Chicago Dermatological Society

February 2010
MONTHLY EDUCATIONAL CONFERENCE

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, February 17, 2010
Donald E. Stephens Convention Center
Rosemont, IL

Conference Host:
Division of Dermatology
Stroger Cook County Hospital
Chicago, Illinois

Program

Venue Information

STEPHENS CONVENTION CENTER
5555 N. River Road; Rosemont, IL
Registration – Ballroom 1, First Floor, Conference Center

- Committee meetings
- Slide & poster viewing
- Lectures, business meeting & case discussions
- Lunch
- Exhibitors

Committee Meetings

8:00 a.m.	CDS Plans & Policies Committee
9:00 a.m.	IDS Board of Directors

Program Activities

9:00 a.m.	Registration for all attendees *Outside Ballroom #1, first floor of the Conference Center*
9:00 a.m. - 10:00 a.m.	*RESIDENT LECTURE – Ballroom #2* "Problem Psoriasis" – *Mark Lebwohl, MD*
9:30 a.m. - 10:45 a.m.	*CLINICAL ROUNDS* Poster viewing – *Ballroom #14* Slide viewing – *Ballroom #14*
10:45 a.m. - 11:45 a.m.	*GENERAL SESSION - Ballroom #2* *Sidney Barsky Lecture:* "Great Cases" – *Mark Lebwohl, MD*
11:45 a.m. - 12:15 p.m.	Lunches & visit with exhibitors
12:15 p.m. - 12:30 p.m.	CDS Business meeting – *Ballroom #2*
12:30 p.m. - 2:30 p.m.	Case Discussions – *Ballroom #2* Moderator: Warren Piette, MD; *Chair, Department of Dermatology; Stroger/Cook County Hospital* Cases presented by Stroger/CCH Residents
2:30 p.m.	Meeting adjourns

Next meeting – Wednesday, April 21, 2010; Stephens Convention Center, Rosemont

Future Meeting Schedule – check the CDS meeting calendar on our website:
www.ChicagoDerm.org

Guest Speaker

Sidney Barsky Lecture

Mark Lebwohl, MD

Professor and Chairman, Department of Dermatology,
The Mount Sinai School of Medicine; New York, NY

Dr. Mark Lebwohl graduated summa cum laude from Columbia College in 1974 and graduated from Harvard Medical School in 1978. He completed residencies in internal medicine and dermatology, both at Mount Sinai.

Dr. Lebwohl has been practicing dermatology since 1983. He is professor and chairman of the Department of Dermatology of The Mount Sinai School of Medicine. Dr. Lebwohl has served as president of the New York Dermatological Society, the Manhattan Dermatologic Society, and the New York State Society of Dermatology, and as chairman of the Dermatology Section of the New York Academy of Medicine. Dr. Lebwohl has served as chairman of the Psoriasis Task Force of the American Academy of Dermatology, and has directed the AAD's annual Psoriasis Symposium, Diagnostic Update Symposium and Therapeutics Symposium. He was a member of the Scientific Assembly Council, and chaired Academy 2001 in California and the AAD annual meeting in Washington, D.C. in 2004. He was elected to the Board of Directors of the AAD for 2010-2014.

Dr. Lebwohl is chairman of the Medical Board of the National Psoriasis Foundation. He is the founding editor of Psoriasis Forum as well as medical editor of the bulletin of the National Psoriasis Foundation, Psoriasis Advance. He is on the editorial board of the Journal of the American Academy of Dermatology and was editor of the Dermatology Section of Scientific American Medicine, now called ACP Medicine. Dr. Lebwohl has chaired numerous symposia and has written, edited, or co-edited several books including the first atlas devoted entirely to cutaneous manifestations of systemic disease, and the leading book on dermatologic therapy, Treatment of Skin Disease. The second edition of The Skin and Systemic Disease has been published in English and in French, and English, Portuguese, and Polish versions of Treatment of Skin Disease have been published. Other books include Difficult Diagnoses in Dermatology, Psoriasis, Mild-to-Moderate Psoriasis and Moderate-to-Severe Psoriasis. He has authored or co-authored over 500 publications including peer-reviewed articles, invited articles and book chapters. Dr. Lebwohl is actively involved in clinical trials of many new dermatologic treatments.

Educational Items

Course Director: Benjamin Dubin, MD

Target Audience: Practicing dermatologists, dermatology residents and fellows

Objectives: At the conclusion of this learning activity, the participant should be able to:

1. Define the clinical features of pyoderma gangrenosum.
2. Discuss the differential presentations of Lyme disease.
3. Interpret the lessons learned from cases presented by the residents with respect to dermatological conditions and general medical impact on the patent.

Continuing Education Credit

Chicago Dermatological Society

"Chicago Dermatological Society Monthly Conference"

February 17, 2010 *Rosemont, Illinois*

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

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

Link address to evaluation form:

www.yourcesource.com/eval?act=399!02172010

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**.

GOAL / PURPOSE

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

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:

1. Define the clinical features of pyoderma gangrenosum.
2. Discuss the differential presentations of Lyme disease.
3. Interpret the lessons learned from cases presented by the residents with respect to dermatological conditions and general medical impact on the patient.

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.

Colorado Foundation for Medical Care designates this educational activity for a maximum of **4.75** ***AMA PRA Category 1 Credits™*****.** Physicians should only claim credit commensurate with the extent of their participation in the activity.

CFMC has no financial responsibility for this activity.

DISCLOSURE STATEMENTS

The following faculty member has disclosed that they have the following financial relationships:

Mark Lebwohl, MD -	Speakers Bureau for:	Consultant for:
	Abbott Laboratories	DermiPsor
	Amgen	Graceway
	Astellas	Megen Biosciences
	Centocor	NeoStrata
	Galderma	Pharmaderm
	Genentech	Sanofi-Aventis
	GlaxoSmithKline	Taro
	Novartis	
	Stiefel	
	Triax	
	Warner Chilcott	

All other members of the faculty and planning team have nothing to disclose nor do they have any vested interests or affiliations. **It is the policy of the Chicago Dermatological Society and Colorado Foundation for Medical Care (CFMC) that the faculty discloses real or apparent conflicts of interest relating to the topics of the educational activity, and also discloses discussions of off-label uses of drugs and devices before their presentation(s).**

Conference Supporters

Chicago Dermatological Society gratefully acknowledges the support of

Unrestricted educational grant provided to our conference by GRACEWAY PHARMACEUTICALS, LLC

And the continued support of our participating conference exhibitors.

TABLE OF CONTENTS

**We extend our sincere thanks to
Dr. Darryl Bronson and Dr. Jesse Jiang
for their review of the histopathology
from these cases.**

Case #1

Presented by August A. Natalie, MD and Warren Piette, MD

History of Present Illness:
This 26 year-old homosexual man was admitted to the hospital with a two day history of high grade fevers, chills, malaise, nausea, and 20-25 episodes of non-bloody vomiting. He denies headache, neck pain, cough, abdominal pain, or dysuria. He denies any sick contacts or recent travel. HIV testing six months prior was negative. In the emergency department, he was found to be hypotensive with a systolic blood pressure of 60 mm Hg, which improved to 100 mm Hg after four liters of intravenous normal saline. He was given 2 grams of intravenous ceftriaxone in the ED before transfer to the MICU.

Past Medical History:
None

Medications/Allergies:
None/NKDA

Social History:
Homosexual male with multiple sexual partners
Tobacco (+), Alcohol (+), IV or recreational drug use (-)

Physical Exam:
Vital signs: T 102.9 BP 100/63 HR 142 RR 36 O_2 92% 4L
Ears: dusky blue, cool to touch
Left eye: conjunctival hemorrhages
Abdomen: scattered petechial hemorrhages
Lower extremities: non-inflammatory retiform purpura extending from lower abdomen to dorsal feet

Laboratory Data:
The following were abnormal or positive:

Bicarbonate	18 mEq/L	[23-31 mEq/L]
Anion gap	16	
BUN	26 mg/dL	[8-20 mg/dL]
Creatinine	2.3 mg/dL	[0.6-1.4 mg/dL]
Albumin	2.5 g/dL	[3.8-5.2 g/dL]
LDH	309 U/L	[85-210 U/L]
Total protein	4.0 g/dL	[6.4-8.3 g/dL]
White blood cell	3.5 k/µL	[4.2-10 k/µL]
Bands %, manual	28%	[0-9 %]
Platelet	74 k/µL → (Day 2) 22 k/µL	[185-395 k/µL]
Prothrombin time	32.0 secs → (Day 2) 22.1 secs	[12.3-14.7 secs]
Partial thromboplastin time	136.9 secs → (Day 2) 56.3 secs	[25.3-36.1 secs]
Lactate	6.40 mmol/L	[0.90-2.47 mmol/L]
Troponin-I	1.5 ng/mL → (Day 2) 222 ng/mL	[0.000-0.034 ng/mL)
HIV 1/2 antibody screen	Nonreactive	
Serum cortisol	52.30 µg/dL	
Protein C function	58% (24 hours after last lesion)	[80-164 %]

Case #1 continued

Diagnostic Procedures and Tests:

1/6/09 Gram stain- blood (within two hours of arrival): gram negative diplococci
1/6/09 Blood cultures: positive, aerobic bottle, *Neisseria meningitidis* (Group C), beta-lactamase negative
1/6/09 Chest X-ray: lung apices/bases with prominent vascular markings, blunting of costophrenic angles

Histopathology:

1/6/09 Left thigh: thrombi within small vessels in the superficial dermis; gram stain negative

Diagnosis:

Purpura fulminans (microvascular occlusion), acute infectious type, secondary to *Neisseria meningitides* (group C) sepsis with presumed protein C depletion

Treatment and Course:

In the MICU, the patient's condition worsened. His antibiotic coverage was broadened to vancomycin, ceftriaxone, azithromycin, and oseltamivir. He developed respiratory distress requiring intubation and sedation; the septic shock required three vasopressors (norepinephrine, dopamine, and vasopressin) and continued IV fluids. Shortly after, he became anuric with progressive renal failure. On hospital day two, he developed ventricular tachycardia which degenerated into asystole. Cardiopulmonary resuscitation was unsuccessful.

Discussion:

Purpura fulminans (PF) means something different to everyone who uses the term. This patient developed generalized intravascular thrombosis secondary to *N. meningitides* sepsis. The two most relevant mechanisms for developing dermal thrombosis in the setting of sepsis are: 1) consumptive coagulopathy leading to severe protein C depletion (usually <20%), or 2) triggering an underlying antiphospholipid antibody syndrome. This patient had evidence of a consumptive coagulopathy (elevated PT and PTT, thrombocytopenia, and histologic evidence of intravascular clot), which suggests that protein C depletion played an important role in his striking presentation. His protein C level was drawn 24 hours after the last lesion.

PF has a high associated mortality rate (>50%) owing to multi-organ dysfunction. Our patient had evidence of myocardial infarction, most likely secondary to intracoronary thrombosis, which led to his fatal arrhythmia.

There are three forms of this disease that are classified by the triggering mechanisms which include neonatal PF (hereditary deficiency of protein C or S), post-infectious PF (acquired antibody interferes with protein S function, usually children after varicella and/or streptococcal infection), and sepsis-related PF (acute severe infection, usually gram negative). The most common form is the sepsis-related PF. In adults, meningococcal sepsis is the most common etiology of sepsis-related PF, followed by pneumococcal sepsis. Physical examination usually reveals diffuse noninflammatory retiform purpuric patches accompanied by hemorrhagic bullae, epidermal necrosis, and distal extremity gangrene.

Successful management is facilitated by early diagnosis, aggressive antibiotic treatment, systemic organ support, and prompt surgical consultation. Areas of full thickness skin loss are expected in patients who survive. Streptococcal-induced PF results in more extensive amputations compared with other infections, with a mean of three amputations per person. Activated protein C appears to be a promising therapeutic option for neonatal protein C depletion and presumably for sepsis-related protein C depletion.

References:

1. Edlich RF, Cross CL, Dahlstrom JJ, Long WB, 3rd. Modern concepts of the diagnosis and treatment of purpura fulminans. *J Environ Pathol Toxicol Oncol* 2008; 27:191-6.
2. Betrosian AP, Berlet T, Agarwal B. Purpura fulminans in sepsis. *Am J Med Sci* 2006; 332:339-45.

Case #2

Presented by Victoria Negrete, MD and Jerry Feldman, MD

UNKNOWN #1

Fifty-three year-old Hispanic woman with 5-year history of asymptomatic solitary linear lesion on the 5th left fingernail

Case #3

Presented by Rachel Neems Pritzker, MD and Warren Piette, MD

History of Present Illness:
A 35 year-old African American male was admitted to the general medical floor for evaluation of progressive lesions which first appeared on his face and scalp 4 months prior as red and tender papules. Within 1-2 weeks the rash involved his entire body including the palms and soles. The lesions are mildly pruritic. The patient recalls helping his sister clean her basement at the time of the original outbreak. Associated symptoms include fevers and transient migratory joint pain. He also reports a morning stiffness of the large joints for the past five months that is improved with ibuprofen. He has no history of similar lesions and denies a history of genital ulcers or other sexually transmitted diseases.

Past Medical History:
Eczema, bronchitis

Medications/Allergies:
None/ NKDA

Family History:
He has a sister with SLE who died at 22 years-old from unknown complications of her disease.

Review of Systems:
Positive findings include fevers, chills, productive cough, shortness of breath, and nausea. He denies urinary urgency, dysuria, hematuria, headaches, and altered mental status.

Physical Exam:
Face: thick pink plaques on eyebrows, cheeks, and ears with fine scale
Arms, legs, and trunk: many diffuse pink hyperkeratotic papules, some coalescing into round pink scaling plaques
Palms and soles: rounds, edematous red papules, some with slight central depression and darkening

Laboratory Data:
The following laboratory values were abnormal or positive:

WBC	2.4 k/µL	[4.2-10.0k/µL]
Platelets	86 k/ µL	[186-395 k/ µL]
UA protein	50 mgs	[negative]
UA blood	trace	[negative]

The following were normal or negative:
HIV, Chest x-ray

Histopathology:
8/30/09 Left arm: interface dermatitis, vacuolar type, with keratin plugging, superficial and deep perivascular inflammatory infiltrate of monocytic cells, and dermal mucinosis. No organisms identified on GMS, PAS or Warthin-Starry stains.

Diagnosis:
Disseminated discoid lupus erythematosus.

Treatment and Course:

The patient was given triamcinolone 0.1% ointment twice daily to all affected areas. Further testing included an ANA and RPR. The initial RPR and repeated RPR diluted for prozone effect was negative, and ANA titer was positive; >1:160, speckled pattern. Subsequently, the patient was lost to follow up by both dermatology and rheumatology before further treatment was initiated.

Discussion:

Cutaneous lupus erythematousus (LE) has extensive variation on clinical presentation. Gilliam first created the widely used systematic approach of categorizing cutaneous LE within the three broad clinical subsets: chronic cutaneous lupus erythematosus (CCLE), subacute cutaneous lupus erthematosus (SCLE), and acute cutaneous lupus erythematosus (ACLE). Within these subsets are different combinations of morphology, configuration, and distribution. In this case, the hundreds of lesions and the generalized distribution, including the palms and soles, made the initial differential diagnosis very broad, including several diffuse papulosquamous diseases.

Discoid lupus erythematosus (DLE) is classically characterized by sharply demarcated round (discoid or disc-like) erythematous scaling plaques with follicular plugging, dyspigmentation, and scarring upon resolution. The distribution of localized DLE is most often on the face, neck and scalp, though it can less commonly involve mucosal surfaces. Generalized DLE is present both above and below the neck. In the generalized form, it is uncommon to have lesions below the neck without lesions above the neck as well.

The generalized form of DLE is important to recognize as these patients are more likely to have systemic disease than patients with localized DLE. Patients with localized DLE have a 50% chance for remission; this number drops to 10% with generalized lesions. Widespread DLE, periungual telangiectasias, persistently elevated erythrocyte sedimentation rates, leukopenia and positive antinuclear antibody titers are all factors of DLE associated with progression to systemic disease. Though variable, most of these patients will develop the ACR criteria for SLE within 1-3 years from the time of diagnosis of cutaneous DLE. Due to the differences in disease progression and prognosis, close clinical follow-up of generalized DLE patients is indicated.

Generalized DLE can rarely present with lesions on the palms and soles, which was evident in our patient. This small subset of generalized DLE patients may be a diagnostic challenge, as there are no appendageal structures on the palms and soles. These lesions are usually painful and erosive. There are no reported clinical or serologic differences between these patients and patients with generalized DLE without palm and sole involvement except that theses particular lesions may be more resistant to treatment.

References:

1. Tebbe B. Clinical course and prognosis of cutaneous lupus erythematous. *Clin Dermatol*. 2004 Mar-Apr; 22(2):121-4.
2. Callen JP. Cutaneous lupus erythematosus: A personal approach to management. *Australas J Dermatol*. 2006 Feb; 47(1):13-27.
3. Goyal S, Nousari HC. Treatment of resistant discoid lupus erythematosus of the palms and soles with mycophenolate mofetil. *J Am Acad Dermatol*. 2001 Jul; 45(1):142-4.

Case #4

Presented by Warren Piette, MD

UNKNOWN #2

Sixty-nine year-old Ukrainian man with 40-year history of recurrent red patches on the legs and 2-year history of leg ulcers.

Case #5

Presented by Joerg Albrecht, MD, Jerry Feldman, MD, and Christina Steil, MD

History of Illness:
This is a 58 year-old female that presents for evaluation of asymptomatic facial lesions which have developed over 2 to 3 years.

Past Medical History:
Hyperparathyroidism, parathyroidectomy, osteopenia, hypercholesteremia, cholescystectomy

Family history:
Her mother, who developed renal cell carcinoma at age 29, had similar skin lesions which were never biopsied. At age 64 the mother was found to have cancer of the other kidney with death likely from lung metastasis. The patient has 6 brothers and one sister. Her sister and one brother have similar skin lesions.

Medications/Allergies:
Calcium, vitamin D, pravastatin, fosamax/ NKDA

Physical Examination:
Forehead: multiple 1-2 mm flesh-to-white colored papules
Medial cheeks: approximately 15 flat, skin colored papules of the same size, which spare the nose and nasolabial folds. Inferior to the breast, there are multiple skin colored pedunculated and sessile papules

Laboratory Data:
PCR amplification of Exon 4-14 of the FLCN (folliculin) genes positive for a single base insertion between nucleotides 1285 and 1286 of the FLCN gene. This mutation has previously been reported in a patient with Birt-Hogg-Dube Syndrome; it results in a shift of the translational frame of the encoded mRNA from the encoded amino acid position 429 to a premature stop codon at position 455.

Histopathology:
6/09 Left cheek: fibrofolliculoma, but also consistent with trichodiscoma and fibrofolliculoma. The biopsy consists of a polypoid nodule that has an unremarkable epidermis. Within the dermis there is a dense fibrous sheath surrounding the hair follicle.

Radiology:
6/09 CT chest/abdomen/pelvis: the lungs have cysts that are smaller than 1 cm in the lower lobes and a small bleb in the right lower lobe. There is minimal intra- and extrahepatic biliary dilatation; there are several 5mm lesions in the liver and multiple 1cm lesions in both kidneys suggestive of cysts.

Diagnosis:
Birt-Hogg-Dubé-Syndrome

Treatment and Course:
The patient was referred to a geneticist, pulmonologist and urologist. The urologist plans to follow her at regular intervals to screen for renal cancer.

Case #5 continued

Discussion:

Birt-Hogg-Dubé syndrome is an autosomal dominant disease that was first described in 1977 based on a family with "fibrofolliculomas with trichodiscomas and achrocordons". It took 16 years until the association with renal cell cancer was described by Roth et al., which arguably is the most clinically relevant aspect of the disease. Birt-Hogg- Dubé syndrome is now defined as a germline mutation of the folliculin (FLCN) gene, and characterized by fibrofolliculomas, pulmonary cysts, spontaneous pneumothorax and renal cell cancer.

Patients with Birt-Hogg- Dubé syndrome develop multiple white to skin colored papules in the midface, neck, oral cavity and upper trunk in their 20s. These have to be biopsied to confirm the diagnosis of fibrofolliculomas; sometimes a single biopsy may be insufficient to make the diagnosis with certainty. There are multiple dermatological syndroms that feature firm facial papules, importantly Cowden's syndrome, Tuberous Sclerosis and Basaloid Follicular Hamartoma.

In one large series about 27% of the patients with Birt-Hogg-Dubé syndrome developed renal tumors often multiple and bilateral, however, some families do not seem to develop these tumors at all. In all likelihood there are several classes of FLCN mutations with different associated risks, but these cannot be distinguished as yet; thus all patients with Birt-Hogg- Dubé syndrome should be monitored for renal cell carcinoma. However, there are no generally accepted monitoring guidelines. The earliest renal cell carcinoma has been reported at 20 years with tumors still developing in the 70's. Careful monitoring should start in the late teens particularly if early cancer has been reported. This is often before skin lesions have developed. Ultrasound, which would be the most convenient screening modality is not sensitive enough to discover small carcinomas (less than 2 cm) but for reasons of practicality is still commonly used. Due to the extended monitoring period, CT scanning has an unacceptable risk of radiation induced cancer, leaving only renal MRI as an acceptable, albeit expensive, long-term screening option. Different screening methods for Birt-Hogg-Dubé syndrome will need to be monitored and compared as the number of discovered families increases to establish efficient and practical monitoring guidelines. Treatment of renal cell carcinoma should be nephron sparing due to the risk of the development of further tumors, but otherwise consists largely of standard therapy.

The lung is another organ that is involved in 80% of patients most commonly with multiple cysts, which in one series lead to pneumothorax in 24% of the patients. Surprisingly the risk seems to decrease with age. In general asymptomatic patients do not need to be screened, and have no restrictions for air travel. However, CT of the lung may be reasonable before general anesthesia and patients who want to go into piloting or deep sea diving should be evaluated by a pulmonologist. Treatment of pneumothorax is the same as for spontaneous pneumothroax. Smoking should be discouraged.

A good reliable and regularly updated source for up to date information on diagnosis and monitoring of Birt-Hogg-Dubé syndrome and other genetic syndromes is the NIH website, the address of which is given below.

References:

1. Menko FH, van Steensel MAM, Giraud S, Friis-Hansen L, Richard S, Ungari S, Nordenskjold M, Hansen TV, Solly J, Maher E, on behalf of the European BHD Consortium. Birt-Hogg-Dube syndrome: diagnosis and management. *Lancet Oncology* 2009; 10; 1199-1206.
2. NIH gene reviews, http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=bhd#bhd.Diagnosis, accessed 12/18/2009.
3. Vincent A, Farley M, Chan E, James WD. Birt-Hogg-Dube syndrome: A review of the literature and the differential diagnosis of firm facial papules. *J Am Acad Dermatol* 2001; 49: 698-704.

Case #6

Presented by Lauren Fine, MD and Warren Piette, MD

UNKNOWN #3

Sixty-eight year-old Nigerian man with multiple, large, firm, ulcerated lesions on his right lower extremity for 1 month.

Case #7

Presented by Hal Weitzbuch, MD and Warren Piette, MD

History of Present Illness:
This 47 year-old HIV positive African American male presented to the emergency room with a three day history of fever and painful left sided facial edema. Initially the lesions were vesicular. The patient also reports discharge and pain from his left ear, along with left facial itching, and dysphagia. He states that he had similar episodes in the past, but none as severe. He denies a history of atopy.

Past Medical History:
Hypertension, syndrome of inappropriate antidiuretic hormone, hemorrhagic stroke (May, 2009)

Medications/Allergies:
Nifedipine, enalapril, amitriptyline, atazanavir, ritonavir, truvada/ penicillin allergy

Review of Systems:
The patient denies shortness of breath, chest pain, headache, visual disturbances, dysuria, hematuria.

Physical Exam:
Vitals: Blood Pressure 176/108 Heart Rate 120 Resp Rate 20 Temp 102.4 SaO2 96%
Left face: marked edema, especially of the palpebral fissure and external auditory meatus. There was yellow, crusty discharge at the external meatus. There is a large eroded plaque along beard line with yellow and brown crust and numerous erosions.
Tongue: sharply demarcated edema and erythema extending from midline fissure to left lateral aspect, including the tip
Bilateral submandibular lymphadenopathy is present. There was no facial weakness.

Laboratory Data:
The following were abnormal or positive:

White blood cell count	3.8 k/µL	[4.2-10 k/µL]
Lymphocytes	54.7%	[16.5-43.4%]
Neutrophils	28.6%	[45.4-75.1%]
CD4 count	373 cells/µL	[590-1,060 cells/µL]
HIV viral load	131 copies/mL	[0 copies/mL]
Wound culture	4+ coagulase negative *S. aureus*	

The following were normal or negative:
Herpes Simplex Virus (HSV) culture: no growth
Varicella Zoster Virus (VZV) culture: no growth

Radiology:
8/09 Sinus CT: right maxillary, frontal and right ethmoid cell sinusitis. An erosion of the left maxillary roof is suspicious for infection or cyst.

Histopathology:
8/10 Lip Tzanck smear: Multinucleate giant cells with eosinophilic inclusion bodies

Diagnosis:
Impetiginized zoster

Case #7 continued

Treatment and Course:

The patient responded well to a course of valacyclovir, levofloxacin, clindamycin, and topical bacitracin. The lesions resolved over the following week and the patient was lost to follow-up.

Discussion:

Herpes zoster (shingles) is a common infection in the US, caused by reactivation of the varicella zoster virus (VZV) in the dorsal root ganglion. VZV is a double-stranded DNA virus in the Human Herpesvirus family. Classically, shingles presents with unilateral distribution along a dermatome of grouped vesicles or pustules with pain. In most immunocompetent individuals, this disease runs an indolent course, however many complications may arise, especially among the elderly and immunocompromised. Impetigo, postherpetic neuralgia (PHN), scarring, and meningoencephalitis, pneumonitis, and hepatitis have been described. Particularly worrisome is involvement of the ophthalmic branch (V1) of the fifth cranial nerve, the trigeminal nerve. Ocular infection carries a high complication rate with blindness possible. It is important to recognize the Hutchinson sign of V1 involvement, which is the presence of vesicles on the tip of the nose. With external ear involvement, the Ramsay Hunt syndrome should be considered, which consists of facial palsy, neurologic symptoms, and occasional oral lesions. This is due to infection of the geniculate ganglion and possible cross infection of nearby nerves. Prompt treatment is necessary to decrease the chance of permanent hearing loss or paralysis.

Zoster infection along the mandibular branch of the trigeminal nerve (V3) has been well documented. However, there is scant literature describing tongue involvement. It is helpful to know the basic anatomy of the tongue in order to understand how the tongue might be involved with V3 infection. The twelfth cranial nerve (glossopharyngeal), controls the motor innervation of the entire tongue. The taste and general sensation of the posterior third of the tongue travels along the ninth cranial nerve (hypoglossal); while a small posteromedial portion of tongue sensation is carried by the tenth cranial nerve (vagus). The special gustatory sensation of the anterior two-thirds of the tongue is carried via the chorda tympani branch of the seventh cranial nerve (facial). Meanwhile, the lingual branch of V3 carries general sensation from the anterior two-thirds of the tongue. Thus, involvement of the lingual branch of V3 or the chorda tympani branch of the facial nerve will result in anterior tongue eruptions.

Treatment for zoster infection usually requires anti-viral, anti-inflammatory, and neurologic medication. Acyclovir is usually the drug of choice, dosed as 500mg by mouth daily for 5-7 days. For PHN, gabapentin or tricyclic antidepressants have been found to decrease duration of symptoms. Occasionally prednisone may be added to the regimen to prevent neuro-inflammation, and subsequent neuralgia. A vaccine is available as well, and is currently used as a prophylactic therapy against zoster for those at higher risk of complications. Additionally, as the live attenuated vaccine for VZV is administered to most infants there is an expected decrease in the number of future cases of shingles. However, it should remain high on any differential of a rash with unilateral dermatome involvement.

References:

1. McCrary ML, Severson J, Tyring SK. Varicella zoster virus. *J Am Acad Dermatol* 1999 Jul; 41(1):1-14; quiz 15-6.
2. Netter FH. Atlas of human anatomy. New Jersey: Icon Learning Systems; 2004. p.58, 112, 116-117.
3. Sweeney CJ, Gilden DH. Ramsay Hunt syndrome. *J Neurol Neurosurg Psych*. 2001 Aug; 71(2):149-54.
4. Andreoli TE, editor. Cecil essentials of medicine, 6th Edition. Pennsylvania: Saunders; 2004. P.880-881.

Case #8

Presented by Morayo Adisa, MD and Warren Piette, MD

History of Present Illness:
This is a 20 year-old African American female with a 2-month history of a worsening pruritic and burning, red scaly "rash" on her extremities, trunk and face. The rash initially started on her legs after working at a construction site where she was in contact with a lot of chemicals – type unknown. Since then, it has progressed to involve her trunk, arms and face. She was treated at an outside hospital with a two week course of diphenhydramine and topical steroids with no improvement.

Past Medical History:
Depression, asthma

Medications/Allergies:
None/ NKDA

Family History:
Depression, diabetes mellitus, hypertension

Review of Systems:
Malaise, myalgias, arthralgias, fevers, anorexia, difficulty walking and bearing weight, dysphagia (both solids and liquids), unintended weight-loss and headaches,

Physical Exam:
Alert and oriented but uncomfortable
Face: facial edema with reticulated bluish-to-brown plaques and few eschar-covered erosions
Bilateral ears: dark brown lichenified scaly plaques with some areas of overlying erosions
Extensor arms and legs: deep-red reticulated patches with some eschar-covered erosions
Negative proximal nail fold capillaroscopy
There were no mucosal lesions

Laboratory Data:
The following were abnormal or positive:

WBC	3.4 k/µL	[4.4-10.6 k/µL]
RBC	4.21 k/ µL	[3.75 -5.01 k/µL]
Hemoglobin	11.5 g/dl	[11.7-14.9g dl]
Hematocrit	35.0%	[34.9-44.3%]
Platelet	110/µL	[161-369/ µL]
MCH	27.3	[27.5-33.2]
RDW	18.8	[12.3 – 15.6]
Sodium	133 mg/dL	[135 -145 mg/dL]
Creatinine	1.6 mg /dL	[0.6-1.4 mg/dL]
LDH	889 U/L	[85-210 U/L]
AST	759 U/L	[0-40 U/L]
ALT	162 U/L	[5-35U/L]
Albumin	2.7 g/dL	[3.8-5.2 g/dL]
Alkaline Phosphatase	223 U/L	[50-120 U/L]
GGT	264 U/L	[3-60 U/L]
ANA screen	positive (Homogenous pattern)	[Negative]

Case #8 continued

ANA titer	>1:160	
Sed. Rate	77	[0- 17]
C3 Complement	<50	[88-201]
C4 complement	<6	[16-47]
Rheum. Factor	225	[-<20]
DS-DNA Ab	3.48	
Smith Antibody	4.48	
Ribonucleoprotein/Smith	3.82	
SSA-Ab	2.62	
SSB-Ab	5.62	
Hepatitis C Ab	Reactive	[Nonreactive]
CK	3402	[0-163]
Urine protein	121	[Negative]
Urine RBC	6-10	[Negative]
Schistocytes	2+	[Negative]

The following were normal or negative:
Anti-centromere antibodies, RPR, bilirubin-total & direct, HIV, hepatitis A & B

Diagnostic Procedures and Tests:
10/09 EMG and Nerve Conduction Study: abnormal
10/09 MRI/MRA Brain: there was diffuse supratentorial dural thickening and contrast enhancement reflecting pachymeningitis and mild diffuse cerebral and cerebellar atrophy.
There was no evidence of lupus cerebritis.

Histopathology:
10/09 Left deltoid muscle: active necrotizing myopathy with few lymphocytes and patchy distribution of myofiber degeneration and regeneration

Diagnosis:
SLE – Dermatomyositis Overlap

Treatment and Course:
She was started on intravenous methylprednisolone with plans to switch to oral prednisone after 3 days. She then developed waxing and waning neurological symptoms, hypoxemia and worsening of her thrombocytopenia, anemia and renal function on day 3 of admission. A diagnosis of thrombotic thrombocytopenic purpura (TTP) was made based on the constellation of clinical signs and symptoms of altered mental status, anemia, thrombocytopenia, renal failure and fevers. She was transferred to the ICU where she underwent plasmapharesis, along with azathioprine and systemic corticosteroids. Her skin lesions resolved while the hematological abnormality and mental status change improved with therapy.

Discussion:
TTP is a rare but life-threatening disorder characterized by the pentad of fever, microangiopathic hemolytic anemia, thrombocytopenia, fluctuating neurological signs and renal involvement. Some known causes of TTP include infection/Inflammation, drugs, pregnancy and ADAMTS13 deficiency (Genetic mutation or acquired antibodies). ADAMTS13 is a metalloproteinase which specifically cleaves von Willebrand factor and a deficiency of this enzyme lead to the presence of unusually large VWF multimers (UL-VWFMs) in the blood circulation. This leads to excessive platelet aggregation under high shear stress within the circulation along with microvasculature luminal narrowing.

Case #8 continued

Both SLE and TTP, share similar symptoms and signs such as anemia (due to hemolysis though more significant in TTP than in SLE), thrombocytopenia, CNS symptoms, renal insufficiency and fevers. Sporadic development of TTP has been reported in patients with SLE and other autoimmune diseases (rheumatoid arthritis, polyarteritis nodosa and Sjogren's syndrome), but the occurrence of TTP in these autoimmune conditions are not well characterized. A series of 56 reported cases of SLE and TTP shows a higher mortality rate amongst patients with a preceding SLE flare prior to the development of TTP development. Active SLE and renal involvement are major risk factors for the development of TTP. Similarly there are few (seven) reported cases of dermatomyositis or polymyositis complicated by TTP. The mechanism of the occurrence is thought to be similar to that of SLE and probably the other autoimmune connective tissue diseases. The cause of death is usually the TTP or superimposed infection.

ADAMTS13 activity is known to be significantly decreased in patients with connective tissue disease- related thrombo-angiopathy, regardless of the underlying disease. There are two phenotypes of ADAMTS13 activity in these patients. In a minority of patients, the deficient ADAMTS13 activity is caused by neutralizing auto antibodies (anti-ADAMTS13 IgG antibodies) while the majority have normal or moderately reduced enzyme activity. The patients reported to have severe deficiency of ADAMTS13 activity were patients with RA- and SLE- thrombo-microangiopathy and this was due to the presence of anti-ADAMTS13 IgG antibodies.

Patients with connective tissue diseases have a high susceptibility to forming thrombi. They have inherent underlying high vWF plasma levels secondary to inflammation. This, along with a deficiency or moderate-to-mild decrease of plasma ADAMTS13 activity leads to a high level of circulating large vWF multimers. They may also have impaired vascular endothelial function from vasculitis and narrowed vessel lumen from the proliferation of vascular endothelium, leading to a high shear stress with platelet aggregation and vascular plugging.

The complication of SLE or other autoimmune diseases with TTP is rare and can be easily missed with fatal results, so clinicians need to have a high index of suspicion to make a prompt diagnosis and initiate therapy.

References:

1. Matsuyama T, Kuwana M, Matsumotos M, Isonish A, Inokuma S, Fujimura Y. Heterogenous pathogenic processes of thrombotic microangiopathies in patients with connective tissue diseases. *Thromb Haemost*. 2009; 102(2):371-8.
2. Hamasaki K, Mimura T, Kanda H, Kubo K, Setoguchi K, Satoh T et al. Systemic lupus erythematosus and thrombotic thrombocytopenic purpura: a case report and literature review. *Clin Rheumatol.*2003 Oct; 22(4-5):355-8.
3. Kwok SK, Ju JH, Chos CS, Kim HY, Park SH. Thrombotic thrombocytopenic purpura in systemic lupus erythematosus : risk factors and clinical outcome : a single center study. *Lupus* 200 ; 18:16.
4. Letchumanan P, Ng HJ, Lee LH, Thumboo J. A comparison of thrombotic thrombocytopenic purpura in an inception cohort of patients with and without systemic lupus erythematosus. *Rheumatology* 200 ; 48: 399-403.
5. Musio F, Bohen EM, Yuan CM, Welch PG**.** Review of Thrombotic Thrombocytopenic Purpura in the setting of Systemic Lupus Erythemaotosus. *Seminars in Arthritis and Rheumatism* 1998; 28(1):1-19.

Case #9

Presented by August Natalie, MD and Warren Piette, MD

UNKNOWN #4

Twenty year-old female with painful and swollen umbilical nodule for 6 months

Case #10

Presented by Jordan Carqueville, MD and Warren Piette, MD

History of Present Illness:
This 50 year-old African American female, recently diagnosed with lupus erythematosus by a community physician, presented to our clinic with a 1-week history of a widespread, erythematous eruption on her back, arms and chest. The lesions were pruritic at the onset and then became tender to palpation. They are not exacerbated by sun exposure. There was no apparent precipitating event, no recent illness, and she did not start any new medications. Recently the eruption has worsened, as her skin was breaking down in the affected areas.

Past Medical History:
Lupus erythematosus, diabetes mellitus type 2

Medications/Allergies:
Glyburide, metformin/ NKDA

Review of Symptoms:
She occasionally had arthritis of the knees and toes. She denies fevers, chills, myalgias, headaches, visual changes, chest pain, shortness of breath, nausea, vomiting, diarrhea, sun sensitivity, dry eyes or dry mouth.

Physical Exam:
On the chest, arms, back and upper thighs are scattered, erythematous macules and 2-zone, dusky-red, targetoid plaques. Many plaques have central necrosis with blister formation; few have erosion. There are hyperpigmented plaques on the forehead. It spares the mucosa, lowers legs, palms and soles.

Laboratory Data:
The following data were abnormal or positive:

ANA screen +	SSA >8.0
ANA pattern speckled	SSB >8.0
ANA titer <1:160	

The following were normal or negative:
Complete blood count and differential, basic metabolic panel, liver function tests, thyroid function tests, hepatitis B and C, ESR, anti-DS DNA, anti-Sm antibody, rheumatoid factor, and C3/C4.

Histopathology:
3/09 Right shoulder: There is interface dermatitis with vacuolar degeneration and dyskeratosis throughout the epidermis. There is a superficial and focal deep perivascular inflammatory cell infiltrate of mostly lymphocytes.

Diagnosis:
Rowell Syndrome type SCLE

Treatment and Course:
A course of oral prednisone (20mg daily) and triamcinolone 0.1% ointment twice daily to affected areas was started, which resulted in significant improvement. At the two-week follow- up, she did not have any new lesions and there were no open erosions.

Case #10 continued

The prednisone was slowly tapered and she was started hydroxychloroquine 200mg twice daily. She was instructed to wear at least SPF 30 sunblock and wear sun protective clothing.

At 1-month follow-up, only post-inflammatory hyperpigmented patches remained. Tapering doses of prednisone were given for two more weeks. She has not developed any new erythematous, targetoid lesions in the last year.

Discussion:

Rowell syndrome was first described in 1963 by Rowell and colleagues as the coexistence of discoid lupus erythematosus and erythema multiforme with laboratory findings including a positive antinuclear antibody (ANA), rheumatoid factor (RF), and precipitation to a saline extract of human tissue (anti-Sj-T). The saline extract of human tissue is now thought to be analogous to anti-Ro (SS-B) and anti-La (SS-A) antibodies. Since then, there have been approximately 30 cases of Rowell syndrome reported in the literature, mostly occurring in middle-aged women and less often in younger women. The term has been loosely applied to any type of cutaneous lupus manifestation occurring concomitantly with erythema multiforme-type lesions with various serologies. While some believe that the occurrence of LE with erythema multiforme is mere coincidence, clinical features and immunologic serologies in multiple reported cases lead others to believe that this is a distinct syndrome.

Zeitouni et al. recently redefined Rowell syndrome by major and minor criteria. To make the diagnosis of Rowell syndrome, the patient should fulfill all three major and at least one minor criterion. The major criteria include lupus erythematosus (systemic LE, discoid LE or subacute cutaneous LE), erythema multiforme-like lesions (with or without involvement of the mucous membranes), and a speckled pattern of antinuclear antibody. The minor criteria are chilblains, positive anti-La (SS-B) or anti-Ro (SS-A) antibody and reactive rheumatoid factor. Speckled pattern of ANA is the most consistent diagnostic feature of Rowell syndrome, and was present in our patient. In addition, our patient had a positive ANA, SS-A and SS-B antibodies with a targetoid, EM-type eruption in an SCLE distribution. She had taken no new medications, and had no recent illness or history of cold sores that may be attributed to the etiology of EM.

Patients with lupus erythematosus may develop erythema multiforme. When there is no identifiable precipitating cause of erythema multiforme-type lesions in a patient with LE, one may consider Rowell syndrome. On the other hand, erythema-multiforme lesions in a patient with a positive SS-A, SS-B may simply be a variant of SCLE with targetoid lesions rather than an entirely distinct syndrome. Regardless of nomenclature, most patients respond to treatment with prednisone, anti-malarials and topical corticosteroids. In our patient the lesions completely resolved with a prednisone taper, hydroxychloroquine and triamcinolone 0.1% ointment.

References:

1. Rowell NR, Beck S, Anderson JR. Lupus erythematosus and erythema multiforme-like lesions. *Arch Dermatol*. 1963 Aug; 88:176-80.
2. Zeitoni NC, Funaro D, Cloutier RA, Gangne E, Claveau J. Redefining Rowell syndrome. *Br J Dermatol*. 2000 Feb; 142(2):343-6.
3. Aydogan K, Karadogan SK, Balaban S, Tunalit S. Lupus erythematosus associated with erythema multiforme: report of two cases and review of the literature. *J Eur Acad Dermatol Venereol.* 2005 Sep; 19(5):621-7.
4. Child FJ, Kapur N, Creamer D, Kobza Black A. Rowell syndrome. *Clin Exp Dermatol.* 1999 Mar; 24(2):74-7.

Case #11

Presented by Erika Music, MD and Warren Piette, MD

UNKNOWN #5

Sixty-two year-old male transferred from an outside hospital with a three day history of skin lesions after one week of antibiotics.

Case #12

Presented by Joerg Albrecht, MD and Jerry Feldman, MD

History of Present Illness:
This is a 68 year-old female admitted to the hospital with facial herpes zoster. At the time of admission an indurated, asymptomatic mass of her left arm with overlying skin changes was noted. The patient's left arm had been non-functional due to years of massive lymphedema occurring after a left mastectomy.

Past Medical History:
Breast carcinoma status post radical mastectomy with chronic lymphedema, hypertension, hypothyroidism, appendectomy, cholecystectomy, right hip replacement, colectomy for benign polyps, anal sphingterotomy

Medications/Allergies:
Metoprolol, enalapril, ASA, levothyroxine/ allergies to Penicillin, iodine, latex, sulfa

Review of Systems:
Her left arm is functionless with increased pressure for the past few months.

Physical Examination:
Left arm: tense edema and erythematous-to-purplish papules and nodules in groups as well as subcutaneous firm tumor

Laboratory Data:
Non-contributory

Histopathology:
3/09 Left arm: There is a dermal infiltrate composed of epithelioid cells in sheets with marked atypia but without vascular channels. There are frequent mitosis (up to 14 per high power field) and apoptotic cells. The tumor stains positive for vascular markers (CD31, CD34 and factor VIII) as well as vimentin. It is negative for epithelial markers (AE1, CK 20, CK 8/18 and EMA), LCA, CD38, factor XIIIa, chromagranin, synaptophysin, S-100, HMB, melanin A, SMA, and MSA.

Diagnostic Procedures and Tests:
2/09 MRI (left upper extremity): There is diffuse edema involving the subcutaneous tissue surrounding the full left extremity and conglomerate amorphous soft tissue lesion involving the subcutaneous tissues of the lateral and posterior compartments of the proximal two-thirds of the left forearm. The lesion abuts the left extensor carpi radialis longus and extensor digitorum muscles
4/09 PET scan (chest): metastatic lesions in left upper, right middle lobe
7/09 PET scan (chest): resolution of chest lesions

Diagnosis:
Stewart-Treves syndrome (High-grade angiosarcoma)

Treatment and Course:
After amputation of her non-functional left arm, the patient was started on a chemotherapy regimen consisting of six cycles of paclitaxel and dexamethasone, with resolution of her metastatic lesions. She experienced neuropathy secondary to paclitaxel treatment and phantom pain after her amputation.

Case #12 continued

Discussion:

Angiosarcoma is a well known complication of breast cancer treatment. It occurs as radiation induced sarcoma within the irradiated field, or as Stewart-Treves syndrome. Stewart-Treves syndrome is angiosarcoma of the upper extremity as a consequence of chronic lymphedema. It was initially described after mastectomy but similarly longstanding lymphedema e.g. congenital, idiopathic, traumatic or secondary to obesity can also cause angiosarcoma, albeit rare. Ninety percent of the cases occur after mastectomy. Lymphedema prior to the discovery of the tumor has been reported between 4 and 27 years, but cases have been reported in which the patient did not have clinically appreciable lymphedema. Clinical presentation is varied. A mottled, hardly visible purple hue on the brawny non-pitting edema of the affected skin may indicate deeper tumors, while superficial lesions may be palpated as erythematous papules that coalesce to form polypoid growths. Later tissue breakdown may lead to ulcerations.

The categorization of angiosarcoma is unclear. There is some debate whether this tumor is of lymphatic origin or a haemeangiosarcoma, however, for most purposes the two possible classifications are merged to denote sarcomas of endothelial origin with no regard for their origin. Tumors that develop within chronic lymphedema are more likely to show lymphatic differentiation, but the range of histological presentations is the same that characterizes angiosarcoma elsewhere. The variability within and between tumors is enough to blur any clear distinction. In extreme cases vessel formation may be practically absent with only high mitotic activity and a picture that may suggest other high grade sarcomas, carcinoma, or melanoma. In general small, capillary sized vessels are composed of obviously malignant cells that infiltrate soft tissue and skin. These vessels may carry clear fluid or erythrocytes. Most angiosarcomas stain for CD34 and CD31, which is more sensitive and endothelium specific. Another insight into the pathogenesis may be so-called lymphangiomatosis which develops as a possibly premalignant lesion of, most likely, lymphatic vessels. The vessels of lymphangiomatosis are lined with plump endothelial cells with hyperchromatic nuclei. The vessels can also dilate and develop branching networks. Lymphangiomatosis may merge with areas of frank angiosarcoma or exist in patients without angiosarcomas. Treatment is scrupulous follow-up.

The prognosis of Stewart-Treves syndrome, if untreated, is poor with an average expected survival of 6 months. Prognosis of treated angiosarcoma is better, but treatment is not standardized and there is no good data. Larger series indicate an average survival of about 20-30 months. Treatment of angiosarcoma once it has developed is primarily surgical with subsequent chemotherapy primarily with paclitaxel. Individual lesions can be treated with radiotherapy.

References:

1. Kirova YM, Feuilhade F, Calitchi E, Otmezguine Y, Le Bourgeois JP. Steward-Treves syndrome after treatment for breast cancer. *Breast* 1999; 8; 282-284.
2. Cozen W, Bernstin L, Wang F, Press MF, Mack TM. The risk of angiosarcoma following primary breast cancer. *BJC* 1999; 81; 532-536.
3. Angiosarcoma, North PE, Kincannon J in Dermatology ed. Jean L. Bolognia, MD and Joseph L. Jorizzo, MD, 2nd edition, 2007, Mosby, St Louis.
4. Roy P, Clark MA, Thomas JM. Stewart-Treves syndrome – treatment and outcome in six patients from a single center. *EJSO* 2004: 982-986.
5. Malignant Vascular tumors in Enzinger and Weiss's Soft Tissue Tumors, Weiss SW and Goldblum JR eds. 5th edition, 2008, Mosby, Philadelphia.

Case #13

Presented by Erika Music, MD and Jerry Feldman, MD

History of Present Illness:
This 29 year-old Hispanic male presented to our clinic with a 15-year history of painful nodules on the right side of his body. The lesions first appeared on his face in his early teens and have slowly increased in number to involve his right neck, chest, and arm. Heat seems to make the lesions more painful. No family members have similar lesions.

Past Medical History:
None

Medications/Allergies:
None/ penicillin

Review of Systems:
He denies fever, chills, cough, shortness of breath, nausea, vomiting, fatigue, and weight loss.

Physical Exam:
Right face, neck, chest, arm, and forearm: multiple flesh-colored-to-pink, firm subcutaneous nodules in a linear distribution. The lesions do not cross the midline.

Histopathology:
9/19/09 Right neck: There are rounded dermal nodules composed of small basophilic cells surrounded by larger, paler cells forming multiple lumens. There is a pink, hyaline membrane separating the nodules.

Diagnosis:
Blaschkoid eccrine spiradenomas with possible *CYLD* Cutaneous Syndrome

Treatment and Course:
The patient is currently awaiting a plastic surgery consultation for possible staged excision. We are attempting to obtain genomic mutation analysis for the known *CYLD* mutations.

Discussion:
In 1956 Kersting and Helwig first described eccrine spiradenomas as rare, benign tumors of sweat gland origin. More than 97% of the time, the lesion presents as solitary, slowly growing, painful, blue-pink dermal or subcutaneous nodule on the head or neck. Typically, these lesions occur in young adults between the ages of 15 and 35. On histologic examination, there are characteristic, well-defined dermal lobules composed of two types of epithelial cells arranged in cords and forming small lumen: central large cuboidal cells with vesicular nuclei and peripheral cells with dark nuclei and scanty cytoplasm. Multiple eccrine spiradenomas are exceedingly rare, comprising less than 2% of all cases. Lesions occurring in Blaschkoid, linear, nevoid, or zosteriform distributions have been described and are even rarer. In a review published in April 2009 by Rodriguez-Martin et al, there have been 21 cases in the literature of linear eccrine spiradenoma, 16 of which were female. Only 2 congenital cases have been reported.

Case #13 continued

Most cases of multiple eccrine spiradenomas are sporadic. It has been hypothesized that the linear or Blaschkoid mosaic distribution represents a de novo, post-zygotic somatic mutation. Three familial cases of eccrine spiradenomas have been reported, all of which support an autosomal dominant inheritance pattern. To date, the gene defect responsible is unknown.

Multiple eccrine spiradenomas may be associated with foci of other appendageal tumors. Cylindromas, eccrine hidradenomas, pilar components, and most recently, chondroid syringomas have been reported to occur along with the eccrine spiradenomas. Because of its association with other appendageal tumors, it has been proposed that linear/Blaschkoid eccrine spiradenomas could represent an organic hamartoma.

The finding of trichoepitheliomas and cylindromas along with eccrine spiradenomas should raise the suspicion of the autosomal dominantly inherited Brooke-Speigler syndrome. In November 2009, Rajan et al reported two families with mutations in the tumor suppressor gene, *CYLD*, and proposes the novel diagnosis "CYLD cutaneous syndrome" to encompass three appendageal tumor predisposition syndromes with *CYLD* mutations: Brooke-Speigler, familial cylindromatosis, and multiple familial trichoepitheliomas. Many of the patients with *CYLD* mutations in these two families had eccrine spiradenomas associated with cylindromas. It is quite possible that our patient has a mutation in the *CYLD* tumor suppressor gene.

Malignant degeneration has been reported with eccrine spiradenomas, potentially more often in the setting of multiple lesions. The majority of cases typically present as a rapidly enlarging or ulcerated nodule within a long-standing lesion.

Staged surgical excision, CO_2 laser ablation, and radiation therapy (1500 rads in 10 sessions) have been described as potential therapies for multiple eccrine spiradenomas.

References:

1. Altinyazar H, Kargi E, Ozen O, et al. Multiple eccrine spiradenoma in zosteriform distribution. *Plast Reconstr Surg* 2003; 112:927-928.
2. Ekmekci T, Koslu A, Sakiz D. Congenital Blaschkoid eccrine spiradenoma on the face. *Eur J Dermatol* 2005; 15:73-74.
3. Gupta S, Jain V, Singh U, Gupta S. Multiple eccrine spiradenomas in zosteriful distribution in a child. *Pediatr Dermaol* 2001;17:384-386.
4. Nath A, Kumari R, Thappa D. Eccrine spiradenoma with chondroid syringoma in Blaschkoid distribution. *Indian J Dermatol Venereol Leprol* 2009; 75:600-602.
5. Rajan N, Langtry J, Ashworth A, et al. Tumor mapping in 2 large multigenerational families with *CYLD* mutations. *Arch Dermatol* 2009; 145:1277-1284.
6. Rodriguez-Martin M, Gonzalez R, Saez-Rodriguez, et al. An unusual case of congenital linear eccrine spiradenoma. *Pediatr Dermatol* 2009; 26:180-183.
7. Ter Poorten MC, Barrett K, Cook J. Familial eccrine spiradenoma: a case report and review of the literature. *Dermatol Surg* 2003; 29:411-414.

Case #14

Presented by Morayo Adisa, MD and Jerry Feldman, MD

History of Present Illness:
This is a 19 year-old Ethiopian male with a ten-year history of a friable mass on his forehead that had started as a much smaller lesion. He reports occasional drainage of oily, non-foul smelling fluid. There were no associated systemic symptoms. He had been evaluated in the past by several non-dermatologist physicians in his home country and had been treated with several courses of systemic antibiotics without any improvement.

Past Medical History:
None

Medications/Allergies:
None/ NKDA

Physical Exam:
Forehead: 5cm x 5cm yellowish- brown verrucous plaque with overlying yellow crust and areas of focal necrosis

Laboratory Data:
The following were abnormal or positive:
Tissue gram stain and culture - + *Staphylococcus aureus*, *Porphyromonas gingivalis*

The following were normal or negative:
CBC, Chemistry panel, HIV, RPR, Fungal cultures

Histopathology:
07/09 Forehead: papillomatous epidermis connected to underlying cystic spaces with papillated projections and a plasma cell infiltrate

Diagnosis:
Syringocystadenoma papilliferum arising in a background of nevus sebaceus

Treatment and Course:
The patient underwent surgical excision by plastic surgery with negative margins.

Discussion:
Syringocystadenoma papilliferum is a skin hamartoma thought to be derived from apocrine glands and less often from eccrine sweat glands. One-third of cases arise within a nevus sebaceus, but there are also reports of their occurrence within epidermal nevi (linear nevus verrucosus). Syringocystadenoma papilliferum commonly presents on the head and neck and less commonly on the thigh and arms. They have a tendency to proliferate during puberty, hence a suspicion that they may be androgen sensitive.

Nevus sebaceus of Jadassohn is a benign hamartoma that was described in 1895 by Jadassohn, comprised of epidermal follicular, sebaceous and apocrine elements. It frequently occurs on the head and neck (scalp 59.3%, face 32.6%, pre auricular area 3.8%, neck and other body parts 1.3%). They occur sporadically and are usually benign, occurring either without any associated abnormalities or as part of a syndrome with associated neurological, ophthalmic or other abnormalities (epidermal nevus syndrome). There are three suggested stages in the lifecycle of these lesions. The first stage is comprised of

Case #14 continued

papillomatous epithelial hyperplasia with underdeveloped hairs. The second stage arises during puberty and is characterized by significant proliferation of sebaceous glands, epidermal verrucous hyperplasia, and apocrine gland maturation. The third stage consists of benign and malignant epithelial neoplasm development. Some of the reported benign neoplasms include trichilemommas, tumor of the follicular infundibulum, sebaceous adenoma, syringocystadenoma papilliferum, and trichoblastomas, with the latter being the most frequently occurring benign lesions.

Basal cell carcinomas (6-50% incidence) were reported to being the most frequent malignant lesion, but more recently it has been determined that many of the previously described cases may actually have been trichoblastomas, a benign follicular tumor. Other malignant neoplasms arising within these lesions tend to occur in older age groups and they include apocrine carcinomas, adnexal carcinomas, squamous cell carcinomas and basal cell carcinomas. The presence of a malignant lesion or transformation can be suspected with the presence of ulcerations, sudden onset of bleeding and increase in size. Multiple tumors or epithelial changes can occur within the same nevus sebaceus, with reports of up to 4 different lesions occurring within a single nevus sebaceus.

Treatment of choice is excision. Other alternative treatments include carbon dioxide laser treatment, photodynamic therapy, and dermabrasion. In the past, prophylactic excision was recommended prior to puberty but more recent studies appear to question this. A study by Cribier et al. retrospectively analyzing 596 cases of excised nevus sebaceus between 1932 and 1998 from patients of all ages determined only a 1.7% incidence of associated benign tumors (11-16 years of age) and no incidence of malignant neoplasm in children less than 16 years (232/596 cases evaluated). However, they did find five cases of basal cell carcinoma (0.8%) and no other malignant tumors in the adult specimens evaluated. In a study by Jaqueti et al. there were no malignant tumors in 155 samples of excised nevus sebaceus in all age groups (including 60 patients who were under age 18) identified. Another study by Santibanez-Gallerani et al. looked at 658 cases of excised nevus sebaceus in children under age 16. They found no basal cell carcinomas or other malignant tumors. An 18-year (1990-2008) database query study by Rosen et al. looking at 690 excised nevus sebaceus lesions in 631 pediatric patients (mean age of 7.2 years, range 0.3–54.3 yrs) revealed five patients (0.8%) with BCC (mean age 12.5 yrs, range 9.7–17.4 yrs) and seven patients (1.1%) with syringocystadenoma papilliferum (mean age 8.8 yrs, range 1.7–16.9 yrs).

Based on the current available data, prophylactic excision of nevus sebaceous without clinical signs of malignancy in children has uncertain benefits. Thus, excision is not warranted but could be considered for aesthetic reasons or if there is an associated benign tumor. Not all authors agree with this recommendation; Rosen and colleagues recommend prophylactic excision of all nevus sebaceus due to the potential risk of malignant transformation and cosmesis.

References:

1. Eisen D.B, Michael D. Sebaceous lesions and their associated Syndromes. *J Am Acad Dermatol* 2009; 61(4):549-78.
2. Nakai K. Sebaceoma, trichoblastoma and Syringocystadenoma papilliferum arising within a nevus sebaceous. *J Dermatol* 2008; 35:365-367.
3. Greer K.E, Bishop G.F, Ober W.C. Nevus Sebaceous and Syringocystadenoma Papilliferum. *Arch Dermatol* 1976; 112:206-208.
4. Cribier B, Scrivener Y, Grosshans E. Tumors arising in nevus sebaceus : A study of 596 cases. *J Am Acad Dermatol* 2000; 42: 263-268.
5. Santibanez-Gallerani A, Marshall D, Duarte AM et. al. Should Nevus Sebaceous of Jadassohn in children be excised? A study of 757 cases and Literature review. *J Craniofac Surg*. 2003 Sep; 14(5):658-60.
6. Jaqueti G, Requena L, Sanchez Yus E. Trichoblastoma is the most common neoplasm developed in nevus sebaceous of Jadassohn. *Am J Dermatopathol* 2000; 22:108-18.
7. Rosen H, Schmidt B, Lam H.P, Meara J G, and Labow BI. Management of Nevus Sebaceous and the Risk of Basal Cell Carcinoma: An 18-Year Review. *Ped Dermatol* 2009; 26(6) 676–681.

Case #15

Presented by Victoria Negrete, MD, Sidney Barsky, MD, and Warren Piette, MD

History of Present Illness:
This 29 year-old man presents with a one year history of multiple lesions on the scrotum associated with intermittent pruritus and extrusion of "white gel" following compression. The lesions have not been previously treated. He denies new sexual partners. He admits to frequently manipulating the lesions in an attempt to remove the "core". An initial shave biopsy revealed nonspecific changes of hyperkeratosis and acanthosis. A conservative trial of triamcinolone ointment 0.1% and then clobetasol ointment 0.05% did not improve the pruritus.

Past Medical History:
None

Medications/Allergies:
None/ NKDA

Review of Systems:
Unremarkable

Physical Exam:
Scrotum: approximately thirty-five grouped 3-6 mm flesh colored papules predominantly located on the midline of the scrotum; many with a dilated central pore

Laboratory Data:
Noncontributory

Histopathology:
8/08 & 1/09 Scrotum: several markedly dilated pilar infundibula filled with keratin showing atrophy near the ostiae and hypertrophy with radiating papillary projections near their bases. Several lesions reveal granulomatous changes.

Diagnosis:
Aggregated dilated pores of Winer

Treatment and Course:
The lesions were individually excised over the course of one year with no recurrences. The pruritis has also improved. Given the extent of the remaining lesions, a wide excision was performed to remove the majority of remaining lesions.

Discussion:
The dilated pore was first described by Winer in 1954 and is considered a benign acquired tumor of the hair follicle epithelium. Clinically, it usually presents as a solitary, enlarged, open comedone on the face or upper body of an elderly male. Since 1954, 115 cases of dilated pore of Winer have been published, with two cases involving aggregated dilated pores of Winer (ADPW). Konohana et al. reported ADPW on the neck of a 74-year-old male, and Resnik et al. reported ADPW on the neck of a 26-year-old female. We present the first case to our knowledge of ADPW on the scrotum of a young adult male. We attribute the histologic findings of granulomatous changes to his frequent manipulation of the lesions.

Case #15 continued

The clinical differential diagnosis for ADPW includes nevus comedonicus and porokeratotic eccrine ostial and dermal duct nevus (PEODDN). These may present as multiple comedones, papules, or nodules with or without a central pore. In contrast to a later onset of ADPW, nevus comedonicus and PEODDN typically appear between birth and childhood.

The histologic differential diagnosis for ADPW includes pilar sheath acanthoma, trichofolliculoma, and tumor of the follicular infundibulum. Of these, dilated pore of Winer, pilar sheath acanthoma, and trichofolliculoma share the histology of a central keratin-filled cavity lined with follicular epithelial tumor cells continuous with surface epithelium via a dilated infundibulum. DPW is characterized by predominantly infundibular differentiation. Although pilar sheath acanthoma may show partial infundibular differentiation with radiating papillary projections, there is primarily isthmic differentiation. Similarly, trichofolliculoma may show partial infundibular differentiation, but it occurs among a background of mature follicular differentiation. This case broadens the clinical picture of DPW and demonstrates successful treatment following wide excision.

References:

1. Winer LH. The dilated pore, a trichoepithelioma. *J of Investigative Dermatol* 1954; 23: 181-8.
2. Klovekorn G, Klovekorn W, Plewig G, Pinkus H. Giant pore and hair-shaft acanthoma. Clinical and histologic diagnosis. [In German]. *Hautarzt* 1983; 34: 209-16.
3. Konohana A, Kobayashi T. Aggregated dilated pores. *J Dermatol* 1999; 26: 332-3.
4. Resnik KS, Kantor GR, Howe NR, Ditre CM. Dilated pore nevus: A histologic variant of nevus comedonicus. *Am J Dermatopathol* 1993; 15: 169-71.
5. Steffen C, Winer's dilated pore: the infundibuloma. *The Am J of Dermatopathol* 2001; 23: 246-253, 2001.

Case #16

Presented by Rachel Neems Pritzker, MD and Lissette Ortiz-Ferrer, MD

Patient A

History of Present Illness:
The patient is a 61 year-old Italian male who presents to clinic with a 6 month history of a rash on both hands and forehead. The lesions appeared at the same time and have remained stable. He denies pain, swelling, or pruritus. He does not have a history of similar lesions. He denies any new medication or trauma. He was initially treated with a hydrocortisone cream and topical antifungal cream and both medications did not improve his lesions.

Past Medical History:
Bipolar disorder; no history of diabetes mellitus

Medications/ Allergies:
None/ NKDA

Physical Exam:
Bilateral dorsal hands: 4cm x 3cm blanching, non-scaly faint violaceous patches
Right forehead: 2cm x 1cm non-scaly pink patch

Histopathology:
8/17/09 Right dorsal hand: granulomatous dermatitis with interstitial histiocytes and giant cells associated with abundant mucin. No polarizable material seen. Stains for mycobacteria (AFB) and fungi (GMS) are negative.

Diagnosis:
Patch granuloma annulare

Treatment and Course:
He was started on fluocinonide 0.05% ointment to the hands twice daily for 3 weeks then daily for an additional 3 weeks. Elidel 1% cream was started twice daily to the forehead lesion. There was no improvement after 6 weeks of treatment and the lesions on the hands became more annular.

Patient B

History of Present Illness:
This 49 year-old female presents with a 6 month history of mildly pruritic, slow-growing lesions on the right lower quadrant of her abdomen and a 1 month history of a similar lesion on her left lower abdomen. She denies any scaling, discharge, or bleeding. She is only using a hydrophilic ointment on the lesions. The patient was previously seen in our clinic in 2006 for generalized pruritus secondary to cirrhosis.

Past Medical History:
Autoimmune hepatitis, cirrhosis, hypertension, thyroiditis, osteopenia, duodenal ulcer, anemia

Medications/ Allergies:
None/ NKDA

Case #16 continued

Physical Exam:
Right lower quadrant abdomen: 7cm x 5cm irregular erythematous patch with central clearing. There is no scale or surface change.
Left lower quadrant abdomen: 3.5cm x 4cm light pink faint patch without central clearing

Histopathology:
7/09 Abdomen, right lower quadrant: There is single-filing of histiocytes between collagen bundles and perivascular lymphocytes associated with abundant mucin.

Diagnosis:
Patch granuloma annulare

Treatment and Course:
The patient was given triamcinolone 0.1% ointment 0.1% twice daily. After three months there was no change in the lesions. She has not developed any new lesions.

Discussion:
Granuloma annulare (GA) is a benign granulomatous dermatitis of unknown etiology that demonstrates a variety of clinical variants. The classic presentation of GA is an annular plaque with a raised border, sometimes beginning as an erythematous dermal papule which spreads peripherally and undergoes central involution. The localized variant is the most common and typically presents on the distal extremities, including the dorsal hands and feet. Other variants include generalized GA, subcutaneous GA, perforating GA, and patch or macular GA. Patch GA is clinically described as patches of erythema possibly lacking the annular configuration. While it is a commonly described variant of GA, patch GA is not represented equally in the journal literature.

In a rare case series solely evaluating patch GA, six cases were evaluated clinically and pathologically. All six of the patients presented with asymptomatic red-brown or violaceous patches, none with evidence of papules, scales, or induration. Only one patient had an annular appearing lesion. Half of the patients had localized lesions present on the extremities and half had more widespread lesions on the extremities and trunk.

There are two major histological types of GA, first being the classic pattern of palisading granulomas around focal necrobiosis and mucin accumulation. The second type is the interstitial pattern with single-filing histocytes between collagen bundles with scattered necrobiosis and mucin deposition. Interestingly, in the same case series all six lesions demonstrated the interstitial pattern.

An interesting feature of patch GA is that it often resolves or improves after biopsy. Levin et al. demonstrated a patient with biopsy-proven patch GA who had resolution of the biopsied patch on two separate occasions. There are other reports of GA responding to trauma- producing treatments such as cryotherapy and sparing sites of trauma such as a vaccination site. This phenomenon may occur by inciting a wound healing process that remodels the extracellular matrix.

References:
1. Harth W, Linse R. Topical tacrolimus in granuloma annulare and necrobiosis lipoidica. *Br J Dermatol* 2004; 150:792-4.
2. Levin NA, Patterson JW, Yao LL, Wilson BB. Resolution of patch-type granuloma annulare lesions after biopsy. *J Am Acad Dermatol*. 2002 Mar; 46(3):426-9.
3. Mauhlbauer JE. Granuloma annulare. *J Am Acad Dermatol*. 1980 Sept;3(3):217-30.
4. Mutasim DF, Bridges AG. Patch granuloma annulare: clinicopathologic study of 6 patients. *J Am Acad Dermatol*. 2000 Mar; 42(3):417-21.

Case #17

Presented by Jordan Carqueville, MD and Jerry Feldman, MD

History of Present Illness:
A 51 year-old Filipino male with multiple small, round plaques on his extremities presents with a one year history of an oval plaque on the anterior tongue. The patient denies bleeding, pruritus, tenderness or growth of the lesion. The lesions on his body had been present for greater than ten years and become more prominent after sun exposure. He had never had radiation therapy or dialysis, and was not immunosuppressed. His father has similar oval lesions on his extremities.

Past Medical History:
Hypertension

Medications/Allergies:
Amlodipine, aspirin, pantoprazole /NKDA

Social History:
He quit smoking 1-year ago (1-pack of cigarettes per day for 20 years).

Family History:
His father has similar oval plaques on arms and legs. The patient was unaware if the mucosa was involved.

Review of Symptoms:
He denies fever, chills, recent illness, weight loss, photosensitivity, gastrointestinal, genitourinary, neurologic, and musculoskeletal symptoms.

Physical Exam:
Forehead, dorsal forearms, hands and lower legs: approximately 50 scattered, round plaques with elevated, hyperkeratotic borders. No lesions on palms, soles or genitalia.
Tongue: 6 mm well-demarcated milky-white, oval plaque on the left anterolateral tongue. It is a fixed lesion that could not be scraped off and it obscures individual filliform papillae.

Histopathology:
09/09 Left lateral tongue: squamous mucosa with column of parakeratosis and underlying dyskeratotic cells, suggestive of cornoid lamella. Minimal inflammation is present in the subepithelial area.
09/09 Right forearm: well-defined column of parakeratotic keratin with loss of granular layer and focal dyskeratosis beneath.

Diagnosis:
Disseminated Superficial (Actinic) Porokeratosis with Mucosal Involvement

Treatment and Course:
The tongue lesion was completely removed with an excisional biopsy, without recurrence over the past six months. The lesions on the extremities have faded with the winter season and lack of sun-exposure. We continue to watch for new and changing lesions or recurrence of the mucosal porokeratosis plaque. The patient is diligent with sunblock use and sun-protective clothing.

Case #17 continued

Discussion:

Porokeratosis is a heterogeneous group of keratinization disorders inherited in an autosomal dominant fashion. It infrequently involves the oral mucosa. We describe a case of disseminated superficial (actinic) porokeratosis with mucosal involvement. The patient presented with porokeratosis on his exposed, dorsal extremities along with porokeratosis on the anterolateral tongue.

There are five clinical variants of porokeratosis which include porokeratosis of Mibelli (PM), disseminated superficial actinic porokeratosis (DSAP) or disseminated superficial porokeratosis (DSP), porokeratosis palmaris et plantaris disseminate (PPPD), linear porokeratosis and punctuate porokeratosis. The forms that have been shown to have mucosal involvement are PM, PPPD and rarely DSP. Risk factors of porokeratosis include ultraviolet radiation, genetic inheritance, immunosuppression, trauma (via koebnerization), and renal transplantation.

DSP is a disseminated form of porokeratosis that occurs on both sun-exposed and non-exposed skin. It is autosomal dominantly inherited, and the age of onset is usually within the first three decades of life. The lesions may be present on the face, whereas in DSAP, the face is paradoxically spared. Our patient had involvement of the face, tongue, and extremities, which is consistent with the diagnosis of DSP. Our patient, however, has seasonal fluctuations with exacerbation in the summer months. Therefore, we still entertain the diagnosis of DSAP with mucosal involvement.

Cornoid lamellae were originally proposed to be derivatives of the acrosyringium of eccrine glands, however, it is now recognized that the lamellae can originate from the epidermis as well. It is possible that the cornoid lamellae on the tongue biopsy of our patient originated from the epidermis, as there are no eccrine glands typically found in the oral mucosa. The squamous hyperplasia appreciated on biopsy may have caused the filliform papillae to be clinically obscured. Cornoid lamellation is a characteristic finding of porokeratosis, but may also be found in other diseases, including basal cell carcinoma, Bowen disease and solar keratosis. Our patient's tongue biopsy did not demonstrate findings of squamous dyplasia or attributes of other processes that would indicate an alternative diagnosis.

Malignant change has been reported in porokeratosis where lesions may develop into basal cell or squamous cell carcinomas. Characteristics associated with higher rates of transformation include larger size of lesions, locations on non-exposed skin, and skin that has previously been irradiated. Long-standing lesions, older patients, linear porokeratosis, and large lesions on extremities also may distinguish lesions at higher risk. At the 6-month follow-up, there was no recurrence of the porokeratosis plaque on the patient's tongue. The lesions on his extremities remain stable. We will continue regular surveillance given the risk for malignant transformation in a non-exposed and uncommon site. Treatment for porokeratosis includes surgical excision, cryotherapy, CO2 laser, oral retinoids, photodynamic therapy, topical 5-fluorouracil and imiquimod cream.

References:

1. Schamroth JM, et al. Porokeratosis of Mibelli: overview and review of the literature. *Acta Derm Venereol*. 1997; 77:207-213.
2. Darling MJ, Lambiase MC, et al. Porokeratosis: a solitary oral lesion. *J Drugs Dermatol*. 2005; 4(1): 89-91.
3. Roson E, et al. Disseminated superficial porokeratosis with mucosal involvement. *Acta Derm Venereol*. 2001; 81(1):64-65.
4. Wade TR, Akerman AB. Cornoid lamellation, a histologic reaction pattern. *Am J Dermatopathol*. 1980; 2:5-15.
5. Otuska F, Someya T, et al. Porokeratosis and malignant skin tumors. *J Cancer Res Clin Oncol*. 1991; 117:55-60.

Case #18

Presented by Lauren Fine MD, Sidney Barsky MD and Warren Piette MD

History of Present Illness:
This is a 30 year-old Caucasian female with a 10-year history of intermittent lip swelling. Episodes can last from 3-8 days and are not painful or pruritic. The episodes are not associated with any other systemic findings. She has previously been treated with loradatine and diphenylhydramine, however both medications did not improve her symptoms.

Past Medical History:
Panic attacks

Medications/ Allergies:
None/ NKDA

Review of Symptoms:
She denies fever, chills, shortness of breath, visual changes, GI symptoms, paresthesias.

Physical Exam:
There is significant swelling of the upper lip. There is no erythema or scale. Her tongue appears slightly enlarged with multiple plications. There is no facial droop or smile asymmetry.

Laboratory Data:
The C1-esterase inhibitor level is within normal limits.

Radiology:
Chest X-ray normal

Pathology:
Patient declined a skin biopsy

Diagnosis:
Chelitis granulomatosa

Treatment and Course:
The patient had previously been followed in the Allergy clinic and had been unsuccessfully treated with diphenylhydramine and loratadine for possible idiopathic angioedema. Her symptoms continued to recur. After our initial visit she was started on hydroxychloroquine 200mg twice daily and hydroxyzine 25mg nightly and also restarted on loratidine 10mg daily. She declined intra-lesional triamcinolone injections. She was referred to Ophthalmology for a complete ocular exam to rule out eyelid or optic nerve involvement. After 1-2 months on this drug regimen she noticed no change in the frequency or intensity of lip swelling episodes so the hydroxyzine and loratadine were discontinued. She remained on hydroxychloroquine and prednisone 10mg daily was started for one month. She continues to have weekly episodes of asymptomatic lip swelling.

Discussion:
Melkersson-Rosenthal syndrome (MRS) is a rare disorder of unknown etiology and is classically defined as a triad of recurrent orofacial edema, recurrent peripheral facial palsy (FP), and fissured tongue (lingua plicata, LP). First described in 1928 by Melkersson, Rosenthal added fissured tongue to complete the triad in 1931. All three symptoms are present in a minority of patients (8% to 18%), making the diagnosis of MRS difficult. When two symptoms are present it is considered oligosymptomatic.

Case #18 continued

Chelitis granulomatosa (CG) is defined as intermittent labial or orofacial edema and is widely considered as a monosymptomatic MRS form; however this is not universally accepted since the majority of CG patients never present with other MRS symptoms. Histologically edematous tissues in CG and MRS demonstrate non-necrotizing lymphoepitheliod granulomas of the dermis, multinucleated Langerhans-type giant cells, dermal edema, and a perivascular lymphocytic infiltrate.

The swelling in CG and MRS is soft to firm, non-painful, asymmetric, and almost always limited to the orofacial location. In the early stages of the condition the swelling is usually intermittent; however at later stages the swelling is often persistent. Less commonly, patients can experience similar changes elsewhere such granulomatous vulvitis or edema of the eyelids, orbital tissue, or optic nerve. The symptoms of MRS can closely mimic angioedema, however MRS is more persistent, it does not respond to antihistamines, and it can lead to fibrosis of the involved tissues. Lingua plicata is congenital in 30%-80% of MRS patients and is an anomaly present in 0.5% to 5% of the general population. It is considered a developmental malformation. Facial paralysis associated with MRS may occur months to years before or after the onset of facial edema and relapses are frequent. Peripheric facial paralysis may be unilateral or bilateral and it may be partial or complete. Other symptoms associated with MRS include migraine-like headaches, swelling of the oral mucosa, salivary or taste complaints, trigeminal neuralgia, paresthesias, and psychotic episodes.

The cause of MRS is unknown, but there are several speculated associations. Some investigators consider MRS to be a manifestation of sarcoidosis or Crohn's disease. A reaction to *Mycobacterium tuberculosis* infection, dental infections, foreign material, or delayed hypersensitivity reactions to cow's milk protein additive, other food additives, or cobalt have also been suggested. Reports of familial occurrence of MRS suggest genetic factors may also play a role. In the differential diagnosis of MRS, Crohn's disease, sarcoidosis, connective tissue disease, infectious etiologies, granulomatous blepharitis, chelitis, contact dermatitis, facial trauma, and Bell's palsy are considered.

Treatment for MRS can be challenging and response to treatment is often unpredictable. Anti-inflammatory and anti-granulomatous agents such as clofazimine, dapsone, sulfapyridine, danazol, and hydroxychloroquine have been used with limited success. Use of the antibiotics tetracycline and metronidazole has also been described. Systemic and intralesional corticosteroid injections are generally attempted but usually only provide short-term benefit. Surgical options can be considered for patients with disfiguring facial swelling or those not responsive to other modalities. Some cases of MRS associated with Crohn's disease have responded well to infliximab and adalimumab.

References:

1. Kakimoto C, Sparks C, White A. Melkersson-Rosenthal syndrome: a form of pseudoangioedema. *Annals of Allergy, Asthma, & Immunology*. 2007; 99: 185-189.
2. Ozgursoy OB, Tulunay O, Kemal O, Akyol A, Dursum G. Melkersson-Rosenthal syndrome as a misdiagnosed disease. *American J of Otolaryngology*. 2009; 30:33-37.
3. Prassler J, Elsner P, Ziemer M. Persistent non-tender swelling of the upper lip. *Amer Jour clin Dermatol*. 2007; 8(4): 251-253.
4. Ratzinger G, Sepp N, Vogetseder W. Chelitis granulomatous and Melkersson-Rosenthal syndrome: evaluation of gastrointestinal involvement and therapeutic regimens in a series of 14 patients. *J Euro Acad of Dermatol and Vener*. 2007; 21: 1065-1070.
5. Wiesen A, David O. Chelitis granulomatosa: Crohn's disease of the lip? *J Clin Gastroenterol.* 2007: 41(9): 865-866.