Chicago Dermatological Society

May 2016
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, May 4, 2016
Rush University Medical Center - Chicago

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

Program

Host: Rush University
Wednesday, May 4, 2016
Rush University Medical Center
Professional Building - 5th Floor
1725 W. Harrison St., Chicago

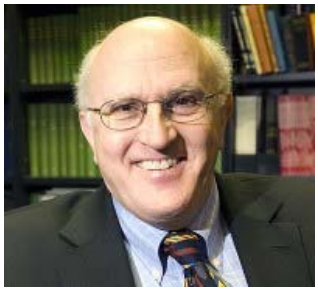
Except for patient viewing, all other meeting activities take place on the 5th floor of the Professional Building.

8:00 a.m.	**Registration & Continental Breakfast with Exhibitors** *Searle Conference Center registration counter and Fenger/Sippy Rooms*
8:30 a.m. - 10:00 a.m.	**Clinical Rounds** Patient viewing/posters – *Rush Dermatology Clinic - Room 264 Professional Building (Elevator III)* Slide viewing – *Blaney Room*
9:00 a.m. - 10:00 a.m.	**Resident/Basic Science Lecture** – *Brainard Room* *RESIDENT LECTURE:* "Cutaneous LE" *Jeffrey P. Callen, MD*
10:00 a.m. - 10:30 a.m.	**Break and Visit with Exhibitors** – *Fenger/Sippy*
10:30 a.m. - 12:00 p.m.	**Resident Case Presentations & Discussion** *Brainard*
12:00 p.m. - 12:15 p.m.	**MOC Self-Assessment Questions** *Brainard*
12:15 p.m. - 12:45 p.m.	**Box Lunches & visit with exhibitors** *Room 500 - Main Dining Room*
12:55 p.m. - 1:00 p.m.	**CDS Business Meeting** *Brainard*
1:00 p.m. - 2:00 p.m.	**General Session** – *Brainard* *MALKINSON LECTURE*: "Safe Use of Systemic Therapies in Dermatology" *Jeffrey P. Callen, MD*
2:00 p.m.	**Meeting adjourns**

Mark the Dates!
Next CDS monthly meeting –
- Wednesday, June 8 at Stephens Convention Center, Rosemont

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

Guest Speaker



JEFFREY P. CALLEN, MD

Professor of Medicine (Dermatology), University of Louisville
Louisville, KY

Delivering the Frederick Malkinson Lecture

Clinical Expertise – Skin signs of systemic diseases; lupus erythematosus; dermatomyositis; pyoderma gangrenosum; psoriasis; systemic therapies for management of skin disease.

Board Certifications – American Board of Internal Medicine; American Board of Dermatology

Education and Training – Medical School: University of Michigan; Residency: University of Michigan Affiliated Hospitals

Recent Publications –

- Campbell C, Callen JP. Misdiagnosed Periocular Pyoderma Gangrenosum Requiring Ectropion Repair With Development of Second Lesion of Pyoderma Gangrenosum at Graft Site. JAMA Dermatol. 2016 Mar 2. doi: 10.1001/jamadermatol.2016.0062. [Epub ahead of print] PubMed PMID: 26934168.
- Tidwell WJ, Malone J, Callen JP. Cutaneous T-Cell Lymphoma Misdiagnosed as Lipodermatosclerosis. JAMA Dermatol. 2016 Feb 24. doi: 10.1001/jamadermatol.2015.6106. [Epub ahead of print] PubMed PMID: 26914225.
- Tidwell WJ, Malone J, Callen JP. Eruptive Keratoacanthomas Associated With Leflunomide. JAMA Dermatol. 2016 Jan 1;152(1):105-6. doi: 10.1001/jamadermatol.2015.2506. PubMed PMID: 26352135.
- Wright NA, Vleugels RA, Callen JP. Cutaneous dermatomyositis in the era of biologicals. Semin Immunopathol. 2016 Jan;38(1):113-21. doi: 10.1007/s00281-015-0543-z. Epub 2015 Nov 12. PubMed PMID: 26563285.
- Thompson L, Abner S, Malone J, Callen JP. Interstitial Granulomatous Dermatitis as the Initial Manifestation of Myeloma. JAMA Dermatol. 2015 Oct;151(10):1141-2. doi: 10.1001/jamadermatol.2015.1160. PubMed PMID: 26039702.
- Norris IN, Haeberle MT, Callen JP, Malone JC. Generalized linear IgA dermatosis with palmar involvement. Dermatol Online J. 2015 Sep 17;21(9). pii: 13030/qt1s3402cj. PubMed PMID: 26437279.
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- Robinson JK, Bhatia AC, Callen JP. Protection of patients' right to privacy in clinical photographs, video, and detailed case descriptions. JAMA Dermatol. 2014 Jan;150(1):14-6. doi: 10.1001/jamadermatol.2013.8605. PubMed PMID: 24305726.

CONTINUING MEDICAL EDUCATION CREDITS

Chicago Dermatological Society

Presents

"Chicago Dermatological Society Monthly Meeting Series"

May 4, 2016 *Chicago, IL*

Please be sure to complete and return the attendance/CME claim form and the evaluation form before you leave the meeting. The information collected in the evaluation form represents an important part of the CME planning process. A certificate of credit will be mailed to you following the conference. Participants must attend entire session to receive full credit. SynAptiv will retain a record of attendance on file for six years.

JOINT SPONSOR STATEMENT

This educational activity is jointly provided by SynAptiv and the Chicago Dermatological Society.

GOAL / PURPOSE

To broaden the clinical knowledge of dermatologists in a number of areas relating to management of patients and new therapy options.

EDUCATIONAL OBJECTIVES

Upon completion of this series of activities, participants will be able to:

1. Discuss key factors in the diagnosis and treatment for viral diseases and bacterial infections.
2. Describe the manifestation of skin cancers and the efficacy of treatments available to the dermatologist.
3. List the therapeutic options available to the dermatologist for a variety of skin diseases, both medical and surgical, and discuss how new emerging treatments can be successfully incorporated into a dermatology practice.

Continued next page

CREDIT STATEMENTS

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of SynAptiv and Chicago Dermatological Society. SynAptiv is accredited by the ACCME to provide continuing medical education for physicians.

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

DISCLAIMER STATEMENTS

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DISCLOSURE STATEMENTS

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

None of our faculty, planners and/or content managers have any conflicts of interest to disclose nor do they have any vested interests or affiliations.

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

TABLE OF CONTENTS

Presented by Magdalena Kobierska, MD, Lisa Arkin, MD, and Warren Piette, MD
Department of Dermatology, Rush University Medical Center

HISTORY OF PRESENT ILLNESS

A 46-year-old white male with known dermatomyositis presented to clinic for discussion of treatment options regarding chronic elbow ulcerations and longstanding violaceous erythema of the face. Dermatomyositis was diagnosed 7 years ago when he presented with polyarthritis, weakness, weight loss and shortness of breath. Skin and muscle biopsies along with pulmonary imaging confirmed the diagnosis of dermatomyositis with associated interstitial lung disease (ILD.)

As part of his malignancy workup at the time of initial diagnosis, the patient had pan-CT imaging of his chest, abdomen, and pelvis. Non-specific findings in the testes and liver prompted additional work up to rule out testicular cancer and hepatocellular carcinoma. Subsequent ultrasonography imaging of the testes showed scrotal calcinosis cutis, and a biopsy of liver found non-alcoholic steatohepatitis without any evidence of malignancy. The patient is currently 7 years from his initial diagnosis and remains without systemic symptoms; however, no additional malignancy surveillance has since been performed.

At our dermatology clinic visit 3 months ago, we noted characteristic cutaneous findings of non-inflammatory acral ulcerations and scaly palmar papules. Given the presence of interstitial lung disease and absence of a prior serologic positivity, we sent a myositis specific and myositis-associated antibody panel, which confirmed the diagnosis of MDA-5+ Dermatomyositis.

Treatment has included IVIG for the chronic ulcerations and tacrolimus and cyclophosphamide for the ILD with little improvement. He is currently being treated with prednisone, Hydroxychloroquine, and methotrexate, and his myositis, arthritis and pulmonary disease have improved on this regimen. In contrast, the patient's cutaneous ulcerations have been quite debilitating. He underwent surgical repair of the right elbow ulceration on the urging of his orthopedist 1.5 years ago, and this was complicated by bacterial osteomyelitis and required several surgical attempts at closure. He recently underwent grafting of the left elbow ulceration in spite of counseling that he might experience impaired wound healing.

PHYSICAL EXAM

Examination revealed bilateral upper eyelid erythema and confluent violaceous erythema of the bilateral malar cheeks, nose, and chin. He had a single, deep, non-inflammatory ulceration with central keratotic plugging overlying the left elbow. Several, pinpoint, subcutaneous white deposits, which were hard and non-tender to palpation, were also noted on his left palm and left distal digits. All ten fingernails showed periungual telangiectasias with capillary loops and drop out as well as hyperplasia and ragged change of the eponychia.

LABORATORY WORKUP

MDA-5 (P140) (CADM-140): **93..**.....	**Strong Positive**
EJ AB: **<20**	**Weak Positive**
TIF1 GAMMA (P155/140): <20	Negative
Anti-Jo-1 Ab: <20	Negative
PL-7: <20	Negative
PL-12: <20	Negative
OJ: <20	Negative

SRP: <20 ..... Negative
MI-2: <20 ..... Negative
NXP-2 (P140): <20 ..... Negative
Anti-PM/Scl Ab: <20..... Negative
Fibrillarin (U3 RNP): Negative ..... Negative
U2 snRNP: Negative..... Negative
Anti-U1-RNP Ab: <20..... Negative
Ku: <20. ..... Negative
Anti-SS-A 52 kD Ab, IgG: <20..... Negative

PRIOR (5/2009)
ANTIJO1 AB: <1.0 ..... Negative
RHEUMATOID FACTOR: <10 ..... Negative
ANTI-DBLE STR DNA: 9 ..... Negative
ANTI-RNPANDANTI-SM: 0.31 ..... Negative
ANTI-SM: 0.13 ..... Negative
SSA: 0.19 ..... Negative
SSB: 0.04 ..... Negative

LUPUS ANTICOAGULANT = **Positive** [Based on confirmatory testing]
PTT-LA SCREEN: **51 seconds**..... [<41]
dRVVT SCREEN: 42 seconds..... [<46]
IFA ANA titer: 1:30..... [<1:40]

MEDICATIONS
Prednisone 5 mg PO once daily
Hydroxychloroquine 400 mg PO once daily
Methotrexate 12 mg PO once weekly

PRIOR
Systemic tacrolimus
Cyclophosphamide (6 month course)
Monthly IVIG infusions (12 month course)
Variable-doses of systemic steroids (continuous therapy since diagnosis)

DIAGNOSIS
Anti-MDA-5 antibody positive dermatomyositis with interstitial lung disease and cutaneous ulcerations

DISCUSSION
Dermatomyositis (DM) is a systemic autoimmune disease characterized by variable involvement of the skin, muscles, and lungs. Approximately 60-70% of patients with DM have detectable myositis-associated (MAAs) or myositis specific- antibodies (MSAs), which may be helpful for risk stratification and prognosis. In certain subsets of DM, MSAs may be detectable in serum prior to symptom onset and titers may correlate with disease activity. We present this case of a Caucasian male with a 7 year history of MDA-5 antibody positive DM in order to illustrate this unique clinical phenotype and to provide a forum for discussion of treatment and malignancy screening.

MDA-5 is the autoantigen recognized by the anti-CADM-140 antibody and functions as an RNA helicase. It is involved in the innate immune response against intracellular viruses, cellular growth suppression, and apoptosis. Found in ~10-30% of DM patients, anti-MDA-5 antibody

positivity can be associated with absent or minimal myositis (amyopathic DM), interstitial lung disease that may be rapidly progressive, and a characteristic cutaneous phenotype consisting of diffuse, non-scarring hair loss, skin ulcerations, and tender palmar papules that demonstrate vasculopathy on histopathology.

MDA-5 is unique among the DM-specific autoantigens in terms of its cellular localization and function. Unlike some of the other DM-specific antigens (p155 or Mi-2), which are nuclear proteins involved in transcriptional or translational regulation, MDA-5 localizes to the cell membrane. It senses intracellular viral infection and subsequently upregulates type I interferons to suppress viral replication and modulate adaptive immunity. Although seropositivity to MDA-5 antibodies can serve as an important marker for risk stratification and disease prognosis, no universally-accepted practice guidelines exist for treatment or monitoring.

Current treatment options for DM include corticosteroids, antimalarials, IVIG, methotrexate, mycophenolate mofetil, and rituximab. Treatment recommendations for refractory cutaneous disease, including chronic ulcerations that characterize the MDA-5 DM phenotype, remain scarce. Sildenafil, a known regulator of vascular tone that induces neovascularization and vasodilation, is a recently reported therapy for patients with digital ulcerations. Friedrichson et al published a case series of successful healing of digital ulcerations in scleroderma patients after 5 weeks of treatment with 75 mg of sildenafil. Extrapolated from this literature, some have suggested Sildenafil therapy may also be effective for chronic ulcerations in dermatomyositis. We discussed the option of Sildenafil therapy with our patient but he declined. Instead, he recently underwent surgical grafting of the left elbow ulceration against our recommendation. We are interested to learn from other experiences in treating chronic ulcerations in patients with dermatomyositis.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 2**

Presented by Andrew Thompson, MD and Lisa Arkin, MD
Department of Dermatology, Rush University Medical Center

UNKNOWN

Presented by Todd Rickett, MD, PhD, Sheetal Mehta, MD, and Arthur Rhodes, MD, MPH
Department of Dermatology, Rush University Medical Center

PATIENT A

HISTORY OF PRESENT ILLNESS

A 43-year-old white man presented to clinic for skin cancer surveillance, concerned about a new growth on his right mid-scapula. The lesion was raised, pruritic, and bled occasionally. The lesion was first noted 6 weeks prior to presentation (PTP). He had attempted no therapies except local dressings. Four months PTP, he had developed a tender red nodule of the left posterior thigh that rapidly tripled in size. Biopsy revealed this to be a sebaceoma and was excised with complete tumor clearance. He also has a history of a basal cell carcinoma and multiple squamous cell carcinomas. He had no personal history of melanoma, but two first degree family members had melanomas removed. He had an osteosarcoma at age 19, treated with surgery and chemotherapy, without recurrence. Except for chronic hearing loss and minor musculoskeletal pain associated with activity, review of systems was unremarkable.

PAST MEDICAL HISTORY

Sebaceoma of left posterior thigh, s/p excision 1 month PTP
Basal cell carcinoma of left occipital scalp, s/p Mohs 2 years PTP
Invasive SCC of the right lateral cheek, s/p Mohs 3 years PTP
Invasive SCC of the mid-back, s/p Mohs 4 years PTP
Superficial SCC of the right posterior thigh, s/p excision 6 years PTP
Osteosarcoma of the right tibia, s/p excision and chemotherapy 24 years PTP
High-frequency sensorineural hearing loss

FAMILY HISTORY

Father with melanoma, gastric cancer, colon cancer, prostate cancer, bladder cancer
Sister with melanoma
Paternal uncle with prostate cancer
Paternal aunt with renal cancer and endometrial cancer
Paternal grandmother with colon cancer and endometrial cancer
Mother with Barrett's Esophagus

PHYSICAL EXAMINATION

Right mid-scapula: 5 mm x 4 mm (2 mm height) yellow-red papule

HISTOPATHOLOGY

Microscopic examination revealed focal fragmentation and ulceration of the epidermis. Extending from the epidermis to the superficial dermis was a cohesive proliferation of atypical epithelial cells with dark-blue, pleomorphic nuclei, scattered mitotic figures, and focal cytoplasmic clear vacuoles. An associated dermal infiltrate consisted of lymphocytes, histiocytes, and numerous plasma cells. Immunohistochemical stains were positive for anti-EMA (epithelial membrane antigen) and negative for CK20 and synaptophysin.

Reevaluation of the recently excised left thigh lesion revealed lobules of cells with foamy, multi-vacuolated cytoplasm in addition to a basaloid lining without significant cytologic atypia. Diagnosis was confirmed as a sebaceoma. There was complete loss of expression for MSH2, while MSH6 was expressed at 6% of the expected level and interpreted as equivocal.

LABORATORY EVALUATION
CBC, CMP, UA, and PSA: Within normal limits
Esophagogastroduodenoscopy: Numerous polyps and adenomas throughout the stomach. One gastric antral polyp with low grade dysplasia.
Colonoscopy: Numerous polyps and adenomas throughout the large intestine.
Adenocarcinoma in situ of distal ascending colon with non-expression for MSH2 and MSH6 (MLH1 and PMS2 were normal/wild type).
Genetic testing: heterozygosity for the MSH2 gene with pathogenic deletion of c2O4deIG

DIAGNOSIS
Sebaceous carcinoma in the setting of Muir-Torre Syndrome

TREATMENT AND COURSE
The sebaceous carcinoma of his right mid-scapula was re-excised with 1 cm margins. He has subsequently developed a keratoacanthoma of the left lateral knee and an invasive squamous cell carcinoma of the right lower chest. He has been evaluated by gastroenterology as noted. The patient was seen by a genetic counselor and elected to inform his family members of the condition; one sister was found to have colonic polyps.

PATIENT B

HISTORY OF PRESENT ILLNESS
A 72-year-old white man presented for skin cancer surveillance, concerned about a new growth on his right zygomatic cheek. He had developed a small raised lesion over the last 1-2 months. The lesion was elevated, asymptomatic, and growing larger. No treatments had been attempted. He has a history of multiple basal cell carcinomas. He had no personal or family history of melanoma, but there were numerous other cancers, detailed below. Review of systems was unremarkable.

PAST MEDICAL HISTORY
Cancer of the small intestine 30 years PTP, s/p excision
Ureteral cancer 24 years PTP s/p excision
Multiple polyps of the colon and small intestine

FAMILY HISTORY
Mother with ovarian cancer
Father with urinary tract carcinoma
One brother with colon cancer
Additional brother with lung cancer
Additional brother with prostate cancer
Two sisters and one daughter with severe endometriosis, each requiring hysterectomies
One daughter with colonic polyps

PHYSICAL EXAMINATION
Right zygomatic cheek: 3mm round pearly papule

HISTOPATHOLOGY
Microscopic examination revealed irregular sebaceous lobules, some connecting to the dermis, with a predominantly immature, basaloid appearance. There were numerous apoptotic cells along with general pleomorphism, and many cells with increased nuclear-cytoplasmic ratios and irregular chromatin patterns. Immunohistochemical stains were positive for EMA and MLH1. There was complete loss of expression for MSH2.

LABORATORY EVALUATION

Colonoscopy: rectal polyp with adenomatous changes and lymphoid aggregates.
Genetic testing: heterozygosity for the MSH2 gene with pathogenic deletion of exons 7 and 8

DIAGNOSIS

Sebaceous carcinoma in the setting of Muir-Torre Syndrome

TREATMENT AND COURSE

The sebaceous carcinoma of his right cheek was excised using Mohs microscopically controlled margin surgery (MCMS), with permanent sections verifying complete clearance. He has since developed four additional basal cell carcinomas, a squamous cell carcinoma, and another sebaceous carcinoma. These tumors have all been treated with MCMS. The patient was seen by a genetic counselor, and he elected to inform his family members of the condition. Most siblings and children elected to pursue testing, and many had the mutation.

DISCUSSION

Sebaceous carcinoma is a very rare cutaneous malignancy with potential for aggressive spread and poor outcome. Arising from the adnexa, more than 70% of sebaceous carcinomas arise on the face, neck, or scalp, body regions where sebaceous glands are at highest density. Within this anatomic distribution of tumors, the most frequent site of involvement is the periocular region. Tumors in this region may be mistaken for chalazia, xanthelasmas, or other malignancies such as a basal cell or squamous cell carcinomas. Sebaceous carcinomas may present as subcutaneous nodules, or yellow, red, tan, or skin-colored papules that may be eroded or ulcerated. Dermoscopy often shows polymorphous vessels and a yellow background.

With such heterogeneous presentations, many cases of Muir-Torre syndrome are only diagnosed after histopathologic results are available. Microscopically, sebaceous carcinomas are composed of sheets or lobules of cells with foamy or vacuolated cytoplasm, often with nuclear atypia and mitotic figures. Sebaceous carcinomas are especially uncommon before age 50. The median age for diagnosis of sebaceous carcinoma is 72 years. Beyond relatively advanced age, which is variable, other reported risk factors for sebaceous carcinoma include Asian or Pacific Islander ethnicity or a history of ionizing radiation to the head or neck. Sebaceous carcinoma may be locally destructive or metastasize via lymphatics. For patients diagnosed with sebaceous carcinoma, the absolute 5 and 10 year survival rates are 71% and 46%, respectively. Treatment consists of MCMS or surgical excision with histopathological verification of margin clearance. Lymph nodes must be evaluated if enlarged. Radiation, cryotherapy, and topical chemotherapy with mitomycin c are potential alternative or adjuvant therapies for patients who have more advanced disease.

History of sebaceous carcinoma is associated with a 43% increase in risk of developing a new malignancy when compared to the general population. One study estimates that two-thirds of all cases of sebaceous carcinoma are associated with cancer syndromes involving microsatellite instability such as Muir-Torre. Sporadic (i.e. non-syndromic) sebaceous carcinoma is frequently caused by mutations in p53 and occurs most commonly in immunocompromised patients, either subsequent to organ transplant immunosuppression or in the setting of AIDS.

Muir-Torre syndrome (MTS) is a rare genetic condition marked by a predisposition to develop sebaceous neoplasms, basal cell carcinomas, squamous carcinomas, and internal malignancies. Sebaceous adenomas, epitheliomas, and carcinomas are the hallmark lesions of MTS, and detection of any one of these neoplasms should prompt consideration of potential

cancer syndromes. MTS is a variant of Lynch syndrome (hereditary nonpolyposis colorectal cancer) and as such is caused by an autosomal dominant mutation in one of the DNA mismatch repair genes. In particular, most cases of MTS are caused by germline mutations in the MSH2, MLH1, or MSH6 genes. Without the ability to repair incorrectly replicated DNA, mutations accumulate throughout the genome, resulting in microsatellite instability and a predisposition to develop malignancies. Approximately 35% of MTS patients do not display microsatellite instability, and likely have a distinct subtype with autosomal recessive inheritance of the MYH gene.

All patients with MTS are at increased risk for cutaneous and visceral malignancies, particularly colorectal adenocarcinoma. Compared to sporadic colorectal cancers, MTS-associated intestinal neoplasms are more likely to occur proximal to the splenic flexure (i.e. affecting the transverse or ascending colon as in patient A) and often display less aggressive clinical behavior. Neoplasia can occur anywhere in the gastrointestinal tract, and some MTS patients may have hundreds of adenomatous polyps. The second most commonly affected organ system is the urogenital tract including kidneys, bladder, ureter, urethra, prostate, ovary, and endometrium. Other cancers reported to be linked to MTS include brain, breast, lung, and hematological malignancies. Accordingly, patients who have sebaceous adenomas, sebaceous carcinomas, or sebaceous epitheliomas should be evaluated for germline mutations in mismatch repair genes and receive genetic counseling for possible MTS. Patients and their first degree relatives should be encouraged to undergo an aggressive screening program for secondary prevention of internal malignancies. These gender-related screenings might include the following:

1) Annual complete mucocutaneous examinations
2) Annual colonoscopy beginning at age 20-25 years
3) Biennial or triennial endoscopy with gastric antrum biopsy starting at age 30-35 years
4) Annual pelvic examinations, endometrial biopsies, and transvaginal ultrasounds beginning at age 30-35 years, with recommended hysterectomy and bilateral salpingo-oophorectomy at age 40 years
5) Annual urinalysis with cytology starting at age 30-35 years
6) Screening for prostate cancer as advocated for the general population
7) Mammograms as advocated for the general population

In summary, we present two adults who had sebaceous carcinomas associated with Muir-Torre Syndrome. Appropriate screening and surveillance for cutaneous and visceral malignancies, along with screening and surveillance of family members is indicated in an attempt to reduce morbidity and mortality related to this syndrome.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 4**

Presented by Andrew Thompson, MD and Lisa Arkin, MD
Physician team included Brandi Kenner-Bell, MD, Megan Curran, MD, and Joan Guitart, MD
Department of Dermatology, Rush University Medical Center

HISTORY OF PRESENT ILLNESS

This 10-year old male initially presented with a red-brown plaque on his right periorbital region. He saw Dr. Kenner-Bell, a pediatric dermatologist at Lurie Children's Hospital, who suspected lymphoid nodular hyperplasia and performed a biopsy, which confirmed the diagnosis. He was prescribed fluocinolone ointment, and the rash resolved within 3 weeks. Several months later, the rash recurred in the same distribution while in Florida. They re-started the fluocinolone ointment, and the eruption resolved within 2 weeks. He subsequently presented to pediatric dermatology at Rush with yet another recurrence. His mom felt that this rash looked similar to the previous eruption, but she believed that the sun was a trigger as he had flared 1-2 days after being outside without sunscreen. He denied any history of fever, chills, sweats, blood in his urine, joint or muscle pains, oral or nasal sores, hair loss, chest pain, shortness of breath, or mood changes. He had no history of recurrent infections or hospitalizations.

PAST MEDICAL HISTORY

Biopsy-proven lymphoid nodular hyperplasia

MEDICATIONS

None

ALLERGIES

No known drug allergies

FAMILY HISTORY

There is no known family history of autoimmune disease. A cousin died of hepatoblastoma in childhood.

PHYSICAL EXAM

At the time of our initial physical exam, there were scattered slightly scaly erythematous to violaceous patches across the nasal bridge, right nose and right periorbital region. The conchal bowls were clear. There was no alopecia. The hard palate was clear. There were no periungual changes or palmar erythema.

HISTOPATHOLOGY

Previous biopsy (2014) from the right medial cheek and right side of the nose demonstrated a brisk perivascular and periadnexal lymphoid infiltrate. The dermis shows a dense superficial and deep lymphoid infiltrate in a perivascular and periadnexal distribution with scattered irregular germinal centers. An interstitial lymphoplasmacytic infiltrate with numerous histiocytes is also noted. Immunohistochemistry was performed on deparaffinized sections. All controls stained simultaneously were reviewed and appeared adequate. Kappa and lambda in situ hybridization and immunohistochemistry demonstrate a ratio of light chains within the normal limits. Light chain restriction was not demonstrated. The infiltrate is mostly CD3 positive with occasional CD4 positive cells.

LABORATORY RESULTS

4/2015 – Normal CBC with diff, normal CMP, ANA negative (ELISA and IFA), Anti-Sm negative, anti-dsDNA negative, SSA and SSB negative, U/A negative, ESR normal, CRP normal, C3 71, C4 10

10/2015 – Normal CBC with diff, normal CMP except for AST 72 and ALT 107, ANA screen > 5.5, ANA titer >=1:1280, speckled ANA pattern, Anti-Sm 1.25, anti-dsDNA negative, SSA and SSB negative, C3 45, C4 5, CH50 < 10

RADIOLOGY

None

TREATMENT AND COURSE

Baseline labs were obtained at the first visit due to the history of photosensitivity with concern for acute cutaneous lupus erythematosus (ACLE); both the C3 and C4 were found to be low. All other initial labs were unremarkable including an ANA and lupus-specific serologies. The patient was subsequently started on topical tacrolimus 0.1% ointment twice daily, and the rash resolved within 1-2 weeks. He was informed about the importance of strict sun protection and wore Neutrogena Helioplex sunscreen 70 SPF, reapplying every 2-3 hours. Six months later, the violaceous dermatitic patches on his nose and periorbital region recurred, again after a trip to Florida. He was otherwise feeling well. Repeat labs were notable for hypocomplementemia and new high-titer ANA (>=1:1280). Anti-Sm was elevated but other lupus-specific serologies were negative. His LFTs were mildly elevated. The EBV IgG and IgM were both positive with a known exposure; an abdominal ultrasound was unremarkable. All other labs were unremarkable. He was started on hydroxychloroquine 200 mg alternating with 100 mg every other day along with Tacrolimus 0.1% ointment.

Rheumatology at Lurie Children's Hospital promptly evaluated the patient and detected a faint effusion in the left knee with mild loss of flexion and a leg length discrepancy (L > R leg). He had experienced one episode of left knee pain after playing basketball that resolved with ice. Additional labs were notable for a C2 level < 10, C2 antigen < 0.2, with low C3 and C4. Based on the above findings, the patient met SLICC criteria for SLE (+ANA, +Smith, hypocomplementemia, arthritis, presumed acute cutaneous lupus). The rash resolved a few weeks after initiation of treatment.

DIAGNOSIS

Lymphoid nodular hyperplasia as the initial presentation of systemic lupus erythematosus (SLE) in the setting of C2 deficiency

DISCUSSION

Inherited homozygous deficiencies of the classical pathway components, especially C1q and C4, are associated with early onset SLE. Early components of the classical complement pathway, including C1q, bind to surface blebs of apoptotic keratinocytes and are essential for clearance of apoptotic cells and circulating immune complexes. These apoptotic cells result in increased exposure to self-antigens, predisposing to autoimmunity.

Cutaneous lymphoid nodular hyperplasia clinically presents as violaceous to erythematous papules, nodules, or plaques on the head, neck and upper extremities. On histopathology, there is marked proliferation of non-neoplastic polyclonal lymphocytes that form follicles. Although the majority of cases have no known etiology, previous trauma, tattoos, arthropod bites, vaccinations, and infections with *Borrelia burgdorferi* have been reported. The histologic findings

may resemble B cell lymphoma, mycosis fungoides, or CD30+ anaplastic large cell lymphoma; however, it is currently thought that this condition is a benign reactive condition that requires only conservative management.

We could find no reports of cutaneous lymphoid nodular hyperplasia associated with either C2 deficiency or SLE. There is a single paper reporting lymphoid nodular hyperplasia as an incidental finding in bone marrow biopsies among patients with SLE and cytopenias. We presume that the immunologic dysregulation associated with this child's inherited complement deficiency predisposed to a local cutaneous reaction, which was distinct from the photosensitive eruption he later developed. This was never biopsied but we presume it was consistent with acute cutaneous lupus. This case underscores the importance of listening closely to families and collaborating with other physicians to optimize patient care.

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Presented by Andrew Nesterovitch, MD and Arthur Rhodes, MD, MPH
Department of Dermatology, Rush University Medical Center

FAST BREAK

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 6**

Presented by Todd Rickett, MD, PhD and Lisa Arkin, MD
Department of Dermatology, Rush University Medical Center

UNKNOWN

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 7**

Presented by Emily Garritson, MD, Michael Tharp, MD, and Lisa Arkin, MD
Department of Dermatology, Rush University Medical Center

HISTORY OF PRESENT ILLNESS

The patient is a 9 year-old Hispanic female who presented to clinic with a 2 year history of evanescent skin lesions. Her father noted that she would develop red, edematous plaques on her face, neck, and extremities immediately following any exposure to cold weather conditions. Individual lesions last for approximately 2 hours and are always asymptomatic. At her initial visit, she had not yet received any treatment specifically for these eruptions. The patient and her family denied any associated episodes of angioedema, dyspnea, nausea, vomiting, or diarrhea. Her mother further denied any history of periodic fevers, frequent headaches, hearing loss, or myalgias.

PAST MEDICAL HISTORY

Prematurity, born at 30 weeks gestation
Allergic rhinoconjunctivitis
Mild persistent asthma requiring 2 hospitalizations
Infantile hemangiomas

PAST SURGICAL HISTORY

Bilateral inguinal hernia repair
Diaphragmatic hernia repair

MEDICATIONS

Fluticasone 50 mcg nasal spray daily
Mometasone-fomoterol 100/5 mcg inhaler 2 puffs BID
Albuterol HFA 90 mcg inhaler 2 puffs q 6 hours prn wheezing
Montelukast 5 mg daily
Zyrtec 10 mg nightly

ALLERGIES

The patient has no known drug allergies.

FAMILY HISTORY

There are no family members with similar cutaneous findings. Furthermore, there is no known family history of autoinflammatory or autoimmune diseases.

SOCIAL HISTORY

The patient is a 4th grader who lives with her mother and father.

PHYSICAL EXAM

The patient had no cutaneous findings of note during the initial evaluation. After 5 minutes of contact with an ice pack, the exposed portion of her left forearm developed multiple edematous, erythematous plaques.

LABORATORY RESULTS

Immunoglobin E 931 (Ref <304 kU/L)

DIAGNOSIS

Cold urticaria

TREATMENT AND COURSE

At the first visit, the patient and her father were instructed on the importance of avoidance of possible triggers including cold and windy weather conditions, cold showers, and swimming in cold water. She was started on cyproheptadine 4 mg BID and continued on cetirizine 10 mg nightly. She had subsequent daily flaring of lesions after 3 weeks of treatment, so her cyproheptadine evening dose was doubled to 8 mg with less frequent episodes of urticaria. The patient and her family also received teaching on how to use an epinephrine autoinjector in instances of possible anaphylaxis.

DISCUSSION

Cold urticaria is one subset of the physical or inducible urticarias and represents approximately 3% of cases of chronic urticaria. Patients with this disorder develop edematous papules and plaques within minutes of exposure to cold air, water, food, or drink. The lesions appear on exposed surfaces upon rewarming and most commonly occur on the face and upper extremities. Primary cold urticaria, accounting for 95% of cases, occurs in patients without an underlying associated systemic disease. In both pediatric and adult case series, about 30% of patients display at least one serious systemic symptom in addition to the cutaneous lesions with cardiovascular and respiratory symptoms being most common (hypotension, dizziness, and respiratory distress). In addition, fatalities from shock have been reported in affected persons swimming and showering in cold water. Primary disease typically begins in early adulthood, but it has been documented in children less than 1 year of age. Patients with suspected cold urticaria can be diagnosed with an in-office ice cube provocation test during which an ice cube wrapped in plastic is applied to bare skin for 5 minutes. Patients with a positive test will demonstrate wheals in the area of cold contact by 10 minutes. The mean duration of disease has been reported to be about 5 years in acquired primary disease.

Secondary cold urticaria occurs in association with an underlying systemic disease. Examples of associated conditions include cryoglobulinemia, cryofibrinogenemia, hepatitis B and C, infectious mononucleosis, syphilis, and multiple myeloma. The ice cube test is not recommended in these patients due to risk of precipitating vascular occlusion and possible tissue ischemia. Patients with the secondary form of cold urticaria are more often adults and have additional cutaneous findings like purpura, ulcers, acrocyanosis, or Raynaud's phenomenon.

The final subgroup of patients with cold urticaria is the syndromic variants. This includes the cryopyrinopathies, a spectrum of rare autosomal dominant syndromes resulting from mutations in the gene NLRP3/CAIS1. All of these syndromes (Familial Cold Autoinflammatory, Muckle-Wells, and CINCA/NOMID) are characterized by cold urticarial eruptions, but the phenotypes vary. Patients with familial cold autoinflammatory syndrome present shortly after birth or during early infancy with atypical delayed cold urticaria, fevers, arthralgias, headaches, generalized malaise, and conjunctivitis, while patients with Muckle-Wells have urticaria, sensorineural hearing loss, and renal amyloidosis. In cases of chronic infantile neurological cutaneous and articular/neonatal onset multisystemic inflammatory disease, patients present with migrating urticarial eruptions, destructive arthralgias, and chronic aseptic meningitis. These syndromic patients typically have a negative ice cube test.

PLCG2 associated antibody deficiency and immune dysregulation (PLAID) syndrome is another recently described autosomal dominant condition which is characterized by cold evaporative urticaria starting in infancy. These patients can also demonstrate a unique blistering acral dermatitis and non-infectious granulomatous lesions. Affected individuals with PLAID have

increased incidence of atopy, autoimmunity, and reduced humoral immunity with increased sinopulmonary infections.

Treatment of cold urticaria includes avoidance of high risk activities such as swimming, cold showering, surgery, and ingestion of cold food or drinks. Patients must be educated on the risks of additional systemic symptoms like hypotension and dyspnea and are given epinephrine autoinjectors for possible episodes of anaphylaxis. Non-sedating H1-antihistamines are the first line therapy and may administered at dosages four times the standard dose. In patients with disease refractory to antihistamines, omalizumab or cyclosporine therapy may be initiated. Patients with a cryopyrinopathy are treated with anakinra.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 8**

Presented by Bryan Sofen, MD, Louisa Gehlmann, MD, and Michael Tharp, MD
Department of Dermatology, Rush University Medical Center

UNKNOWN

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 9**

Presented by Neal Kumar, MD, MBA and Lisa Arkin, MD
Department of Dermatology, Rush University Medical Center

HISTORY OF PRESENT ILLNESS

A 12 day old ex 31 2/7 week infant twin A was born due to precipitous pre-term labor. Dermatology was consulted for evaluation of multiple vascular lesions, two of which were noted on day 2 of life. The lesions had not bled or ulcerated. His hospital course was complicated by hemolytic anemia and thrombocytopenia of unknown etiology requiring pRBC transfusion, with resolution and no recurrence. A cardiac murmur had been noted prior to consultation and a subsequent echocardiogram confirmed a PFO with left to right shunt. An abdominal x-ray was notable for mild hepatomegaly without splenomegaly.

PAST MEDICAL HISTORY

Preterm labor
Thrombocytopenia (resolved)
Hemolytic anemia (resolved)
PFO

PAST SURGICAL HISTORY

None

MEDICATIONS

None

ALLERGIES

No known drug allergies

FAMILY HISTORY

Twin B
Mom with 2 other healthy children without any medical problems

SOCIAL HISTORY

Single mom. No smoking at home.

PHYSICAL EXAMINATION

Skin: On the left forearm, left back, right hand 3rd digit, right abdomen, right medial forearm, chest, left abdomen, right anterior shin, left shin, left lateral thigh, and left parietal scalp there were 15 well demarcated red to violaceous papules, the largest lesion measuring 4 mm on left back. There was no evidence of ulceration, bleeding, telangiectasias, or peripheral pallor.

Cardiac: Regular rate and rhythm. I/VI systolic murmur. No jugular venous distention appreciated.

Pulmonary: Mild tachypnea and subcostal retractions. No rales appreciated on auscultation.

HISTOPATHOLOGY

None

LABORATORY EVALUATION

Date	TSH [0.35-4.94 uIL/mL]	Free T4 [0.7-1.5 ng/dL]	Reverse T3 [8-25 ng/dL]
11/10/15	3.7		270 (H)
11/23/15	3.9	1.0	
12/4/15	5.1 (H)	1.4	157 (H)
12/7/15	4.6	1.8 (H)	
12/14/15	2.9	1.4	192 (H)
12/21/15	5.1 (H)	1.3	
1/4/16	6.5 (H)	1.5	
2/15/16	6.9 (H)	1.3	
4/12/16	1.739	1.3	

IMAGING

Complete abdominal ultrasound with Doppler revealed at least 3 hepatic lesions which appear rounded, predominantly centrally hypoechoic with increased peripheral echogenicity. Some of the lesions appeared to demonstrate increased peripheral color flow. There was dilatation of hepatic arteries and veins, most compatible with vascular shunting.

Echocardiogram revealed mild dilatation of the left atrium and left ventricle with increased systemic venous flow return to the heart. Systolic function was normal.

Chest x-ray was significant for moderate enlargement of the cardiac silhouette and mild pulmonary edema.

DIAGNOSIS

Multifocal infantile hemangiomas with extra-cutaneous involvement of the liver and high output shunting leading to congestive heart failure

TREATMENT AND COURSE

Initial abdominal ultrasound with Doppler revealed at least 3 hepatic masses as well as dilatation of hepatic arteries and veins compatible with high out-put vascular shunting. An echocardiogram was performed and confirmed early signs of heart failure. Screening for hypothyroidism revealed a high reverse T3, which has trended down after initiation of therapy, with normal TSH and T4.

Propranolol was initiated for the liver involvement at 0.5 mg/kg/day and titrated to 3 mg/kg/day divided q8 hours. Due to the risk of hypoglycemia, the baby was fed prior to every dose and monitored for bradycardia and hypotension. He tolerated the propranolol escalation without complication.

After consultation with Dr. Steven Fishman at the Vascular Anomalies Center at Boston Children's Hospital, liver ultrasounds were repeated every 2 weeks until stabilization. Two weeks after propranolol initiation, there was an interval increase in number of liver lesions from 3 to at least 9. A subsequent ultrasound (12/14/15) confirmed that the lesions had stabilized in size and number, and he was discharged home. The ultrasound schedule was lengthened by 2 weeks from the date of the 1st stable ultrasound. A repeat echocardiogram 1 month after discharge demonstrated resolution of cardiac failure. Propranolol has been weight adjusted monthly (total dose 3 mg/kg/day). Six weeks after discharge, a repeat abdominal ultrasound demonstrated a significant decrease in the size of the liver hemangiomas (at 4 months 2 weeks gestational age), suggesting involution.

DISCUSSION

This neonate with multiple infantile hemangiomas (IH) on the skin demonstrates the importance of screening for hepatic hemangiomas. The actual number of cutaneous IHs required to precipitate concern remains a floating target, but most people use > 5 as a guideline for hepatic screening based on an a retrospective review of hepatic hemangiomas by Dickie et al. The screening test of choice is a complete abdominal ultrasound with Doppler imaging.

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The infantile hepatic hemangioma is the most common hepatic vascular tumor in the pediatric population and can be divided into focal, multifocal, or diffuse subtypes. Dickie et al suggest that patients with diffuse or multifocal hepatic hemangiomas should be screened for congestive heart failure and hypothyroidism. Large infantile hemangiomas elaborate type 3 iodothyronine deiodinase, which catalyzes the conversion of thyroxine (T4) to reverse triiodothyronine (T3) and T3 to diiodothyronine (T2). Hypothyroidism develops when the rate of inactivation of thyroid hormones surpasses the rate of production, leading to consumptive hypothyroidism.

While there are no consensus guidelines for the use of propranolol for hepatic infantile hemangiomas, several case reports and case series support its use. Clear indications for starting propranolol include vascular shunting, high output heart failure, hypothyroidism, and rapidly increasing hemangioma size. A review of 26 cases of diffuse infantile hepatic hemangiomas noted a mortality rate of 17% and a >70% incidence of hypothyroidism. More than one-third of these patients developed heart failure. Propranolol doses can be escalated to as high as 3-5 mg/kg/day in 0.5 or 1 mg/kg increments under close monitoring. In a retrospective French study of 1130 children with cutaneous infantile hemangiomas treated with propranolol, 0.9% were resistant to propranolol treatment at doses of 2-3 mg/kg/day after at least 4 weeks of treatment. Half of the non-responders responded to adjuvant systemic steroids.

In our case, both the vascular shunting and hepatic hemangiomas have responded to 3 mg/kg/day of propranolol, and he is thriving on this regimen.

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Presented by Neal Kumar, MD, MBA and Michael Tharp, MD
Physician team Included Joan Guitart, MD
Department of Dermatology, Rush University Medical Center

HISTORY OF PRESENT ILLNESS

This is a 27 year black male who initially presented to our clinic on 8/2014 with a 1.5 year history of diffuse pruritic plaques. He reported that his eruption started as a single red plaque on the right forearm, but progressed to widespread, numerous plaques with islands of sparing over his entire body. According to the patient, he had been seen by multiple dermatologists with biopsies showing "inflammation" or psoriasis. At his initial presentation to our clinic a skin biopsy was performed which was read as "consistent with psoriasis". He was treated with midpotency and then potent topical steroids with only mild improvement. Because adalimumab was not approved by his insurance, he was started on cyclosporine (CsA) 3 mg/kg/day along with methotrexate (titrated up to 12.5 mg weekly). After 6 weeks of treatment, there was no improvement; however, adalimumab was approved and thus his treatment was switched to this biologic (40 mg every 2 weeks). Because of joint complaints, the patientwas also referred to Rheumatology and diagnosed as having mild psoriatic arthritis. After 4 months of adalimumab and triamcinolone ointment, there was no improvement. Some lesions were becoming hyperkeratotic, and facial involvement was worsening. As a result, two additional skin biopsies were performed. Despite the concern for CTCL, these biopsies again showed a "psoriasiform dermatitis". Given his lack of response to adalimumab and repeat biopsies showing only psoriasiform changes, methotrexate (20mg weekly), and NB-UVB (twice weekly) therapy were instituted. He received only three sessions of NB-UVB before moving to Indiana for the following 7-8 months.

While living in Indiana, the patients was seen in the dermatology department at Indiana University and given the diagnosis of psoriasis. He also was seen by a private dermatologist in Indiana who performed two additional biopsies, both reported "compatible with psoriasis". The patient continued to follow with dermatologists in Indiana and was started on ustekinumab (1/2016 and 2/2016) without improvement. During this time, he developed skin ulcers on his back, shoulder, posterior neck, and extremities. Due to social reasons, the patient moved back to Illinois in 3/2016 and presented to the Rush ED for acute onset low back pain. MRI of his low back was unremarkable, but a culture of a back ulcer was positive for MRSA. The patient was admitted to the hospital and Dermatology was consulted. The patient complained of significant pruritus (10/10), but denied fevers, chills, night sweats, weight loss, or family history of psoriasis. Additional biopsies were obtained with one suggesting a T-cell lymphoproliferative disorder; the other two showed non-specific findings without atypical lymphocytes (see histopathology).

PAST MEDICAL HISTORY

None

PAST SURGICAL HISTORY

None

MEDICATIONS

Stelara

ALLERGIES

None known

FAMILY HISTORY
No family history of psoriasis or skin cancer

SOCIAL HISTORY
Daily to weekly marijuana use. Regular alcohol use.

PHYSICAL EXAMINATION
At the time of the initial examination, the patient was afebrile and well-appearing. Widespread thick hyperkeratotic and lichenified erythematous plaques and nodules were noted over his entire body, Some lesions had a finer scale. Dusky areas within the center of some nodules were noted. Palmar and plantar involvement was noted. An oral palatal ulcer was present. BSA was approximately 80% with islands of sparing. There was no nail pitting.

HISTOPATHOLOGY
8/2014 (right abdomen): Consistent with psoriasis

4/2015 (right shoulder, right posterior hip): Psoriasiform dermatitis with hypogranulosis, consistent with psoriasis

3/3/2016 (left shoulder, upper back): T-cell lymphoproliferative disorder. Psoriasiform dermatitis. Sections of the left shoulder lesion show ulcerated epidermis with epidermal hyperplasia and a band-like infiltrate of mostly small to medium and a striking patchy infiltrate of large and irregular lymphoid cells. The lymphocytes are predominately located in the superficial dermis with epidermotropism. The larger cells are atypical with irregular and convoluted nuclei.

3/17/2016 (left leg, left neck): Epidermal hyperplasia and superficial perivascular dermatitis with eosinophils and plasma cells (A). Lichenoid dermatitis (B). Atypical lymphoid infiltrates seen in previous biopsy (S16-4687) are not identified in the present biopsies.
A. There is hyper and parakeratosis, epidermal hyperplasia which is psoriasiform in some areas and verrucous in others and perivascular mixed inflammatory cell infiltrate consisting of lymphocytes, eosinophils and plasma cells. The overall histologic changes are not quite typical of psoriasis although verrucous psoriasis may be a possibility.
B. There is hyperkeratosis, irregular epidermal hyperplasia and a lichenoid inflammatory cell infiltrate consisting of lymphocytes and frequent melanophages and associated with occasional necrotic keratinocytes. Scattered eosinophils and plasma cells are present.

The following biopsies was reviewed by Dr. Joan Guitart:
8/2014 (right abdomen), 3/3/2016 (left shoulder, immunohistochemistry):

Atypical intraepidermal lymphoid infiltrate consistent with cytotoxic T-cell lymphoma, not otherwise specified. The tumor cells lack expression of both TCR heterodimers based on the initial markers tested and have a null CD4-/CD8- phenotype with cytotoxic markers consistent with an aggressive lymphoma with Berti's like features. Tumor cells are negative for gamma-delta marker (GM3) and CD45RA and positive for CD7, granzyme B and CD2.

LABORATORY EVALUATION
Right groin lymph node; excision: Follicular hyperplasia with interfollicular expansion by histiocytes and pigment-laden macrophages, suggestive of dermatopathic lymphadenopathy. No morphologic or flow cytometric evidence of lymphoma seen.

Bone marrow biopsy and touch prep, aspirate smears, and peripheral blood smear: Normocellular marrow with tri-lineage maturation. No morphological or flow cytometric evidence of lymphoma.

IMAGING

CT of chest, abdomen, and pelvis revealed multiple enlarged bilateral axillary, inguinal lymph nodes and prominent to borderline enlarged mediastinal lymph nodes which are increased in size from prior recent CTs dated 03/04/2016 and 03/14/2016. These are nonspecific. Given the extensive distribution, an inflammatory or neoplastic process should be considered.

DIAGNOSIS

CD4-/CD8- Aggressive T-Cell Lymphoma

TREATMENT AND COURSE

On March 2nd 2016 the patient was admitted for acute onset low back. CT T-spine and MRI were negative for infectious etiology. Dermatology was consulted and two skin biopsies were performed, one of which was consistent with T-cell lymphoproliferative disorder, the other a psoriasiform dermatitis. Immunostaining on the CTCL suggestive skin biopsy failed to reveal a specific subtype. Oncology was consulted who recommended staging with a CT of the chest/abdomen/pelvis, lymph node biopsy, and bone marrow biopsy; all of which failed to showed evidence of lymphoma. Skin cultures grew MRSA for which he was started on Vancomycin with decreased drainage of the ulcer as well as decreased crusting and scaling of his other skin lesions.

Due to unclear CTCL subtype on initial inpatient skin biopsy, repeat punch biopsies were performed which showed epidermal hyperplasia with eosinophils and plasma cells on the left leg, and lichenoid dermatitis on the left neck. However since the previous biopsy suggested CTCL, bexarotene was ordered but was denied by insurance due to the fact that he had not received other treatments. He was discharged on acitretin 25 mg daily and triamcinolone 0.1% ointment with plans to start NB-UVB as outpatient. The patient was also seen my hematology/oncology who recommended starting romidepsin.

DISCUSSION

CTCL patients expressing a CD8+ T cell phenotype are rare but have been well-defined. Berti et al described 17 patients with CD8+ CTCL with eight having a distinctive clinical and immunopathological presentation. In this patient subgroup, all presented with widespread, erythematous scaling patches, plaques, and verrucous or hemorrhagic papulonodular and tumoral lesions. Unlike classic MF, these patients did not generally progress through patch-, plaque, and tumor-stage disease, but rather presented with widespread plaques and tumors from the onset. Additionally oral mucosal involvement was observed in 3/8 patients, and metastatic spread to unusual sites including lungs, testis, and CNS but typically sparing the lymph nodes was noted.

On histology, early lesions showed intraepidermal pagetoid spreading of atypical lymphocytes. Epidermotropism was noted in all stages of the disease which is unlike most cases of MF. Fully developed lesions demonstrated band-like/lichenoid infiltrates of atypical lymphocytes varying in size. In the center of these lesions, intercellular edema, blister formation and necrosis was often observed while pagetoid lymphocytes changes occured at the periphery. Immunohistochemistry demonstrated CD3+, CD8+, CD7+,TIA-1/GMP17+,CD45RA+ cellular infiltrates which were CD2-,CD30-and HECA 452-. All 8 patients in this series died with disseminated disease 14 to

50 months after diagnosis (median, 32 months) despite PUVA, oral retinoids, total skin electron beam irradiation, polychemotherapy and/or allogenic bone marrow transplantation.

Nofal et al. have recently reviewed the literature on CD8+ T cell lymphomas and proposed diagnostic criteria listed in the table below:

Table II. Differences between mycosis fungoides and primary cutaneous aggressive epidermotropic $CD8^+$ T-cell lymphoma

	Mycosis fungoides	Primary cutaneous aggressive epidermotropic $CD8^+$ T-cell lymphoma
History	Long, usually years	Short, weeks to months
Clinical features		
Symptom	Itching is common	Pain is common
Precursor lesions	Usually patches at first	Plaques and tumors from start
Central ulceration	Uncommon	Very common
Extent	Localized or generalized	Generalized
Mucosal involvement	Very rare	Common
General condition	Usually good	Usually bad
Histopathology		
Epidermotropism	Early, less pronounced	All stages, marked
Keratinocyte necrosis	Rare	More common
Depth	Less deep	More deep to subcutaneous fat
Adnexal structures	In syringotropic and folliculotropic variants	Usually involved
Angiocentricity and angioinvasion	Very rare	Relatively common
Immunophenotype		
CD4	+	−
CD8	Rarely positive	Always positive
Course	Indolent, even in $CD8^+$ cases	Aggressive
Metastatic spread		
Incidence	Rare and late	Common and early
Nodal	Common	Lymph nodes are usually spared
Extranodal	Lung, spleen, and liver	Lung, testis, and CNS
Therapy		
Conventional therapy for $CD4^+$ CTCL	Usually effective	Not effective, some may worsen
Systemic chemotherapy	Rarely needed	Almost always needed
Prognosis	Good	Poor

CNS, Central nervous system; *CTCL*, cutaneous T-cell lymphoma.

While numerous therapies including PUVA, interferon, localized and total body radiotherapy, bexarotene, gemcitabine and other systemic chemotherapies as well as bone marrow transplantation have been used, to date there is still no effective treatment for CD8+ CTCL.

What makes our patient unusual is that he has the clinical presentation of CD8+ CTCL but lacks the characteristic immunophenotyping in several skin biopsies. Hodak et al. described CD3+,CD4-/CD8- lymphocytic infiltrates in lesional skin of 18/140 patients with CTCL. However, none of their patients had the clinical presentation of our patient and all had indolent disease responsive to conservative therapy. Because of the aggressive clinical presentation of our patient, we consider him most like CD8+ CTCL. Therapies in consideration are romedepsin, gemcitabine, total skin electron beam and possibly bone marrow transplantation.

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