiation of the types of primary cutaneous B-cell lymphoma. Immunohistochemistry staining is particularly helpful.

	Primary Cutaneous Follicle Center Lymphoma	Primary Cutaneous Marginal Zone B-Cell Lymphoma	Primary Cutaneous Diffuse Large B-Cell Lymphoma, Leg Type
CD20	+	+	+
CD79a	+	+	+
CD5	-	-	-
CD10	+	-	+/- (usually negative)
Bcl-2	-	+	+
Bcl-6	+	-	+/- (usually positive)

In addition to primary cutaneous B-cell lymphomas, the skin may be a site of secondary involvement for B-cell lymphomas. A complete staging is required for any patient with a biopsy confirmed B-cell lymphoma of the skin to rule out systemic involvement. This work-up includes complete blood examination, flow cytometry of the peripheral blood, and CT (chest, abdomen, and pelvis). Bone marrow biopsy and flow cytometry may also be performed.

Treatment of cutaneous B-cell lymphomas depends on several factors, including type, location, and number of lesions. Local radiotherapy is often the treatment of choice, as it is considered safe and effective. It is most suited for patients with a small number of localized lesions. Radiotherapy is not ideal for patients with numerous, widespread lesions. Excision may also play a role in a patient with one or few small lesions. Intralesional interferon-alpha has also been used with some success. Rituximab, a chimeric, monoclonal anti-CD20 antibody, has been used both intralesionally and systemically for the treatment of cutaneous B-cell lymphoma. Systemic rituximab may be useful in more widespread cases. Rituxamab may also be employed in cases where radiotherapy might be less desirable secondary to potential side effects, including scarring or alopecia. Combination therapy should be limited to cases with diffuse disease that are not responsive to rituximab or those with systemic disease. Relapses are common. The approach to relapses may be similar to the initial approach.

REFERENCES

1. Cerroni L. B-Cell Lymphomas of the Skin. From Dermatology, Bolognia J, Jorizzo J, and Rapini R (eds). Spain, 2007; Mosby: 1855-1865.
2. Good LM, Miller MD, High WA. Intralesional agents in the management of cutaneous malignancy: a review. J Am Acad Dermatol. 2011;64(2):413-422.
3. Morales AV, Advani R, Horwitz, Riaz N, Reddy S, Hoppe, RT, Kim YH. Indolent primary cutaneous B-cell lymphoma: experience using systemic rituximab. J Am Acad Dermatol. 2008;59(6):953-957.
4. Senff NJ, Noordijk EM, Kin YH, Bagot M, Berti E, Cerroni L, Dummer R, Madelein D, Hoppe RT, Pimpinelli N, Rosen ST, Vermeer MH, Whittaker S, Willemze R. European Organization for Research and Treatment of Cancer and International Society for Cutaneous Lymphoma consensus for the management of cutaneous B-cell lymphoma. Bood. 2008;122(5):1600-1609.
5. Willemze R, Jaffe ES, Burg G, Cerroni L, Berti E, Swerdlow SH, Ralfkiaer E, Chimenti S, Diaz-Perez JL, Duncan LM, Grange F, Harris, NL, Kempf W, Kerl H, Kurrier M, Knobler R, Pimpinelli N, Sander C, Santucci M, Sterry W, Vermeer MH, Wechsler J, Whittaker S, Meijer CJLM. WHO-EORTC classification for cutaneous lymphomas. Blood. 2005;105(10):3788-3785.

6. Zackheim H, Vonderheid EC, Ramsay DL, LeBoit PE, Rothfleisch J, Kashani-Sabet M. Relative frequency of various forms of primary cutaneous lymphomas. J Am Acad Dermatol. 2000;43(5):793-796.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 10a**

Presented by Andrea Kassim, MD and Mark D. Hoffman, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 55-year-old white woman with a history of epidermolysis bullosa (EB) of unknown subtype presented with a four-month history of a worsening skin lesion on the posterior neck. The lesion was tender and associated with paresthesias of the neck and head. A complete review of symptoms, including review for any fevers, night sweats or weight loss, was negative.

The patient describes recurrent bullous lesions within skin folds (groin/genital areas, perianal area, axillae, neck, inframammary creases) as well as on the ears; dorsal hands; shins; oral mucosa and esophagus since birth with resultant scarring. Her skin lesions would ordinarily heal within one to two weeks, and none had previously persisted for greater than three months. The patient had been under the care of Dr. Roger Pearson for EB, but had been lost to follow up since 1985. No records could be retrieved.

PAST MEDICAL HISTORY

Ulcerative colitis: quiescent for fifteen years without therapy.

FAMILY HISTORY

The patient has four siblings: two affected brothers, two unaffected sisters. Parents were unaffected.

PHYSICAL EXAM

There were two 3-4 cm exophytic, hyperkeratotic, and verrucoid noduloplaques on the left and right posterior neck, with pink to white cicatricial changes extending circumferentially along the posterior to lateral neck. A single subcentimeter node was palpated within the right cervical chain.
The posterior scalp displayed a large patch of scarring alopecia, with surrounding erythema and psoriasiform scale with crusting. Erythema and scarring were also present within the inframammary folds.
Erosions were noted on the sternal chest and within the inframammary regions. A few collapsed bullae were found on the upper abdomen.
Toenails were hypoplastic.

HISTOPATHOLOGY

Shave biopsy with immunomapping of an induced blister on the upper abdomen disclosed a subepidermal cleft with attenuated and intermittent expression of type VII collagen. There was normal expression of CK, plectin, BP180, α6β4-integrin, and laminin 332.

Two 4-mm punch biopsies of the neck mass revealed invasive squamous cell carcinoma.

LABORATORY RESULTS

The following labs were abnormal: serum iron 21 ug/dl (25-170), % iron saturation 6% (25-66%), vitamin D 22 ng/ml (30-100), zinc 42 mcg/dl (60-130) total carnitine 26 umol/l (34-78), free carnitine 22 umol/l (25-54)

The following labs were normal: ferritin 89 ng/ml (40-260), total iron-binding capacity 332 ug/dl (196-364), folic acid 17.4 ng/ml (5.3-17.1)selenium 170 mcg/l (120-200)

DIAGNOSIS

Recessive Dystrophic Epidermolysis Bullosa Inversa with Squamous Cell Carcinoma of the Posterior Neck

TREATMENT AND COURSE

The patient was referred to Rush University Otolaryngology and underwent imaging studies for staging purposes, which included positron emission tomography (PET) and computed tomography (CT) scanning. The PET and CT scans demonstrated bilateral cervical lymph node, left supraclavicular lymph node and bilateral parotid gland involvement without obvious lung involvement.

Treatment was initiated with three courses of cisplatin chemotherapy and thirty-three sessions of radiotherapy without any surgical intervention, as she was deemed not to be an appropriate surgical candidate.

Five months status post chemotherapy and radiation treatment, total body PET-CT scanning was repeated. No metabolically active nodes were apparent. There was significant interval decrease in the metabolically active nodular skin thickening (squamous cell carcinoma) at the posterior aspect of the neck. Clinically, the tumor site was re-epithelializing without obvious sign of persistent squamous cell carcinoma.

A few weeks ago, a pebbly keratotic plaque developed within the treatment field, which was biopsied, demonstrating squamous cell carcinoma. After consulting with Rush University Otolaryngology, the decision was made to surgically excise the squamous cell carcinoma rather than initiating a second course of radiation and chemotherapy.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 10b**

Presented by Andrea Kassim, MD and Arthur Rhodes, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A one-year-old Hispanic female infant presented with a five-month history of pruritic lesions on the bilateral hands, feet and lower legs. According to the patient's mother, the patient develops several new lesions a week. New lesions appeared as blisters predominantly at sites of trauma. The patient's mother ruptured the blisters, which produced a clear fluid. The resultant erosions then healed with scarring and milia. Mother reports dystrophic nail changes with loss of toenails in the past. Review of symptoms was negative for fever or other systemic symptoms. Family history of similar lesions and consanguinity was denied. Past treatment included oral cephalexin and clindamycin, bacitracin ointment and permethrin cream, with no response.

PHYSICAL EXAMINATION

Bilateral dorsal hands and feet, lower legs, thighs, dorsal forearms, elbows, abdomen, back, forehead and nose: multiple pink plaques with overlying vesicles and milia, erosions, some with hemorrhagic crusts, as well as rare intact bullae, and pink or hypopigmented scars. At initial presentation, there were numerous pustules, which were no longer present on subsequent examinations. Several nails were dystrophic and there were no oral lesions. Total body surface area of involvement was approximately 2.5%.

HISTOPATHOLOGY

Immunomapping of an intact blister on the right great toe (4-mm punch biopsy): subepidermal blister with all components of the basement membrane present at the roof of the blister with irregular expression of type VII collagen as globular aggregates.

Direct immunofluorescence of perilesional skin was negative for IgG, IgM, IgA, C3, C5/C9 complex and fibrinogen deposition.

LABORATORY

Aerobic bacterial culture: moderate growth of methicillin-resistant *Staphylococcus aureus*

DIAGNOSIS

Dominant dystrophic epidermolysis bullosa

TREATMENT AND COURSE

Treatment since presentation has included empiric PO cephalexin for the patient's MRSA-positive bacterial culture with clearing of infection. The parents were counseled regarding the avoidance of aggravating factors (including trauma, friction, heat and increases in humidity) as well as the signs and symptoms of infection. Topical treatment included mupicorin ointment to the erosions. Genetic counseling consisted of a discussion of the recurrence risk for any future siblings and the probably of the patient's children being affected by dominant dystrophic epidermolysis bullosa.

DISCUSSION

The mechanobullous disorders of epidermolysis bullosa (EB) are a group of inherited diseases characterized by skin fragility with numerous variants and different underlying genetic bases, inheritance patterns and clinical presentations. Dystrophic epidermolysis bullosa (DEB) is caused by mutations in the gene encoding type VII collagen (COL7A1), leading to either complete absence or reduced numbers of poorly functioning anchoring fibrils.

In order to distinguish among the EB variants, diagnostic studies beyond standard microscopy are necessary. Immunomapping, transmission electron microscopy and molecular genetics, help to determine ultrastructural defects, level of expression of various disordered components of the basement membrane zone, and nature of causative mutation involved.

There are both dominant and recessive inheritance patterns of DEB, dominant dystrophic epidermolysis bullosa (DDEB) and recessive dystrophic epidermolysis bullosa (RDEB), respectively. The recessive form is classically further subdivided into the Hallopeau-Siemens and the non-Hallopeau-Siemens types, while the dominant form consists of the Cockayne-Touraine, Pasini, and Bart variants. The Hallopeau-Siemens subtype of RDEB is due to a premature stop codon, whereas the non-Hallopeau-Siemens subtype of RDEB is due to missense or frameshift mutations of collagen VII. The dominant dystrophic forms of EB are due to glycine substitutions in type VII collagen. The types of mutations in type VII collagen may in part explain the variation in phenotypes of the different DEB subtypes with the Hallopeau-Siemens RDEB variant having the most severe clinical manifestations.

The Hallopeau-Siemens subtype of RDEB is characterized by a complete lack of anchoring fibrils, which results in generalized bullae that heal with atrophic scarring, dyschromia and milia. Bullae and scar formation with resultant digital fusion on the hands and feet may lead to the characteristically debilitating “mitten deformities,” whereas erosions, bullae, stricture and scar formation in the eye, upper respiratory, digestive and genitourinary tracts may result in conjunctivitis, keratitis, blindness, hoarseness and gastrointestinal as well as genitourinary strictures. Nail findings include dystrophic changes and onychomadesis, while tooth involvement is manifested by tooth dysplasia and dental caries. Patients with the Hallopeau-Siemens recessive DEB subtype are also prone to flexural contractures, short stature and invasive squamous cell carcinomas, often arising within scars. The recessive DEB-associated squamous cell carcinomas are aggressive in nature, tend to recur, and are frequently resistant to treatment, commonly resulting in premature death.

The non-Hallopeau-Siemens type of RDEB, is considered a milder variant of RDEB, characterized by defective anchoring fibrils instead of a paucity of anchoring fibrils as in the Hallopeau-Siemens type. As a result, patients have a less severe clinical picture, with bullae, erosions, scarring, dyschromia and milia generally limited to bony prominences. Furthermore, patients often note improvement of their disease with time, with severity and frequency of skin lesions typically decreasing by the third decade of life.

In the early 1970s, a new variant of recessive DEB was proposed, namely dystrophic epidermolysis inversa. This variant of recessive DEB is also due mutations in the collagen VII gene, most typically missense mutations involving arginine or glycine residues within the carboxyl portion of the triple helix domain, leading to a reduction in number as well defective functioning of anchoring fibrils. The inversa variant shows a predilection for truncal, extremity and even generalized involvement early in life followed by the propensity for flexural, oral and genital mucosal as well as esophageal involvement later. Inguinal, perineal, axillary, neck and inframammary areas are the most commonly affected flexural sites. Teeth manifestations are characterized by dental caries. Nail involvement and milia are variable. Patients with the inverse variant of recessive DEB are prone to developing aggressive squamous cell carcinomas (SCC), but at a slightly decreased rate compared with patients with the Hallopeau-Siemens variant of recessive DEB. The inversus subtype has the second highest frequency of SCC (18%), only exceeded by the Hallopeau-Siemens type (23%). The risk of death from SCC at age 45 is 12% for the inversus type compared to 70% for Hallopeau-Siemens type of RDEB.

There is no effective therapy for either recessive or dominant dystrophic epidermolysis bullosa. Supportive treatment consists of avoidance of trauma and prevention of infection coupled with proper wound care. Bullae, erosions, scarring and strictures leading to ophthalmologic, upper respiratory, gastrointestinal and genitourinary complications require appropriate specialists. Nutritional support, dental evaluation and periodic surveillance for the development of squamous cell carcinomas are critical issues. As demonstrated in our patient, chemotherapy combined with radiation therapy may be beneficial to patients with advanced invasive squamous cell carcinoma, although surgical excision may prove to be more definitive treatment. Although not currently available to patients, gene therapy may eventually prove to be a curative intervention.

REFERENCES

1. Kahofer, P. *et al.,* Dystrophic Epidermolysis Bullosa Inversa with COL7A1 Mutations and Absence of GDA-J/*F3Protein, Pediatric Dermatology, Vol. 20 No. 3 243–248, 2003.*
2. *Chiaverini , C. et al., Inversa* Dystrophic Epidermolysis Bullosa Is Caused by Missense Mutations at Specific Positions of the Collagenic Domain of Collagen Type VII, *Journal of Investigative Dermatology*, 2010: 130, 2508–2511.
3. Murauer, E. *et al*., Functional correction of type VII collagen expression in dystrophic epidermolysis bullosa, *Journal of Investigative Dermatology*, 2011 Jan;131(1):74-83.
4. Spitz, J. Genodermatoses: *A Clinical Guide to Genetic Skin Disorders*, Second Edition, Lippincott, Williams & Wilkins, 2005.
5. Fine, J. *et al.,* Eye involvement in inherited epidermolysis bullosa: experience of the National Epidermolysis Bullosa Registry, *American Journal of Ophthalmology*, 2004 Aug;138(2):254-62.
6. Fine, J. *et al*., Genitourinary complications of inherited epidermolysis bullosa: experience of the national epidermylosis bullosa registry and review of the literature, *The Journal of Urology*, 2004 Nov;172(5 Pt 1):2040-4.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 11**

Presented by William Huang, MD, MPH and Katherine Brown, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This 40-year-old African American male presented to the dermatology clinic with a one-week history of a diffuse rash. The patient stated the rash started approximately one day after taking ibuprofen for headaches, for which he denied previous use. Review of systems was remarkable for headaches, arthralgias, and fatigue, and negative for shortness of breath, palpitations, chest pain, swelling, or dizziness. The patient denied any recent travel, outdoor travel, or any new or unusual exposures. Of note, the patient was recently admitted to the hospital three weeks prior to presentation for complaints of fever and malaise. During his hospitalization he was found to have an asymptomatic elevation of his liver enzymes. Extensive work-up at that time, including imaging and a hepatology consult, was inconclusive and the patient was sent home after near normalization of his liver function tests.

PAST MEDICAL HISTORY

Asthma

MEDICATIONS

Albuterol
Ibuprofen

ALLERGIES

Penicillin
Clindamycin

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Patient works as a barber.
Denies tobacco, alcohol, or illicit drug use.

PHYSICAL EXAM

Abdomen, bilateral lateral torso, thighs, and ventral forearms: approximately a dozen non-scaling large (4-12 cm) annular and polycyclic plaques with grayish dusky centers and peripheral pink slightly elevated borders.

Mucosa: clear

Neuro: Alert and oriented to person, place, time, and situation. Sensation and cranial nerves II-XII intact grossly. No focal deficits or facial palsies. Gait normal.

HISTOPATHOLOGY

Punch biopsy, left thigh: superficial to mid-dermal moderate perivascular infiltrate consisting of primarily lymphocytes with rare neutrophils.

LABORATORY RESULTS

The following labs were abnormal (hospital lab values in parentheses):
Borrelia burgdorferi IgG Abs–ELISA……2.96 H (Reference Range: < 0.80)
Borrelia burgdorferi IgM Abs–ELISA……5.22 H (Reference Range: < 0.80)

Borrelia burgdorferi IgG Abs –Western Blot Positive A

p18 Present	p41 Present
p23 Present	p45 Present
p28 Absent	p58 Present
p30 Absent	p66 Present
p39 Present	p93 Absent

INTERPRETIVE CRITERIA: Lyme IgG IB is considered as POSITIVE if any FIVE of the following bands are present: 18, 23, 28, 30, 39, 41, 45, 58, 66 or 93 kd

Borrelia burgdorferi IgM Abs –Western Blot Positive A
p23 Present
p39 Present
p41 Present
INTERPRETIVE CRITERIA: Lyme IgM IB is considered as POSITIVE if any TWO of the following bands are present: 23, 39 or 41 kd

Total Bilirubin	0.8 MG/DL **(5.0)**	[0.1-1.3]
Alk Phosphatase	165 U/L **(240)**	[30-125]
AST	30 U/L **(190)**	[3-44]
ALT	59 U/L **(366)**	[0-40]
ESR	59 MM/HR	[0-17]
C Reactive Protein	49.1 MG/L	[0.0-8.0]
Ferritin	1097 NG/ML	[12-410]

The following labs were normal:
Basic Metabolic Panel, WBC, Platelets, Total Protein, Albumin, Calcium, C3, C4, HIV Antibody, CPK, PT, INR, PTT, Lipase, Blood Culture, Urine Culture, Acetaminophen Level, Hepatitis Panel, ANA Screen, Anti-Smooth Muscle Antibody, Anti-Mitochondrial Antibody.

RADIOLOGY

None

DIAGNOSIS

Disseminated Lyme Borreliosis

TREATMENT AND COURSE

Lyme titers and an EKG were ordered based on clinical suspicion, and the patient was started on doxycycline 100 mg twice daily, as well as, triamcinolone 0.1% ointment twice daily as needed for itch and hydroxyzine 25 mg every eight hours as needed for itch. Further interviewing revealed that the patient had been recently in a “wooded area” in Indiana to visit his children, who live with his ex-wife. Upon diagnosis of disseminated lyme disease, the patient was referred to infectious disease for further management considerations. The patient noted rapid improvement in his skin rash at follow-up a week later with resolution of his arthralgias and headaches.

DISCUSSION

Lyme disease is the most common tick-borne disease in the United States (reported in all 50 states), in Europe, and in Asia. The characteristic expanding annular rash, known as erythema migrans, was first described in the early 1900s and found to be associated with tick bites and systemic illness in the 1940s. In 1977, the condition was named Lyme disease after groups of children in Lyme, Connecticut presented with erythema migrans and arthritis. In 1982, it was established that the spirochete *Borrelia burgdorferi* is the causative agent of Lyme disease, transmitted to humans through the bite of the Ixodes tick.

Each of the three stages of Lyme disease can present with specific clinical findings. Early localized infections present as a single erythematous annular lesion resembling a bulls-eye or target (erythema migrans) accompanied by non-specific complaints of fevers, chills, malaise, fatigue, and headache. Early disseminated infections typically occur within a few days to weeks after contact with the infected tick and patients present with multiple lesions of erythema migrans. In addition, patients can have musculoskeletal symptoms (60%) including migratory joint or muscle pain, neurologic symptoms (15%), including meningitis, radicular neuropathies, or facial nerve paralysis, and cardiovascular symptoms (8%), including atrioventricular blockades. If left untreated, early disseminated infections can progress to late disseminated infections with joint pain and swelling (usually the knees or hips), chronic neuropathies and encephalopathies, and rarely death.

The diagnosis of Lyme disease is typically based on the clinical presentation of erythema migrans and systemic symptoms. Patients will often not recall traveling to an endemic area or having had a tick bite. Common laboratory tests, including a complete blood cell count, erythrocyte sedimentation rate, comprehensive metabolic panel, and c-reactive protein, are often not helpful in making the diagnosis. When confirmation is necessary or the diagnosis unclear, the Centers for Disease Control (CDC) recommends serologic tests for Lyme disease, including the enzyme-linked immunosorbent assay (ELISA) followed by Western blot testing which can support the diagnosis, but can be prone to false positives and false negatives. The ELISA test for Lyme disease is sensitive, but can be falsely positive with mononucleosis, auto-immune conditions, and *Treponema pallidum* infections. In addition, antibodies to *Borrelia burgdorferi* may not be present in early disease presentations, potentially leading to a false negative ELISA. Western blot testing, which is more specific, examines IgM and IgG responses to various proteins of *Borrelia burgdorferi*. To be considered positive, IgM blots are required to be positive in at least 2 of 3 specific bands and IgG blots are required to be positive in at least 5 of 10 specific bands.

The treatment of Lyme disease as recommended by the Infectious Disease Society of America includes doxycyline 100 mg orally twice daily (patients 9 years of age or older) or amoxicillin 50 mg/kg/day orally (patients younger than 9 years of age). Other second line treatments include cefuroxime and erythromycin. Duration of therapy depends on the stage and severity of disease. For early localized infections, treatment should continue for at least 14 days. For early disseminated infections, treatment should continue for at least 21 days. For Lyme-disease-associated arthritis, treatment should continue for 30-60 days. Patients with late or severe disease, including neurologic and cardiovascular complications, may require intravenous antibiotics, such as ceftriaxone, cefotaxime, or penicillin G.

REFERENCES

1. Lelovas P, Dontas I, Bassiakou E, Xanthos T. Cardiac implications of Lyme disease, diagnosis and therapeutic approach. Int J Cardiol. 2008 Sep 16;129(1):15-21. Epub 2008 May 27.

2. Bratton RL, Whiteside JW, Hovan MJ, Engle RL, Edwards FD. Diagnosis and treatment of Lyme disease. Mayo Clin Proc. 2008 May;83(5):566-71.
3. Oksi J, Nikoskelainen J, Hiekkanen H, Lauhio A, Peltomaa M, Pitkäranta A, Nyman D, Granlund H, Carlsson SA, Seppälä I, Valtonen V, Viljanen M. Duration of antibiotic treatment in disseminated Lyme borreliosis: a double-blind, randomized, placebo-controlled, multicenter clinical study. Eur J Clin Microbiol Infect Dis. 2007 Aug;26(8):571-81.
4. Benedix F, Weide B, Broekaert S, Metzler G, Frick JS, Burgdorf WH, Röcken M, Schaller M. Early disseminated borreliosis with multiple erythema migrans and elevated liver enzymes: case report and literature review. Acta Derm Venereol. 2007;87(5):418-21.
5. Salzman BE, Stonehouse A, Studdiford J. Late diagnosis of early disseminated lyme disease: perplexing symptoms in a gardener. J Am Board Fam Med. 2008 May-Jun;21(3):234-6.
6. Shadick NA, Phillips CB, Sangha O, Logigian EL, Kaplan RF, Wright EA, Fossel AH, Fossel K, Berardi V, Lew RA, Liang MH. Musculoskeletal and neurologic outcomes in patients with previously treated Lyme disease. Ann Intern Med. 1999 Dec 21;131(12):919-26.
7. Steere AC, McHugh G, Damle N, Sikand VK. Prospective study of serologic tests for lyme disease. Clin Infect Dis. 2008 Jul 15;47(2):188-95.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 12**

Presented by William Huang, MD, MPH and Michael Tharp, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This 16-year-old African American female presented to the dermatology clinic with a four-month history of dyspigmentation around her eyelids. The lesions began as a single hyperpigmented macule that spread to involve both eyelids. The patient denied any symptoms or skin lesions elsewhere including the face, chest, or back. There was no obtainable history of a prior rash, cosmetic product use, use of bleaching agents, or scaling.

PAST MEDICAL HISTORY

Acne
Asthma

MEDICATIONS

Benzoyl Peroxide 2.5% gel
Tretinoin 0.025% cream
Albuterol inhaler

ALLERGIES

NKDA

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Student in high school

PHYSICAL EXAM

Bilateral eyelids: medium-brown, minimally scaly oval and round macules without erythema
Face: acneiform papules and comedones
Chest, back, and proximal upper extremities: clear

HISTOPATHOLOGY

Punch biopsy, lateral canthus: unremarkable epidermis with spores and hyphae in the stratum corneum. These are highlighted by a PAS stain.

LABORATORY RESULTS

KOH: “negative”

RADIOLOGY

None

DIAGNOSIS

Tinea Versicolor of the Eyelids

TREATMENT AND COURSE

At presentation a KOH scraping was negative. A 3-mm punch biopsy was obtained from lesional skin and revealed numerous spores and hyphae. Following the biopsy result, the patient was started on econazole 1% cream to be applied daily for six weeks. At follow-up the lesions had completely resolved.

DISCUSSION

Tinea versicolor, or pityriasis versicolor, is a common superficial cutaneous mycoses caused by lipophilic yeasts and fungi of the genus *Malassezia*. Although yeasts of the genus *Malassezia* are considered a normal part of skin flora, they are associated with several common dermatoses including seborrheic dermatitis, *Malassezia* folliculitis, and tinea versicolor. Tinea versicolor is characterized by the appearance of asymptomatic round to oval lesions most commonly found on the trunk and upper arms. Patients can present with hypopigmented or hyperpigmented skin lesions.

Tinea versicolor is most commonly diagnosed in adolescents and young adults when sebaceous gland activity increases. One theory regarding this disease is that the *Malassezia* yeasts that normally colonize the skin convert from the round, yeast forms to the pathogenic mycelial forms that invade the stratum corneum of the skin. Potassium hydroxide preparations reveal classically “spaghetti and meatballs” on light microscopy reflecting both hyphae and spores.

Although considered a very common dermatosis, tinea versicolor has rarely been reported to involve the eyelids. Reports from the ophthalmology literature of dermatophytosis of the eyelid and periorbital area involve non-*Malessezia* species of fungi including *Microsporum* and *Trichophyton*. These case reports are also not clinically consistent with tinea versicolor as patients presented with complaints of loss of eyelashes, erythema, or pruritus.

Among the most common *Malassezia* species are *M. globosa*, *M. sympodialis*, and *M. furfur*. Treatment of tinea versicolor typically involves the use of topical imidazole preparations including ketoconazole, bifonazole, miconazole, econazole, and clotrimazole. For cases that are widespread or recalcitrant to topical therapies, treatment with systemic antifungals including ketoconazole, itraconazole, or fluconazole can be considered.

REFERENCES

1. Hu SW, Bigby M. Pityriasis versicolor: a systematic review of interventions. Arch Dermatol. 2010 Oct;146(10):1132-40.
2. Mendez-Tovar LJ. Pathogenesis of dermatophytosis and tinea versicolor. Clin Dermatol. 2010 Mar 4;28(2):185-9.
3. Machado AP, Hirata SH, Ogawa MM, Tomimori-Yamashita J, Fischman O. Dermatophytosis on the eyelid caused by Microsporum gypseum. Mycoses. 2005 Jan;48(1):73-5.
4. Derbel M, Benzina Z, Ghorbel I, Abdelmoula S, Makni F, Ayadi A, Feki J. Malassezia fungal blepharitis: a case report. J Fr Ophtalmol. 2005 Oct;28(8):862-5.
5. Finger Basak SA, Berk DR, Lueder GT, Bayliss SJ. Common features of periocular tinea. Arch Ophthalmol. 2011 Mar;129(3):306-9.
6. Gupta AK, Batra R, Bluhm R, Boekhout T, Dawson TL Jr. Skin diseases associated with Malassezia species. J Am Acad Dermatol. 2004 Nov;51(5):785-98.

7. Hort W, Mayser P. Malassezia virulence determinants. Curr Opin Infect Dis. 2011 Apr;24(2):100-5.
8. Bonifaz A, Gómez-Daza F, Paredes V, Ponce RM. Tinea versicolor, tinea nigra, white piedra, and black piedra. Clin Dermatol. 2010 Mar 4;28(2):140-5.
9. Kaur I, Handa S, Kumar B. Tinea versicolor: involvement of unusual sites. Int J Dermatol. 1996 Aug;35(8):604-5.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 13**

Presented by William Huang, MD, MPH and Michael Tharp, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This 57-year-old African American gentleman presented to the dermatology clinic for evaluation of a widespread pruritic rash. The patient had a recent diagnosis of non-Hodgkin's lymphoma and was undergoing chemotherapy with adriamycin, bleomycin, vinblastine, and dacarbazine. The patient's other medical problems included hypertension, which was well-controlled, and a remote history of a cerebrovascular accident. The patient stated that the rash is recurrent and begins a few days after each dose of bleomycin. Review of systems was otherwise unremarkable except for pruritus.

PAST MEDICAL HISTORY

Hypertension
Cerebrovascular Accident
Non-Hodgkin's Lymphoma

MEDICATIONS

Adriamycin
Bleomycin
Vinblastine
Dacarbazine
Hydrochlorothiazide
Lisinopril

ALLERGIES

NKDA

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Non-contributory

PHYSICAL EXAM

Chest, back, abdomen, upper extremities, lower extremities: multiple linear, curvilinear, and flagellate hyperpigmented plaques

HISTOPATHOLOGY

None

LABORATORY RESULTS

None

RADIOLOGY

None

DIAGNOSIS

Flagellate Hyperpigmentation Following Systemic Bleomycin

TREATMENT AND COURSE

Given the patient's history of non-Hodgkin's lymphoma and concurrent chemotherapy, the use of systemic steroids was avoided. The patient's symptoms improved significantly on topical steroids (triamcinolone ointment 0.1% twice daily) under occlusion and systemic gabapentin. The patient's chemotherapy is ongoing.

DISCUSSION

Flagellate hyperpigmentation following systemic bleomycin sulfate as a chemotherapeutic agent is a well-known cutaneous reaction occurring in approximately 10% of exposed individuals. Bleomycin sulfate, an antibiotic derived from *Streptomyces verticillus*, is a commonly used anti-tumor agent for both hematologic and solid organ malignancies. Many patients develop a generalized pruritus within several days after receiving bleomycin sulfate followed by the characteristic linear and hyperpigmented streaks. The exact mechanism of this characteristic rash is unknown. Suggested pathways include induction of neutrophilic eccrine hidradenitis, post-inflammatory pigmentary incontinence, and altered levels of melanin due to a toxic effect of the medication. Other commonly reported adverse events to bleomycin sulfate include alopecia and stomatitis.

Although a diffuse linear eruption is the most commonly reported cutaneous reaction to systemic bleomycin, there have been reports of hyperpigmentation only in areas of pressure and palmar creases. Another case by Tsuji et al. reported a patient with hyperpigmentation limited to areas of striae distensae after systemic bleomycin. Flagellate hyperpigmentation has also been reported following intralesional bleomycin for the treatment of verruca plantaris. In that case, the patient had received 14 units of intralesional bleomycin sulfate injected at different sites of recalcitrant verruca and developed urticaria, generalized pruritus, and flagellate hyperpigmentation.

Treatment of flagellate hyperpigmentation includes cessation of the medication although this is not always possible due to the need for an effective chemotherapeutic regimen. Most cases are reversible following discontinuation of bleomycin, and care is directed at symptom relief, such as antipruritics, antihistamines, systemic steroids, and topical steroids.

REFERENCES

1. Watanabe T, Tsuchida T. 'Flagellate' erythema in dermatomyositis. Dermatology. 1995;190(3):230-31.
2. Yagoda A, Mukherji B, Young C, Etcubanas E, Lamonte C, Smith JR, Tan CT, Krakoff IH. Bleomycin, an antitumor antibiotic. Clinical experience in 274 patients. Ann Intern Med. 1972 Dec;77(6):861-70.
3. Susser WS, Whitaker-Worth DL, Grant-Kels JM. Mucocutaneous reactions to chemotherapy. J Am Acad Dermatol. 1999 Mar;40(3):367-98; quiz 399-400.
4. Tsuji T, Sawabe M. Hyperpigmentation in striae distensae after bleomycin treatment. J Am Acad Dermatol. 1993 Mar;28(3):503-5.
5. Abess A, Keel DM, Graham BS. Flagellate hyperpigmentation following intralesional bleomycin treatment of verruca plantaris. Arch Dermatol. 2003 Mar;139(3):337-9.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 14**

Presented by Jill C. Anderson, MD, and Michael D. Tharp, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This 65-year-old female was initially referred to our clinic in 1996 with a two-year history of diffuse pruritic red-brown macules on her lower extremities and torso. A biopsy at the time demonstrated increased mast cells, and she was diagnosed with cutaneous mastocytosis. At the time of diagnosis, a thorough review of systems was negative; her CBC and CMP were within normal limits; and a skeletal survey was unremarkable. She was treated with antihistamines. Her skin lesions continued to progress, but she remained asymptomatic for 3 years. In 1999, she began experiencing episodes of flushing, nasal congestion, nausea, vomiting, diarrhea, hypotension, and abdominal cramping. While these symptoms were not controlled with combined antihistamines alone, the addition of prednisone and subsequently high dose aspirin eliminated symptoms of mast cell mediator release, suggesting the overproduction of prostaglandins. Cromolyn sodium and montelukast were added to control symptoms of abdominal cramping and diarrhea. A colonoscopy was performed, which demonstrated increased colon mast cells on biopsy. Her total serum tryptase at the time was ~300 (normal range 1.9-13.5). She was diagnosed with systemic mastocytosis. In 2001, she was noted to have mild pancytopenia and extensive involvement of her bone marrow with mast cells. Her advancing disease has been difficult to manage, requiring various treatments, including interferon-α, aspirin therapy, high dose anti-histamines, prednisone, narrow band UVB, and imatinib, none of which controlled her progressive mast cell disease. In addition, she developed splenomegaly and pancytopenia, requiring splenectomy in 2006. Following splenectomy, she did note some improvement in the frequency of her mast cell mediator release episodes.

In January 2010, she was found to have further progression of her mastocytosis, with increasing hepatomegaly, a leukocytosis with greater than 60% eosinophils, and increasing serum tryptase levels (~1300, normal range 1.9-13.5). The decision was made to treat her advancing disease with dasatinib and cladribine.

PAST MEDICAL HISTORY

Mastocytosis
Hypothyroidism
Peptic Ulcer Disease
Anemia
Depression
Hyperlipidemia
Hysterectomy
Splenectomy
Tonsillectomy
Breast Augmentation

MEDICATIONS

cetirizine 10 mg nightly
aspirin five 325 mg tablets twice daily
fexofenadine 180 mg every morning
prednisone 2.5 mg every other day
dasatinib 100 mg every morning
pantoprazole 40 mg twice daily
zolpidem 12.5 mg nightly
omeprazole 40 mg twice daily
escitalopram 20 mg nightly
fenofibrate 160 mg nightly
omega-3-acid ethyl esters 1 g twice daily
levothyroxine 50 mcg every morning
furosemide 20 mg every morning
misoprostol 200 mcg twice daily

ALLERGIES

No known drug allergies.

FAMILY HISTORY
Non-contributory.

SOCIAL HISTORY
Retired teacher. Remote tobacco use (one pack per day for eight years from 1962 to 1970). Denies history of alcohol or illicit drug use.

PHYSICAL EXAM
Generalized, too numerous to count, red-brown macules overlying the trunk, bilateral upper and lower extremities, and face.

Hepatomegaly and cervical lymphadenopathy present.

HISTOPATHOLOGY
Bone Marrow Biopsy (October 2009): Almost 100% cellular marrow, in which, greater than 90% of the space was occupied by sheets of spindled mast cells with surrounding areas of dense fibrosis. The remaining cellularity was composed of erythroid and myeloid precursors with normal maturation.

Punch biopsy, trunk (1996): Increased numbers of spindle-shaped mast cells.

LABORATORY RESULTS
The following were positive or abnormal:

Alkaline phosphatase (12/7/09):	218	(normal 30-125)
Tryptase (12/7/09):	1330.0	(normal 1.9-13.5)
WBC (12/7/09):	23.73	(normal 4.0-10.0)
Neutrophils % (12/7/09):	13.0%	(normal 36.0-72.0%)
Lymphocytes % (12/7/09):	12.0%	(normal 18.0-52.0%)
Eosinophil % (12/7/09):	64.0%	(normal 0.0-6.0%)
Hemoglobin (12/7/09):	9.8	(normal 12.0-16.0)
Platelets (12/7/09):	737	(normal 150-399)

D816V c-kit mutation: Positive

The following were negative or within normal limits:
BMP, AST, ALT

RADIOLOGY
CT Chest, Abdomen, and Pelvis (10/2009) remarkable for:

1. Hepatomegaly extending to the pelvic brim.
2. Surgically absent spleen.
3. Interval increase in size and number of epigastric lymph nodes involving the gastric hepatic ligament and portacaval space.
4. New mesenteric lymphadenopathy.
5. Skeleton significant for diffuse osseous sclerosis with few minimal punctate scattered lytic foci.

DIAGNOSIS
Aggressive Systemic Mastocytosis

TREATMENT AND COURSE

In January 2010, the patient was started on dasatinib 100 mg every morning (which she is currently taking) and cladribine (2-chlorodeoxyadenosine, 2-CdA). She completed a total of six cycles of cladribine (her last treatment was in June 2010). She tolerated the treatment very well. Her skin lesions appeared to become less red and decreased in number. The frequency of her mast cell mediator release episodes has decreased, and as a result, her aspirin has been discontinued.

A repeat CT scan of the chest, abdomen, and pelvis in September 2010 revealed interval near resolution of her abdominal lymphadenopathy. Her hepatomegaly and skeletal changes were stable. In addition, a repeat bone marrow biopsy in September 2010 was much less cellular with significantly fewer mast cells. Her tryptase level in October 2010 decreased from ~1300 (in January 2010) to 502.0 (normal range 1.9-13.5). Her most recent complete blood count with differential in February 2011 is still abnormal, but has improved since treatment with cladribine and dasatinib. She is anemic with a hemoglobin of 9.0 (normal range 12.0 to 16.0) and leukopenic at 3.34 (normal range 4.0 to 10.0) with 23.7% eosinophils (normal range 0.0 to 6.0%). Her current daily regimen is fexofenadine 180 mg every morning, cetirizine 10 mg nightly, aspirin six 325 mg tablets daily, and misoprostol 100 mcg twice daily.

DISCUSSION

Mastocytosis represents a heterogeneous spectrum of disorders all characterized by mast cell hyperplasia. The accumulation of mast cells may be located in one or more organs. The skin is most commonly involved, but not all cases have skin involvement. Presentation may occur during childhood or adulthood. Some forms are relatively asymptomatic with a normal life span, while others are highly aggressive. The World Health Organization classification includes the following types of mastocytosis: Type Ia, Cutaneous mastocytosis; Type Ib, indolent systemic mastocytosis; Type II, systemic mastocytosis with associated clonal hematological non-mast cell lineage disease (AHNMD); Type III, aggressive systemic mastocytosis; and Type IV, mast cell leukemia.

Our patient represents a case of aggressive systemic mastocytosis. She has cutaneous lesions, as well as documented involvement of her bone marrow, GI tract, liver, spleen, and lymph nodes. She also has a marked eosinophilia. Due to her progressive disease, dasatinib and cladribine therapy was initiated. She has had a partial response to therapy.

Cladribine is also known as 2-chlorodeoxyadenosine (2-CdA), which acts as a purine nucleoside analogue. The main toxicities of cladribine are myelosuppression and infection. It is unknown if cladribine poses a risk of future malignancies. Cladribine treatment for mastocytosis was first described by Terreri *et al*. in 2001 in a 57-year-old male with systemic mastocytosis, who had failed treatment with interferon-α, but responded to this medication. Kluin-Nelemans *et al.* described a study of 10 patients with either indolent systemic mastocytosis, aggressive mastocytosis, or AHNMD, all of whom achieved a partial response to 2-CdA. In this study, none had a complete response and one patient had a relapse after 11 months. In a study of 4 patients with aggressive systemic mastocytosis, 75% of the patients had a major or partial response to 2-CdA (Pardanani *et al*., 2004). The duration of response ranged from 2 months to over 4 years. In Pagano *et al.* (2008), three patients treated with 2-CdA achieved a partial response. In 2009, Lim *et al.* reported a 55% overall response rate to cladribine in a group of 22 patients, with 1 patient having a complete response, 7 patients with a marked response, and 4 patients with a partial response.

Patients with mastocytosis, including our patient, often show mutations in the c-kit proto-oncogene, leading to activation of tyrosine kinase KIT (CD117). This is thought to play a pathogenic role in mastocytosis (Longley *et al*, 1999). Dasatinib is an oral, multi-targeted kinase inhibitor. It has been shown to inhibit KIT^{D816V} (Shah *et al.*, 2006). In addition, it is structurally unrelated to imatinib. Therefore, it may be useful in patients who have previously failed imatinib therapy. A case report of 2 patients with systemic mastocytosis treated with dasatinib noted that both patients had a partial response (Pregno *et al.*, 2008). A case report of a 71-year-old patient with aggressive systemic mastocytosis treated with both cladribine and dasatinib noted treatment failure and disease progression with resultant death (Aichberger *et al.*, 2008). Purtill *et al*. (2008) reported 4 cases of systemic mastocytosis treated with dasatinib. All four patients tolerated dasatinib. Two of the patients had symptomatic improvement of diarrhea and pruritus. Of these two patients, one patient had a histologic response in their bone marrow at 7 months, but later developed acute myeloid leukemia at 11 months. The other two patients did not have a response to dasatinib.

In conclusion, our patient tolerated dasatinib and cladribine and was found to have a partial response to treatment. There remains a need for novel treatments of aggressive systemic mastocytosis.

REFERENCES

1. Aichberger, KJ, Sperr, WR, Gleixner, Kretschmer, A, Valent, P. Treatment responses to cladribine and dasatinib in rapidly progressing aggressive mastocytosis. Eur J Clin Invest. 2008;38(11):869-873.
2. Kluin-Nelemans, HC, Oldhoff, JM, van Doormaal, JJ, van't Wout, JW, Verhoef, G, Gerrits, WBJ, van Dobbenburg, OA, Pasmans, SG, Fijnheer, R. Cladribine therapy for systemic mastocytosis. Blood. 2003;102(13):4270-4276.
3. Lim, KH, Pardani, A, Butterfield, JH, Li, C, Tefferi, A. Cytoreductive therapy in 108 adults with systemic mastocytosis: outcome analysis and response prediction during treatment with interferon-alpha, hydroxyurea, imatinib mesylate, or 2-chlorodeoxyadenosine. Am J Hematol. 2009;84(12):790-794.
4. Longley, BJ, Metcalfe, DD, Tharp, M, Wang, X, Tyrrell, L, Lu, SZ, Heitjan, D, and Ma, Y. Activating and dominant inactivating c-KIT catalytic domain mutations in distinct clinical forms of human mastocytosis. Proc Natl Acad Sci USA 96: 1609-14, 1999.
5. Pagano, L, Valentin, CG, Caira, M, Rondoni, M, Van Lint, MT, Candoni, A, Allione, B, Cattaneo, C, Marbello, L, Caramatti, C, Pogliani, EM, Iannitto, E, Giona, F, Ferrara, F, Invernizzi, R, Fanci, R, Lunghi, M, Fianchi, L, Sanpaolo, G, Stefani, PM, Pulsoni, A, Martinelli, G, Leone, G, Musto, P. Advanced mast cell disease: an Italian hematological multicenter experience. Int J Hematol. 2008;88(5):483-488.
6. Pardanani, A, Hoffbran, AV, Butterfield, JH, Tefferi, A. Treatment of systemic mast cell disease with 2-chlorodeoxyadenosine. Leuk Res. 2004;28(2):127-131.
7. Pregno, P, Rondoni, M, Chiappella, A, Paolini, S, Griso, L, Martinelli, G, Vitolo, U. Dasatinib is effective and safe in systemic mastocytosis with D816V mutation: case report of two patients. Haematol. 2008;93(s1):496.
8. Purtill, D, Cooney, J, Sinniah, R, Carnley, B, Cull, G, Augustson, B, Cannell, P. Dasatinib therapy for systemic mastocytosis: four cases. Eur J of Haem. 2008;80(5):456-458.
9. Shah, NP, Lee, FY, Luo, R, Jiang, Y, Donker, M, Akin, C. Dasatinib (BMS-354825) inhibits KIT^{D816V}, an imatinib-resistant activating mutation that triggers neoplastic growth in most patients with systemic mastocytosis. Blood. 2006;108(1):286-291.

10. Tefferi, A, Li, C, Butterfield, JH, Hoagland, HC. Treatment of systemic mast-cell disease with cladribine. N Engl J Med. 2001;344(4):307-308.

11. Tharp, MD. Mastocytosis. From Dermatology, Bolognia J, Jorizzo J, and Rapini R (eds). Spain, 2007; Mosby: 1845-1853.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 15**

Presented by Jill C. Anderson, MD, and Brian K. Bonish, MD, PhD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This 57-year-old male was admitted in August 2010 for evaluation and treatment of a new diagnosis of acute myeloid leukemia. He was enrolled in a chemotherapy trial (CALGB10603) and was started on induction chemotherapy with daunorubicin, cytarabine, and either the study drug, midostaurin, or placebo. Ten days after starting induction chemotherapy, he noted lesions on his torso and around his eyes. He reported that the periorbital lesions were pruritic, and felt that his eyelids were swollen. The abdominal lesions were asymptomatic. He denied any new topical medications (including eye drops) or any vigorous rubbing of the eyes or trauma. His review of symptoms at the time was positive for intermittent fevers for seven days, fatigue, diarrhea, and dry cough, but was otherwise negative.

PAST MEDICAL HISTORY

Acute myeloid leukemia, M4 (acute myelomonocytic leukemia)
Tonsillectomy

MEDICATIONS

daunorubicin
cytarabine
midostaurin or placebo
acyclovir
loperamide
caspofungin
acetaminophen
guaifenesin-dextromethorphan
lorazepam
piperacillin
vancomycin
metronidazole
allopurinol
cefepime
prochlorperazine

ALLERGIES

No known drug allergies

FAMILY HISTORY

Denies family history of hematologic malignancies.

SOCIAL HISTORY

Former smoker, half a pack per day for 10 years (quit in 1974). Denies alcohol or illicit drug use.

PHYSICAL EXAM

Bilateral periorbital areas: erythematous, edematous plaques
Left upper back: well-demarcated, erythematous to violaceous, firm plaque
Abdomen and upper thighs: few scattered, erythematous papules

HISTOPATHOLOGY

Punch biopsy, left upper back (9/2010): dense neutrophilic infiltrate within and around eccrine glands with necrosis of eccrine epithelial cells

LABORATORY RESULTS

The following were positive or abnormal:

White blood count:	0.08	(normal 4.0 – 10.0)
Neutrophil %:	5.3	(normal 46.0 – 78.0)
Lymphocyte %:	94.7	(normal 18.0 – 52.0)
Hemoglobin:	8.3	(normal 13.5 – 17.5)
Platelets:	15	(normal 150 – 399)
Albumin:	2.2	(normal 3.5 – 5.0)
Total protein:	5.8	(normal 6.0 – 8.2)
Calcium:	7.7	(normal 8.7 – 10.7)
Lactate Dehydrogenase:	259	(normal 84 – 240)
Phosphorus:	2.2	(normal 2.5 – 4.6)
Activated Partial Thromboplastin Time:	42.7	(normal 23.0 – 33.0)

Blood cultures from catheter: Vancomycin resistant *enterococcus faecium*

The following were negative or within normal limits:
Sodium, Potassium, Chloride, Creatinine, AST, ALT, Alkaline Phosphatase, Bicarbonate, Total Bilirubin, Glucose, INR, PT, TSH, MCV

DIAGNOSIS

Neutrophilic Eccrine Hidradenitis.

TREATMENT AND COURSE

The patient's lesions improved without treatment over the next week and did not recur. The patient completed induction chemotherapy, but with persistent disease. He completed re-induction chemotherapy with cytarabine and daunorubicin (with either midostaurin or placebo). He then received consolidation chemotherapy with high dose cytarabine in November 2010. In January 2011, he underwent busulfan and fludarabine conditioning followed by allogeneic peripheral stem cell transplant.

DISCUSSION

Neutrophilic eccrine hidradenitis (NEH) is a rare, self-limited, disorder of the eccrine sweat duct. NEH was first reported in 1982 by Harrist et al. in a patient undergoing chemotherapy for acute myelogenous leukemia (AML). NEH is most often documented in patients with AML being treated with chemotherapy, as in the case of our patient, most commonly with cytarabine. NEH has also been reported in otherwise healthy individuals and in patients with conditions such as HIV infection, lupus, and Behçet's. NEH can affect both adults and children. The pathogenesis remains largely unknown, but is likely related to the cytotoxicity of the chemotherapy, which may lead to necrosis of the sweat ducts.

The lesions of NEH usually present 7 to 14 days after administration of chemotherapy. It is often associated with neutropenia and fever. Clinically, the lesions appear as erythematous papules and plaques, most frequently involving the trunk. Lesions may also involve the extremities and face. Our patient's lesions were noted on the trunk, bilateral thighs, and bilateral periorbital areas. To our knowledge, only three case reports of NEH involving the periorbital region have been reported. This presentation may mimic infectious and infiltrative processes. NEH should be considered in the differential diagnosis of perioribital erythematous plaques in individuals undergoing chemotherapy for AML. Lesions usually spontaneously resolve over several days to weeks after cessation of chemotherapy, but may recur. Due to the self-limited nature of NEH, no treatment is needed. Dapsone, non-steroidal anti-inflammatory drugs, and intravenous corticosteroids have been reported to be useful.

REFERENCES

1. Bardenstein, DS, Haluschak, J, Gerson, S, Zaim, MT. Neutrophilic eccrine hidradenitis simulating orbital cellulitis. Arch Ophthalmol. 1994;112(11):1460-1463.
2. Crawford, GH, Chu, AY, Halpern, M, James, WD. Erythematous facial plaques in a patient with leukemia. Arch Dermatol. 2003;139(4):531-536.
3. Harrist, TJ, Fine, JD, Berman, RS, Murphy, GF, Mihm, MM. Neutrophilic eccrine hidradenitis: A distinctive type of neutrophilic dermatosis associated with myelogenous leukemia and chemotherapy. Arch Dermatol. 1982;118(4):262-266.
4. Miller, JL, Hurley, HJ. Diseases of the eccrine and apocrine sweat glands. From Dermatology, Bolognia J, Jorizzo J, and Rapini R (eds). Spain, 2007; Mosby: 531-547.
5. Srivastava, M, Scharf, S, Meehan, SA, Polsky, D. Neutrophilic eccrine hidradenitis masquerading as facial cellulitis. J Am Acad Dermatol. 2006;56(4):693-696.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 16**

Presented by William Huang, MD, MPH and Jessie Cheung, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This 58-year-old Hispanic female with a past medical history significant for systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and gastroesophageal reflux disease (GERD) presented to our institution for evaluation of new pruritic lesions on her right flexor forearm. Her home medications included oxaprozin, hydroxychloroquine, estrostep, and lansoprazole, none of which were started or changed within the past six months. She had previously been given a diagnosis of lichen planus in the emergency department, and prescribed triamcinolone ointment without resolution of her lesions. She denied any constitutional symptoms, joint complaints, or history of HSV infection. Review of previously performed labs revealed an elevated ANA titer with a nucleolar pattern consistent with her previous diagnosis of SLE.

PAST MEDICAL HISTORY

Systemic Lupus Erythematosus (SLE)
Rheumatoid Arthritis (RA)
Gastroesophageal Reflux Disease (GERD)

MEDICATIONS

Oxaprozin
Hydroxychloroquine
Estrostep
Lansoprazole

ALLERGIES

NKDA

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Denies tobacco use

PHYSICAL EXAM

Flexor right forearm: several red-purple targetoid flat-topped papules and vesicles
Oral mucosa: clear

HISTOPATHOLOGY

Shave biopsy, right forearm: interface dermatitis with dyskeratosis and extravasated red blood cells consistent with erythema multiforme (EM).

LABORATORY RESULTS

None

RADIOLOGY

None

DIAGNOSIS

Rowell’s Syndrome

TREATMENT AND COURSE

The patient was subsequently started on clobetasol propionate 0.05% ointment applied twice daily with resolution of her lesions and symptoms within two weeks. The patient continued hydroxychloroquine for her systemic lupus erythematosus managed by her rheumatologist.

DISCUSSION

Rowell's Syndrome (RS) is a rare entity in which lesions of erythema multiforme (EM) are seen in patients with lupus erythematosus (LE). The presence of LE with skin lesions of EM was first described by Scholtz in 1922. Subsequently, in 1963, Rowell et al. reported four patients with DLE and EM-like lesions associated with specific immunologic abnormalities of the serum including a speckled ANA pattern and positive rheumatoid factor. Review of the literature reveals approximately 40 reported cases of RS since its original description.

Several reviews have stated that Rowell's original criteria were not preserved in several of these case reports. For example, one case did not have the characteristic histopathologic findings of EM, and another involved a patient with a homogeneous ANA pattern. Two additional reported cases of RS had a negative rheumatoid factor, and another reported RS in patients with SLE, as opposed to DLE. The EM-like lesions of the original paper by Rowell et al. were reportedly idiopathic, but other reported cases have associated the lesions to medications.

As a result of the aforementioned controversies, several publications have attempted to redefine the criteria for diagnosing RS. A review of 18 cases of RS between 1963 and 2000 demonstrated that the speckled ANA pattern was the most consistent feature observed (88% of cases) while RF is the least prevalent feature (41% of cases). Patients in this review had either DLE or SLE. Our patient had a nucleolar ANA pattern and a negative RF.

Some authors consider RS to be merely the co-existence of EM and LE rather than a distinct entity. However, in these patients, as in ours, no precipitating factors are elucidated and mucous membranes are never involved. Additionally, in patients with EM, positive serological findings are not consistently found. Most cases demonstrate a good response to prednisone with azathioprine or antimalarials, including chloroquine or hydroxychloroquine. Our patient's lesions demonstrated a favorable response to clobetasol propionate ointment although the patient was previously on hydroxychloroquine. As cases continue to be reported in the literature, it will become increasingly clear if Rowell's Syndrome is indeed a distinct entity, or rather, an incidental finding.

REFERENCES

1. Scholtz M. Lupus erythematosus acutus disseminates haemorrhagicus. Arch Dermatol Syphilol 1922; 6: 466.
2. Rowell NR, Beck JS, Anderson JR. Lupus erythematosus and erythema multiforme-like lesions. A syndrome with characteristic immunological abnormalities. Arch Dermatol 1973; 88: 176-80.
3. Fiallo, P, et al. Rowell's syndrome. Int J Dermatol 1995; 34: 635.
4. Maciejewski W. Annular erythema as an unusual manifestation of chronic disseminated lupus erythematosus. Arch Dermatol 1980; 116: 450.
5. Parodi A, et al. Rowell's syndrome: report of a case. J Am Acad Dermatol 1989; 21: 374.
6. Dogra A, Minocha Y, Gupta M, Capalash P. Rowell's Syndrome. Indian J Dermatol Venereol Leprol 2000; 66: 324-5.

7. Khandpur S, et al. Rowell's syndrome revisited: report of two cases from India. Int J Dermatol 2005; 44: 545.
8. Child FJ, Kapur N, Creamer D, Kobza Black A. Rowell's syndrome. Clinical and Experimental Dermatology 1999; 24: 74-77.
9. Duarte AF, et al. Rowell syndrome – case report and review of literature. Dermatol Online J 2008; 44: 545.

CHICAGO DERMATOLOGIC SOCIETY **CASE #17**

Presented by: Mark Romanelli, MD, Marianne O'Donoghue, MD, and Michael Tharp, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This 17 year old Hispanic female presented to the dermatology clinic for evaluation of multiple dark lesions on her tongue for at least 10 years, gradually increasing in number over that time. The patient's primary doctor was concerned about the increase in the number of lesions and was unsure of their significance. The patient was not concerned about the lesions and they were not symptomatic. She denied prior injury to the oral cavity, a history of dental hardware, pain, burning, and bleeding of the lesions. She denied halitosis, dysguesia, and the prolonged intake of oral antibiotics or bismuth.

PAST MEDICAL HISTORY

None

MEDICATIONS

Ibuprofen

ALLERGIES

No known drug allergies

FAMILY HISTORY

No skin cancer or melanoma. No known blood relatives with similar lesions.

PHYSICAL EXAM

Dorsal and anterolateral tongue with medium brown papules with areas of sparing anteriorly. No dental, gingival, buccal, labial, or palatal hyperpigmentation noted. No erosions or ulcers. Dentition intact without visible caries or implants.
Total mucocutaneous exam revealed a benign nevus pattern. No lesions were suspicious for melanoma.

REVIEW OF SYSTEMS

Negative

HISTOPATHOLOGY

Not performed

DIAGNOSIS

Pigmented Fungiform Papillae of the Tongue

TREATMENT AND COURSE

No treatment was indicated. The lesions remain stable and have not progressed.

DISCUSSION

Pigmented fungiform papillae of the tongue first were described by Leonard in 1905 as a possible sequela of parasite infection by *Ankylostoma duodenale*. Subsequent prevalence studies, mostly in African, Caribbean, and Asian populations have demonstrated a prevalence varying from 0.4 % to 30 %, with some studies showing a slightly increased prevalence in females. It has been observed across a broad range of ages from 2 years to 83 years, though usually is evident by the end of the second decade. A positive association has been suggested between prevalence of pigmented fungiform papillae of the tongue and darker skin types. Rarely, it has been reported in Caucasian, Hispanic, and Ashkenazi Jewish individuals. Histologic evidence of pigmented fungiform papillae of the tongue has been shown in whites in the absence of clinical evidence of pigmentation.

The tongue surface has three different type of papillae - filiform, fungiform, and circumvallate. Filiform papillae cover the dorsal surface of the tongue and are the smallest and most numerous. Fungiform papillae are confined to the anterior two thirds of the tongue as well as the lateral tongue and are larger and less numerous than filiform papillae. Circumvallate papillae are confined to the posterior third of the tongue and are the largest and least numerous. A fourth type of papillae, foliate papillae are found on the base of the tongue.

Three types of pigmented fungiform papillae of the tongue have been described, based on distribution. Type I pigmented fungiform papillae of the tongue describes a cluster of pigmented fungiform papillae on the anterolateral or tip of the tongue. In type II pigmented fungiform papillae of the tongue, 3 to 7 affected papillae are randomly distributed. Type III pigmented fungiform papillae of the tongue involves all of the fungiform papillae on the dorsal tongue.

Histologically, melanin is observed within macrophages in the papillary dermis in the absence of evidence of inflammation. In conjunction with the acquired nature of the condition, the microscopic evidence raises the possibility of a preceding period of temporary inflammation leading to the condition.

The majority of individuals with pigmented fungiform papillae of the tongue are healthy. Case reports describe its occurrence with systemic diseases including hemochromatosis, iron deficiency, pernicious anemia, icthyosis linearis circumflexa, scleroderma, Peutz Jeghers, and Addison disease. Our patient did not have evidence of any of these disorders.

Heavy metal salts and amalgam tattoo also can lead to tongue pigmentation. Very rarely, melanoma of the tongue occurs. A careful history, review of systems, and astute physical exam can help differentiate these other disorders. If diagnostic uncertainty remains, it can be clarified with laboratory and histologic evaluation.

Pigmented fungiform papillae of the tongue are considered a normal variant of lingual pigmentation that occur more commonly in individuals with darker skin pigment. It should be included in the differential of acquired focal hyperpigmentation of the tongue and may prevent unwarranted invasive diagnostic procedures.

REFERENCES

1. Das, Prasenjit, N Kumar, A Ahuja, J Ayushi, R Ray, C Sarkar, and SD Gupta. Primary malignant melanoma at unusual sites: and institutional experience with review of literature. Melanoma Research 2010; 20: 233-239.

2. Romiti, Ricardo, and LM De Medeiros. pigmented fungiform papillae of the tongue. Pediatric Dermatology 2010; 27: 398-399.
3. Scarff, Catherine, and R Marks. Pigmented fungiform papillae on the tongue in an Asian man. Australasian Journal of Dermatology 2003; 44: 149-151.
4. Koplon, Burton, and HJ Hurley. Prominent pigmented papillae of the tongue. Archives of Dermatology 1967; 95: 394-396.
5. Dummett, Clifton, and G Barens. Oromucosal pigmentation: an updated literary review. Journal of Periodontology 1971; 42: 726-736.
6. Pehousehek, James, and S Norton. Black taste buds. Archives of Family Medicine 2000; 9: 219-220.
7. Millington, GWN, and S N Shah. A case of pigmented fungiform lingual papillae in an Indian woman. Journal of the European Academy of Dermatology and Venereology 2007; 21: 705.
8. Holzwanger, Jay Marc, R Rudolph, and C Heaton. Pigmented fungiform papillae of the tongue: a common variant of oral pigmentation. International Journal of Dermatology 1974; 13: 403-408.
9. Leonard TMR. Ankylostomiasis or uncinariasis. *JAMA.* 1905;45:588-594.

CHICAGO DERMATOLOGIC SOCIETY **CASE #18**

Presented by Mark Romanelli MD, and Arthur Rhodes MD, MPH
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This 5 year old African American male presented to the dermatology clinic for evaluation of lesions on the trunk, upper extremities, and lower extremities for 1 month. The lesions were persistent, appearing first on the chest and subsequently on the trunk, upper extremities, and lower extremities over one month. They were pruritic to the point of sleep disturbance. Hydrocortisone ointment 2.5% was attempted for 1 month without improvement. The patient had not been sick and had no sick contacts prior to the onset of his lesions. Full review of systems was otherwise unremarkable. Skin care included bubble baths, soap to entire body, and washcloth scrubbing.

PAST MEDICAL HISTORY

Autism
Attention deficit hyperactivity disorder (ADHD)

MEDICATIONS

Guanfacine (Tenex, Intuniv) 1.5 mg daily started 4 months prior to presentation

ALLERGIES

No known drug allergies

FAMILY HISTORY

Atopic dermatitis
Asthma

PHYSICAL EXAM

On the trunk, upper extremities, and lower extremities were scattered, 5-30 mm, dark brown and pink, oval and annular plaques with slight scale, most numerous on the trunk. Follicular prominence was noted. Neither bullae nor crusting lesions were observed. No mucosal or nail lesions were observed. Total mucocutaneous examination was otherwise unremarkable.

REVIEW OF SYSTEMS

Negative

HISTOPATHOLOGY

Lichenoid lymphocytic infiltrate with interface dermatitis and pigment incontinence at the dermal-epidermal junction.

DIAGNOSIS

Lichenoid drug eruption due to guanfacine.

TREATMENT AND COURSE

The biopsy was delayed due to guardianship issues. Instruction on skin care was given. Hydrocortisone ointment 2.5% and hydroxyzine for 2 months, followed by 10% liquor carbonis detergens in aquaphor for 1 month were prescribed without relief. Once the biopsy was obtained and results were interpreted, guanfacine was discontinued. Triamcinolone ointment 0.1% for 2 weeks was prescribed but not used.

Narrow band UVB therapy was started, but stopped after one treatment due to the guardian's concerns of adverse effects on her skin while she accompanied the patient in the UVB light treatment chamber. Two weeks after discontinuation of the suspected medication, pruritus improved. Hydrocortisone ointment 2.5% BID was resumed for 6 weeks with improvement of pruritus. One month later, the patient reported no pruritus and no active lesions. Hyperpigmented macules and patches remained. The patient has not returned for further treatment.

DISCUSSION

Lichen planus is believed to be a T-cell mediated response to altered self antigens on basal keratinocytes. While many cases are idiopathic, viruses, vaccinations, dental hardware, graft versus host disease, and medications reflect some of the known causes of this condition. Skin and mucosae can be affected, with a minority of patients having lesions limited to the oral mucosae.

Lichenoid drug eruptions can be caused by a wide range of agents. Some of the most common include antibiotics, antiparisitics, antidepressants, antipsychotics, anticonvulsants, antihypertensives, nonsteroidal anti-inflammatory drugs, and metals. While withdrawal of the offending drug permits gradual resolution of the condition, some patients have improved without discontinuation of the drug, while others have experienced intermittent recurrences. Furthermore, rechallenge with the suspected drug does not always induce a recurrence of the condition. The latency period can vary widely, from weeks to years after the initiation of the drug, with certain drugs having a more narrowly defined latency period. Similarly, the time to improvement or resolution after discontinuing a drug can vary from months to years.

Clinically, the appearance of a lichenoid drug eruption can resemble classic idiopathic lichen planus. While no single finding is pathognomonic, there can be clinical and histologic clues that may help in differentiation:

	Idiopathic Lichen Planus	**Lichenoid Drug Eruption**
Mean Onset Age	50 years	66 years
Distribution	Flexural wrists and forearms, genitals, presacrum	Generalized with sparing of typical sites
Morphology	Planar violaceous shiny polygonal papules and plaques	Psoriasiform or pityriasis rosea like
Wickham Striae	Frequent	Rare
Mucosal Involvement	Frequent	Rare
Residual Hyperpigmentation	Rare	Frequent
Photodistribution	Rare	Frequent
Histopathologic findings	Eosinophils rare Dense lymphocytic band infiltrate	Eosinophils, plasma cells +/- deep infiltrate Cytoid bodies Focal parakeratosis Focal interruption of granular layer

Adapted from Bolognia

Guanfacine (Tenex, Intuniv) is an alpha$_{2\alpha}$ adrenergic agonist approved for the treatment of hypertension and attention deficit hyperactivity disorder in the pediatric population. In addition, it is used to treat symptoms of Tourette syndrome and post traumatic stress disorder.

There have been 5 reports of dermatologic reactions in children likely due to this drug; 3 specified as rash generalized and 2 as rash macular.

Autism and ADHD are being diagnosed at an increasing rate in the general population. The estimated worldwide prevalence of autism spectrum disorders is estimated at 6 per 1000 children, while that of ADHD in worldwide systematic reviews varies from 5% to 10%. Pharmacologic therapies for these disorders provide symptomatic improvement to varying degrees, prompting therapeutic trials of multiple drugs in some patients. In addition to trial treatments for more than one type of medication, the treatment of comorbidities associated with these conditions may increase the possibility of exposure to multiple drugs and drug interactions affecting metabolism.

Lichenoid drug eruptions may or may not resemble classic lichen planus. With the increasing prevalence of autism spectrum disorders as well as the increased exposure of these children and children with ADHD to systemic drug therapies, the possibility of cutaneous reactions to drugs may similarly increase. When suspected, a detailed drug history extending more than a few months prior to the onset of lesions, and a careful physical examination for the distinguishing features of lichenoid drug eruptions may aid in the diagnosis.

REFERENCES

1. Polanczyk, Guilherme, and LA Rohode. Epidemiology of attention-deficit/hyperactivity disorder across the lifespan. Current Opinion in Psychiatry 2007: 386-392.
2. Faras, Hadeel, N Al Ateeqi, and L Tidmarsh. Autism spectrum disorders. Annals of Saudi Medicine 2010; 30: 295-300.
3. Scahill, Larry, PB Chappell, YS Kim, RT Schultz, L Katsovich, E Shepherd, AFT Arnsten, DJ Cohen, FJ Leckman. A placebo controlled study of guanfacine in the treatment of children with tic disorders and attention deficit hyperactivity disorder. American Journal of Psychiatry 2001; 158: 1067-1074.
4. Bolognia, Jean, J Jorizzo, and R Rapini. Lichen planus and lichenoid dermatoses. Dermatology. Dermatology. 2nd Edition. Spain: Elsevier; 2008. ExpertConsult Web site. Available at http://www.expertconsult.com. Accessed February 27, 2010.
5. LexiComp. Guanfacine: drug information. In: UpToDate. Basow, DS (Ed). UpToDate, Waltham, MA. 2011.
6. Boyd, Alan, and KH Neldner. Lichen planus. Journal of the American Academy of Dermatology. 1991; 25: 593-619.
7. Halevy, Sima and A Shai. Lichenoid drug eruptions. Journal of the American Academy of Dermatology. 1993; 29: 249-255.
8. Weedon, David. The lichenoid tissue reaction. International Journal of Dermatology. 1982; 21: 203-206.
9. Van den Haute, V, JL Antoine, and JM Lachapelle. Histopatholgical discriminant criteria between lichenoid drug eruptions and idiopathic lichen planus: retrospective study on selected samples. Dermatologica. 1989; 179: 10-13.
10. MM Black. Lichen planus and lichenoid eruptions. In: A Rook, DS Wilkinson, FJG Ebling, et al., (Ed). Textbook of Dermatology. 4th Edition. Oxford: Blackwell. 1986: 1665-1685.