Chicago Dermatological Society

Monthly Educational Conference

Program Information
CME Certification
and
Case Presentations

Wednesday, May 10, 2017
Gleacher Center – Chicago, IL

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

Program

Host: Rush University

Conference Location

Gleacher Conference Center
450 N. Cityfront Plaza Dr., Chicago

All meeting activities take place on the 6th Floor of the Gleacher Center.

8:00 a.m.	**Registration & Continental Breakfast with Exhibitors** *6th Floor Lobby and Room 600*
8:30 a.m. - 10:00 a.m.	**Clinical Rounds** Posters – *Room 602/604 (available throughout the morning)* Slide viewing – *Room 608 (available throughout the morning)*
9:00 a.m. - 10:00 a.m.	**Resident/Basic Science Lecture** – *Room 621* "Lessons from Mucous Membrane Pemphigoid" *Kim B. Yancey, MD*
10:00 a.m. - 10:30 a.m.	**Break and Visit with Exhibitors** – *Room 600*
10:30 a.m. - 12:15 p.m.	**Resident Case Presentations & Discussion** **MOC Self-Assessment Questions** *Room 621*
12:15 p.m. - 12:45 p.m.	**Box Lunches & visit with exhibitors** *Room 600*
12:45 p.m. - 1:00 p.m.	**CDS Business Meeting** *Room 621*
1:00 p.m. - 2:00 p.m.	**General Session** – *Room 621* *MALKINSON LECTURE*: "Patients Matter, People Matter" *Kim B. Yancey, MD*
2:00 p.m.	**Meeting adjourns**

Mark the Date!
President's Conference and Annual Awards Luncheon – Wednesday, June 7, 2017 at the Stephens Convention Center in Rosemont

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

Guest Speaker

KIM B. YANCEY, MD

Professor and Chair
Department of Dermatology
UT Southwestern Medical Center
Dallas, TX

Delivering the Frederick Malkinson Lecture

A native of Georgia, Kim B. Yancey, M.D., is Professor and Chair of the Department of Dermatology at UT Southwestern Medical Center. After graduating from the University of Georgia, summa cum laude and valedictorian, he earned his medical degree (Alpha Omega Alpha) from the Medical College of Georgia and performed his residency training there.

A National Institutes of Health-funded researcher for more than 25 years, Dr. Yancey completed a postdoctoral fellowship in immunodermatology in the dermatology branch of the National Cancer Institute at the National Institutes of Health (NIH). He is certified by the American Board of Dermatology, and also holds special competence in dermatologic immunology and diagnostic laboratory immunology.

In 2007, he received the American Academy of Dermatology's Marion Sulzberger Award. He has published numerous research manuscripts, monographs, and chapters, served on an array of grant review panels, and presented more than 150 scientific abstracts and invited lectures in the U.S. and abroad.

CME Information

This educational activity is jointly provided by the Chicago Dermatological Society in partnership with the Indiana Academy of Ophthalmology

Overview

The Chicago Dermatological Society was established in 1903 and has strived to provide meaningful educational opportunities to dermatologists in the Chicago area for more than a century. Guest speakers from across the country share their expertise with CDS members, as well as residents in training medical students doing their dermatology rotation. CDS schedules six day-long meetings each year which are "hosted" by one of the dermatology residency programs in the city. In addition to two lectures given by the guest speaker, the residents of the host institution present cases which are offered for audience discussion. In addition, live patients, posters and microscopic slides prepared by the residents are made available during the "clinical rounds" portion of the meeting. CDS also offers a session that qualifies for "Maintenance of Certification" self-assessment questions under the auspices of the American Board of Dermatology.

Target Audience

This activity has been designed to meet the educational needs of dermatologists. CDS members, residents in training and medical students engaged in their dermatology rotation are invited to attend.

Learning Objectives

At the conclusion of the 2016/17 series of meetings, the participant should 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.

Physician Accreditation Statement

This activity is planned and implemented by Indiana Academy of Ophthalmology (IAO) and the Chicago Dermatological Society. IAO is accredited by the Indiana State Medical Association to provide continuing education for physicians.

Credit Designation for Physicians – IAO designates this live activity for a maximum of 4.75 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Attendees are required to submit a CME claim form upon departure from the conference. Please leave your form, along with the evaluation form, at the registration table when you leave the meeting. Thank you for your attention to this important item. Note - You may complete the paper version of the evaluation form or submit your evaluation online.

Disclosure of Conflicts of Interest

The IAO and CDS require instructors, planners, managers and other individuals and their spouse/life partner who are in a position to control the content of this activity to disclose any real or apparent conflict of interest they may have as related to the content of this activity. All identified conflicts of interest are thoroughly vetted by IAO and CDS for fair balance, scientific objectivity of studies mentioned in the materials or used as the basis for content, and appropriateness of patient care recommendations. All speakers are asked to follow the "first slide" rule to repeat their conflict of interest disclosures during their talk.

Today's guest speaker, Dr. Kim Yancey, has disclosed the following potential conflicts of interest: Author royalties - UpToDate; Consulting fee - Ashland Chemical Company. Dr. Yancey has no other relevant conflicts of interest. None of the planning committee members have any conflicts of interest to disclose.

Continued next page

Contact Information

For information about the physician accreditation of this program please contact the CDS administrative office at: 847-680-1666; email: Rich@RichardPaulAssociates.com

Americans with Disabilities Act

In compliance with the Americans with Disabilities Act, we will make every reasonable effort to accommodate your request. For any special requests, contact CDS at: Rich@RichardPaulAssociates.com

Disclaimer

Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed in this activity should not be used by clinicians without evaluation of patient conditions and possible contraindications on dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities.

Dislosure of Unlabeled Use

This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. The planners of this activity do not recommend the use of any agent outside of the labeled indications. The opinions expressed in the educational activity are those of the faculty and do not necessarily represent the views of the planners. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

Chicago Dermatological Society
Patient Privacy and HIPAA Compliance

APPROVED
June 3, 2015

Purpose

The purpose of this policy is to reaffirm the intent of the Chicago Dermatological Society (CDS) to appropriately safeguard patient privacy with respect to CDS conferences, publications and its website, and also to adhere to HIPAA requirements. All CDS members are expected to be aware of and conform to all regulations concerning patient privacy when attending a conference or utilizing any materials produced by CDS which contains any form of patient information which could be considered to be Protected Health Information.

Background

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) and its implementing regulations restrict health care providers and others to use and disclose protected health information (PHI). Protected health information means information that is created or received by an entity and relates to the past, present, or future physical or mental health condition of a patient; the provision of health care to a patient; or the past, present, or future payment for the provision of health care to a patient; and that identifies the patient or for which there is a reasonable basis to believe the information can be used to identify the patient. Protected health information includes information of persons living or deceased.

Some examples of PHI are:
- Patient's medical record number
- Patient's demographic information (e.g. address, telephone number)
- Information doctors, nurses and other health care providers put in a patient's medical record
- Identifiable images of the patient
- Conversations a provider has about a patient's care or treatment with nurses and others
- Information about a patient in a provider's computer system or a health insurer's computer system
- Billing information about a patient at a clinic
- Any health information that can lead to the identity of an individual or the contents of the information can be used to make a reasonable assumption as to the identity of the individual

Policy

The CDS takes seriously compliance with HIPAA regulations and safeguards concerning protected health information. Accordingly, the Chicago Dermatological Society has adopted the following provisions:

1. Case descriptions included in clinical conference "protocol books" and posters may not include information that could potentially identify a particular patient.

2. Photos of patients will not be published in clinical conference handout materials, including the protocol book.

3. To the extent possible, posters, slide presentations and videos displayed at CDS clinical conferences should avoid using photos that display a patient's full face or other features that could identify a particular patient. When a full-face photo must be used for clinical/educational reasons, the photo must be altered as much as possible to disguise the identity of the patient.

4. At all times, all attendees of CDS clinical conferences must adhere to appropriate behavior that respects the patient's right to privacy. Taking personal photos of posters or other displays, images included in general session lectures/presentations, and live patients at CDS conferences is strictly prohibited. Making audio recordings of any session at a CDS conference also is prohibited.

5. Attendees may not share materials distributed by CDS as part of the clinical conference or on its website with others who are not participating in the conference or who are not members of the CDS.

6. It is the responsibility of the "host" department partnering with CDS for a clinical conference to obtain all appropriate patient waivers and/or informed consent regarding the patient's participation in the CDS conference, including presentation of their case and display of posters or photos.

7. CDS will include a copy of its patient privacy policy in every meeting packet, and it will display a poster reiterating this policy at the entrance to live patient and poster viewing areas.

TABLE OF CONTENTS

Presented by Neal Kumar, MD, MBA, and Morayo Adisa, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This is a 75-year-old woman who presented for evaluation and management of a widespread eruption distributed on her head, face, trunk, and extremities. She first noticed the blistering eruption about a year prior to her presentation and had been managed by a Dermatologist in Indiana. She described the lesions as blisters which later "pop", drain and crust over. Once crusted over, the lesions were associated with pain which worsens with rubbing on clothing. She also reports oral mucosa involvement. She denied any fevers, chills, or shortness of breath. Prior to her presentation, she had been initially treated with prednisone for 2 weeks with good control. This was followed by Doxycycline which improved her initial flare but did not prevent new lesions from appearing. After 2 months of inadequate treatment with doxycycline, she was switched to Mycophenolate mofetil monotherapy with poor control of her disease and development of ankle swelling, so this was discontinued. Prednisone was then re-initiated at a high dose (80mg) but her disease continued to progress. She was then referred to Rush Dermatology.

PAST MEDICAL HISTORY

Hypertension

PAST SURGICAL HISTORY

None

MEDICATIONS

Hydroxyzine 25 mg TID
Mupirocin ointment
Clobetasol cream

ALLERGIES

None known

FAMILY HISTORY

No family history of blistering skin diseases or skin cancer

SOCIAL HISTORY

Former smoker

PHYSICAL EXAMINATION

- Scalp has thick crust atop pink eroded plaques
- Bilateral cheeks, nasal tip, chin pink eroded plaques with thick hemorrhagic crust
- On hard palate of mouth is a large ulceration >1cm in diameter
- Neck, chest, back, extremities have numerous pink erosions topped with hemorrhagic crust
- Right hand with two tense bullae on palmar hands
- Upper legs few pink erosions free of crust
- Knees down with scattered hemorrhagic crusted eroded plaques

> 50% of BSA involvement

HISTOPATHOLOGY

9-3-2015 (Right arm, punch): Supra-basilar bulla and chronic superficial dermal inflammation with numerous eosinophils. The epidermis is mostly absent, making evaluation somewhat difficult.

DIF: There is linear/granular IgG deposition throughout the epithelial cell surfaces. There are also linear/granular C3 deposits on the lower-two thirds of the epithelial strata. There are no immune-reactants at the basement membrane zone and no IgA, IgM, C5b-9 or fibrinogen deposits seen in this specimen.

DIAGNOSIS

Pemphigus Vulgaris

TREATMENT AND COURSE

Because of the widespread involvement upon presentation and poor control with prednisone 80 mg daily, the patient was directly admitted from clinic for IV steroid treatment and wound care. She was started on solumedrol 1mg/kg, non-adherent wound dressings, and hydrogen peroxide soaks for crusting. A wound culture obtained from the crusted lesions on the neck was positive for pseudomonas and MSSA and the patient was treated with Levaquin and Keflex for the superinfection. She continued to improve in the hospital and she was transitioned to oral prednisone and started on Rituximab 375mg/m2 weekly x 4 weeks. She received her first rituximab infusion in the hospital, and subsequent infusions locally in Indiana. After completing the 4-week course of Rituximab, she demonstrated significant improvement with only a few active lesions on her flanks. She was started on Mycophenolate Mofetil 1g BID and Clobetasol ointment for maintenance with continued improvement. The Mycophenolate Mofetil was titrated up to 1500mg BID due to development of occasional new lesions and she was also started on nicotinamide 500 mg TID. Since then she has only had few sporadic breakouts well controlled with topical steroids.

DISCUSSION

Our patient demonstrated progressive disease which became refractory to oral steroids and Mycophenolate Mofetil within 1 year of onset. Long-term corticosteroid treatment can cause severe and even life-threatening side-effects, especially in elderly patients such as our patient. Rituximab offers an alternative treatment option which can improve the proportion of patients achieving complete remission off-therapy, while decreasing treatment side-effects of chronic corticosteroids.

Rituximab is a chimeric murine-human anti-CD20 monoclonal antibody which binds to the CD20 antigen on all B-cells except stem and plasma cells. Rituximab induces a reduction of circulating anti-desmoglein autoantibodies as well as desmoglein-specific auto-reactive T cells. Studies have shown that while rituximab causes an initial remarkable decline in anti-Dsg1 and anti-Dsg3 antibodies, titers can still remain positive even during disease remission in select patients.

The medication is typically dosed in one of two protocols. The rheumatoid arthritis (RA) protocol involves a 1000mg infusion which is repeated after 2 weeks. After that it can be repeated every 24 weeks or based on clinical evaluation (but no sooner than 16 weeks). The lymphoma protocol involves four weekly infusions of 375 mg/m^2. Blackbox warnings for rituximab include anaphylaxis, hepatitis B reactivation, and progressive multifocal leukoencephalopathy. Other side effects can include cytokine release syndrome in up to 10% of patients which can present with hypotension and/or bronchospasms.

Studies have demonstrated impressive disease control with both protocols. A prospective randomized trial published in the Lancet this year compared rituximab (RA dosing) combined with short-term prednisone to prednisone alone in 90 patients with newly diagnosed pemphigus. 89% of patients in the rituximab group demonstrated complete remission at month 24, compared to only 34% of patients assigned to prednisone alone. A study of 12 patients with refractory/severe pemphigus vulgaris treated with four weekly infusions of 375 mg/m^2 (lymphoma protocol) as well as a prednisone taper until the last infusion. Six months after the infusions, 9/12 patients showed complete response and 3/12 patients with partial response. Four patients experienced a long-lasting complete response for up to one year. In one case, 1 additional infusion of rituximab was given after 6 months. In another study a retrospective review of 17 patients treated with four weekly infusions of 375 mg/m^2 showed significant improvement in 88% of patients. At 6 months 53% of patients remained clear. Only 1/17 patients had no response, and serious infections were noted in 3/17 patients.

Table 1. Patients with pemphigus vulgaris treated with Rituximab at Rush University Medical Center *(M: male, F: female, RA: rheumatoid arthritis, MMF: mycophenolate mofetil)*

Sex	Protocol	Response	Maintenance	Adverse Events	Concurrent Treatment
M	RA	almost clear	yes	none	none
F	RA	almost clear, 1 oral lesion	no	pruritus	MMF 3g
F	RA	clear	no	none	none
F	RA	lost to follow-up	-	-	-
F	RA	clear x 4 years	no	none	none
F	RA	clear	no	none	Prednisone 5 mg
F	RA	clear since 2nd course	yes	none	none
M	RA	clear	no	none	Azathioprine 50mg
F	Lymphoma	almost clear	no	none	MMF 3g
M	Lymphoma	clear x 1 year, then recurred	no	deceased, pneumonia, 2016	Prednisone 80mg, MMF 3g

A review of 10 patients with pemphigus vulgaris treated with rituximab at Rush demonstrated significant improvement or complete clearance in 9/10 patients (Table 1). One patient was lost to follow up and response to rituximab was not noted. All other patients were seen in regular follow up for at least 3 months after infusions. 80% of patients received the rheumatoid arthritis (RA) protocol, and 20% received the lymphoma protocol. The lymphoma protocol was selected for the two patients primarily because it involved more frequent visits to monitor for adverse events given their elderly age and severe disease. The RA protocol was used in a majority of patients as rituximab infusions are administered through the Rheumatology department at Rush. Of the 7 patients who received the RA protocol and were seen in follow up, 5/7 were completely clear and 2/7 were almost clear at follow up. Of the 2 patients treated with the lymphoma protocol, 1/2 were almost clear and 1/2 were clear for one year before experiencing recurrent lesions. 2/7 patients treated with the RA protocol received a single maintenance infusion of 1000mg 6-9 months after their initial course due to mild disease activity with subsequent improvement. 1 patient demonstrated infusion related pruritus which resolved with co-administration of Benadryl. 1 patient, an 83-year-old male, passed away while admitted with pneumonia approximately 3 years after his rituximab course. He was also on prednisone 80mg and mycophenolate mofetil 3g at that time.

In March of 2017, the Food and Drug Administration (FDA) granted Breakthrough Therapy Designation status to rituximab for pemphigus vulgaris. This Designation allows the company to expedite the development and review of medications based on early evidence of clinical benefit in serious diseases. The Designation status was granted based on the data published by Joly et al in The Lancet in March of 2017.

REFERENCES

1. Joly, P. First-line rituximab combined with short-term prednisone versus prednisone alone for the treatment of pemphigus (Ritux 3): a prospective, multicenter, parallel-group open-label randomized trial. (2017). Lancet.
2. Reguiai Z, Tabary T, Maizieres M, Bernard P. Rituximab treatment of severe pemphigus: long-term results including immunologic follow-up. J Am Acad Dermatol. 2012;67:623–629.
3. Cianchini, G. Treatment of Severe Pemphigus With Rituximab. Arch Dermatol. 2007;143(8):103-1038.
4. El Tal, A. Rituximab: A monoclonal antibody to CD20 used in the treatment of pemphigus vulgaris. J Am Acad Dermatol 2006;55:449-59.
5. Mouquet H, Musette P, Gougeon ML et al. B-cell depletion immunotherapy in pemphigus: effects on cellular and humoral immune responses. J. Invest. Dermatol. 128(12), 2859–2869 (2008).

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 2**

Presented by Stacie Clark, MD, Peter Revenaugh, MD, Vijaya Reddy, MD, MBA, and Sheetal Mehta, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS
This 31-year old male presented to clinic for evaluation of a lesion on the left inferior lip. The lesion had been present for 2 months. It had grown rapidly over 1 month and then stabilized in size. The lesion was not painful and the patient denied any associated drainage or discharge. The patient participates in martial arts and endorses possible trauma to the area.

PAST MEDICAL HISTORY
None

MEDICATIONS
Creatine monohydrate supplement

ALLERGIES
Penicillin

FAMILY HISTORY
There is no known family history of skin cancer or melanoma.

SOCIAL HISTORY
Former smoker, quit in 2003

PHYSICAL EXAM
Clinical examination revealed a 1.5 cm, firm, mobile, non-tender mass, apparent on both the cutaneous and mucosal surfaces of the left inferior lip.

HISTOPATHOLOGY
Histopathology revealed a spindle cell proliferation with areas of myxoid change, extravasated red blood cells and peripheral lymphocytic aggregates. Immunohistochemical staining was diffusely positive for smooth muscle actin (SMA) and focally positive for desmin. S100, CK8/18 and p63 stains were negative.

LABORATORY RESULTS
None

RADIOLOGY
None

TREATMENT AND COURSE
The patient was referred to otolaryngology for wedge excision of the lesion.

DIAGNOSIS
Nodular fasciitis

DISCUSSION

Nodular fasciitis, also known as subcutaneous pseudosarcomatous fibromatosis or pseudosarcomatous fasciitis, was first described in 1955. It presents as a rapidly growing subcutaneous nodule or mass, but is generally self-limited in size to 1-5 cm. The underlying pathogenesis of this entity is unclear, however it has been postulated that it is a reactive process with trauma playing an important role. Most commonly it presents on the upper extremities or trunk of young to middle aged adults. Although the head and neck is commonly affected in the pediatric population, it is estimated that only 20% of adult cases occur in this location, with far fewer occurring in the oral mucosa. According to Lloyd et al, 45 cases of oral nodular fasciitis had been reported between 1966 and 2013, only 1 of which was present on the lower lip mucosa. The rare occurrence of nodular fasciitis in the oral cavity is thought to be secondary to the paucity of a fascial layer in this region.

Histologically, nodular fasciitis classically manifests as a well-circumscribed proliferation of spindle and stellate shaped fibroblasts and myofibroblasts, often in intersecting fascicles, referred to as a tissue culture-like pattern. Fibroblasts are generally arranged within a myxomatous stroma containing well-defined blood vessels and extravasated erythrocytes. Numerous mitoses can be seen. Immunohistochemical staining can help to differentiate this benign lesion from other more aggressive malignant entities, such as fibrosarcoma or leiomyosarcoma. Nodular fasciitis typically stains positive for SMA, desmin and vimentin and negative for S100, cytokeratin, cluster of differentiation (CD) 34 and h-caldesmon.

Treatment is generally successful with conservative local excision. There have been reports of spontaneous regression. Recurrence is rare (0.4-2%) and aggressive therapy is not indicated. Given its rapid growth rate, dense cellularity and high mitotic index, nodular fasciitis is often misdiagnosed, both clinically and histologically, as a sarcoma or other aggressive malignancy.

This case represents the third documented occurrence of nodular fasciitis of the lower lip and emphasizes the importance of appropriate diagnosis to avoid unnecessary radical surgical dissection.

REFERENCES

1. Lloyd AA, Witheiler D, Menter A. Nodular fasciitis of the lip mucosa: a rare but clinically important entity. *Clinical and Experimental Dermatology* 2015; 40:408-412.
2. Kamino H, Reddy VB, Pui J. Fibrous and fibrohistiocytic proliferations of the skin and tendons. In: Bolognia JL, Jorizzo JL, Schaffer JV, ed. *Dermatology*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2012: 1961-1977.
3. Haddad AJ, Avon SJ, Clokie CML, Sandor GKB. Nodular fasciitis in the oral cavity. *J Can Dent Assoc* 2001; 67(11):664-7.
4. de Carli ML, Fernandes KS, dos Santos Pinto D Jr, Witzel AL, Martins MT. Nodular fasciitis of the oral cavity with partial spontaneous regression (nodular fasciitis). *Head Neck Pathol* 2013; 7(1):69-72.
5. Subramaniam P, Balakrishna R, Mahendra P, Gilhotra K. Nodular fasciitis of the oro-facial region*. Contemp Clin Dent* 2012; 3:S16–18.

Presented by Magdalena Kobierska, MD, and Claudia Hernandez, MD
Department of Dermatology, RUSH University Medical Center

Unknown

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 4**

Presented by Nick Blickenstaff, MD, and Warren Piette, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

This patient is a 30 year-old female who was initially evaluated by rheumatology at Little Company of Mary Hospital for Sjogren's syndrome in 2014 with bilateral parotid enlargement, dry eyes, and recurrent bouts of macular purpura. She was treated with Hydroxychloroquine 300 mg daily for 9 months before self-discontinuing therapy. In March 2015 she developed a small, indurated area on the right anterior lower leg. A biopsy obtained by dermatologist, Dr. Louisa Gehlmann, was consistent with nodular amyloidosis and the patient was referred to Rush Dermatology. There was no evidence of systemic involvement at that time, including negative SPEP and immunofixation studies. A once yearly visit for bloodwork and repeat immunofixation testing was recommended.

Scheduled to return in 1 month, the patient did not return to clinic until 9 months later. There were now many new hyperpigmented papules and plaques on the chest, bilateral forearms, and lower legs. The lesions were asymptomatic. Repeat biopsy of a new lesion on the right lateral leg was obtained given the suspicion for systemic amyloidosis.

PAST MEDICAL HISTORY

Sjogren's syndrome
Cervical Intraepithelial Neoplasia II

MEDICATIONS

Triamcinolone 0.1% ointment BID
Hydroxychloroquine 300 mg daily
Prednisone 20 mg daily
Hydroquinone 4% topical cream daily

ALLERGIES

No Known Drug Allergies

FAMILY HISTORY

Unremarkable

SOCIAL HISTORY

Rare alcohol consumption. No tobacco or recreational drug use.

PHYSICAL EXAM

At the time of the initial physical exam (4/2015), a small hyperpigmented area of induration was noted on the right shin at the prior biopsy site. Widespread 1-5 mm macular purpura and a few hyperpigmented macules were present on the bilateral lower legs.

During follow-up (6/2016) new minimally elevated, hyperpigmented and slightly yellow papules and plaques were seen on the left chest, bilateral forearms and bilateral lower extremities. These lesions were not distinctly nodular on palpation.

HISTOPATHOLOGY
Previous biopsy (3/2015) from the right anterior lower leg demonstrated an unremarkable epidermis. Deposits of amyloid were seen within the dermis confirmed by a positive amyloid stain and a surrounding infiltrate of plasma cells with some admixed lymphocytes.

Repeat biopsy (6/2016) from the right lateral lower leg demonstrated eosinophilic, amorphous, nodular deposits in the dermis and in the walls of the dermal blood vessels. Congo red stain was positive in the nodular deposits.

LABORATORY RESULTS
OSH (2014) – SS-A AB >8.0, SS-B AB >8.0, IgG 3710, IgA 533, IgM 231, Kappa 2990, Lambda 1880, normal CBC, normal CMP, normal urinalysis, negative cyroglobulin, negative c-ANCA, negative p-ANCA

5/2015, 1/2016, 7/2016 – SPEP: diffuse hypergammaglobulinemia, elevated kappa light chains, no paraprotein detected; Immunofixation electrophoresis: no monoclonal proteins

2/2016 – C3 84, C4 7, RF 95, ANA screen positive, ANA titer > 1:2560, speckled ANA pattern, IgG 2699, IgA 518, normal IgM, ESR 73, ESR 73, negative CCP Ab, negative MPO Ab, negative Proteinase-3 Ab, negative c-ANCA, negative p-ANCA

6/2016 – Congo red stain: positive amyloid deposits present; Laser microdissection and tandem mass spectrometry: peptide profile consistent with AL (kappa)-type amyloid deposition

7/2016 – Bone marrow biopsy: normocellular marrow with trilineage maturation. No increase in plasma cells or atypical plasma cells and no material suspicious for amyloid; Flow cytometry: no immunophenotypic evidence of lymphoma

1/2017 – ESR 73, IgG 2881, IgA 616, normal IgM, normal CBC with diff, normal CMP, normal LDH, normal bilirubin

RADIOLOGY
Staging PET CT (7/2016) - no evidence of amyloid

TREATMENT AND COURSE
During the patient's initial evaluation at Rush Dermatology, her lesions were best explained by two different, unrelated dermatologic conditions. The recurrent bouts of macular purpura were suggestive of Benign Hypergammaglobulinemic Purpura of Waldenstrom. The patient was restarted on Hydroxychloroquine 300 mg daily per rheumatology. She self-discontinued the medication after 1 month once the flares stopped and she was feeling well.

Repeat biopsy of a new lesion at the time of her second visit was consistent with nodular amyloidosis. Rescreening for systemic gammopathy by SPEP and immunofixation was again negative. Staging PET scan and bone marrow biopsy showed no evidence of clonal disease. The hematopathologist counted 400 cells surrounding an amyloid deposit that were predominately plasma cells. A slight increase in kappa light chains was seen but no clear clonality could be identified. This left only a new limited availability procedure to establish the protein substrate of amyloid. Laser-capture microdissection and tandem mass spectrometry performed at the Mayo Clinic demonstrated AL (kappa)-type amyloid deposition. A multidisciplinary care conference concluded that a trial of therapy directed at plasma cells was appropriate given the increasing number of lesions and typing results suggestive of light chain-derived amyloid in multiple sites. The patient is undergoing a trial of Bortezomib and

Dexamethasone for 12 weeks and is now status-post 2 cycles. She is tolerating therapy well without any new lesions, significant side effects, or complications.

DIAGNOSIS

Primary localized cutaneous nodular amyloidosis in association with Sjogren's syndrome

DISCUSSION

Amyloidosis is a spectrum of diseases consisting of abnormal deposition of amyloid protein in various tissues, leading to impairment of organ function. Clinically, amyloidosis may be classified into systemic forms with involvement of several organ systems, and localized forms, in which deposits are limited to a particular organ, such as the skin. Systemic amyloidosis with cutaneous involvement can result from immunoglobulin light chains [AL], serum amyloid A protein [AA], beta-2 microglobulin with older dialysis filters, and amyloid transthyretin [ATTR] seen in senile wild type and >100 familial amyloidoses. Systemic light chain [AL] amyloidosis can be mimicked by some senile wild type and subsets of familial ATTR amyloidoses including skin involvement and cardiomyopathy.

Primary localized cutaneous amyloidosis (PLCA) presents with local deposition of amyloid material in the skin, without evidence of systemic involvement. There are 3 main forms of PLCA: macular, lichen, and nodular amyloidosis. Macular and lichen amyloidosis are derived from keratins, whereas, amyloid deposits of nodular amyloidosis primarily consist of immunoglobulin light chains [AL]. Rare cases of amyloid transthyretin, beta-2 microglobulin amyloid and injection site insulin-derived amyloidgenesis have been shown to cause nodules. Immunoglobulin light chain [AL] amyloid is the same type of amyloid fibril protein seen in primary systemic amyloidosis and myeloma-associated systemic amyloidosis. Primary localized cutaneous nodular amyloidosis (PLCNA) is the rarest form of PLCA, accounting for around 1.5% of PLCA cases. It presents as single or, more rarely, multiple firm, waxy or rubbery, yellow to tan nodules measuring up to several centimeters. The acral region is the most common location, followed by the legs, head, trunk, arms, and genitalia, respectively. Our patient had multiple hyperpigmented lesions that were not distinctly nodular on palpation, which is uncommon. She also presented with an existing diagnosis of Sjogren syndrome (SjS). Sjogren syndrome was originally described as sicca syndrome with rheumatoid arthritis, but newer classifications include most sicca patients under the term SjS. Varying forms of PLCA have been uncommonly associated with autoimmune connective tissue disorders. A review of the literature by Yoneyama et al demonstrated 14 cases of PLCNA associated with SjS. Our patient further supports the notion that SjS can predispose individuals to PLCNA.

In patients with amyloidosis, correct identification of the causal amyloid protein is crucial for clinical management in order to avoid misdiagnosis and inappropriate, potentially harmful treatment. Our patient was diagnostically challenging because she had a widespread distribution of new cutaneous lesions suggestive of a circulating clonal process, but no evidence of systemic gammopathy. Serum protein electrophoresis and immunofixation electrophoresis showed no evidence of paraprotein or monoclonal proteins, nor did lesional cellular immunotyping. Staging PET scan and bone marrow biopsy were also unremarkable. To facilitate amyloid typing we turned to laser-capture microdissection with liquid chromatography-coupled tandem mass spectrometry. Findings were consistent with localized AL (kappa)-type amyloid deposition.

This rare case of PLCNA has many unique characteristics. Most cases of nodular amyloidosis are associated with plasmacytoid lymphomas, not true cutaneous plasmactyomas as seen in our patient. The case also demonstrated that lesions in PLCNA can be multiple, widespread, and of variable morphology. It provided further support to the uncommon association between

SjS and PLCNA. Lastly, laser-capture microdissection with liquid chromatography-coupled tandem mass spectrometry provides a new diagnostic avenue for amyloid typing in a select patient population. Given that nodular amyloidosis can progress to systemic involvement in approximately 7% of cases, our patient needs long-term follow up to monitor for systemic change as well as recurrence of PLCNA.

REFERENCES

1. Kyle RA, Bayrd ED. Amyloidosis: review of 236 cases. *Medicine.* 1975;54:271-299.
2. Konishi A, Fukuoka M, Nishimura Y. (2007), Primary localized cutaneous amyloidosis with unusual clinical features in a patient with Sjögren's syndrome. *The Journal of Dermatology,* 34: 394–396.
3. Black MM. Primary localized amyloidosis of the skin: clinical variants, histochemistry and ultrastructure. In: Wegelius O, Paternak A, eds. *Amyloidosis.* London, England: Academic Press; 1976:479-513.
4. Yoneyama K, Tochigi N, Oikawa A, et al. Primary localized cutaneous nodular amyloidosis in a patient with Sjögren's syndrome: a review of the literature. *J Dermatol.* 2005;32:120-123.
5. Pepys MB. Amyloidosis. *Annu Rev Med*. 2006;57:223–41.
6. Vrana JA, Gamez JD, Madden BJ, Theis JD, Bergen HR 3rd, Dogan A. Classification of amyloidosis by laser microdissection and mass spectrometry-based proteomic analysis in clinical biopsy specimens. *Blood*. 2009;114(24):4957–9.
7. Sethi S, Vrana JA, Theis JD, Leung N, Sethi A, Nasr SH, et al. Laser microdissection and mass spectrometry-based proteomics aids the diagnosis and typing of renal amyloidosis. *Kidney Int.* 2012;82(2):226–34.
8. Woollons A, Black MM. Nodular localized primary cutaneous amyloidosis: a long-term follow-up study. *Br J Dermatol.*2001;145:105-109.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 5**

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

FAST BREAK

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 6**

Presented by Neal Kumar, MD, MBA, Vijaya Reddy, MD, MBA, Kerstin Stenson, MD, Nicklas Pfanzelter, MD, and Sheetal Mehta, MD,
Department of Dermatology, Rush University Medical Center

HISTORY OF PRESENT ILLNESS

This is a 66 year old Caucasian male who initially presented to an outside provider with a sore throat in late 2016. He was first diagnosed with tonsillitis or an abscess but his symptoms were refractory to multiple courses of antibiotics. He then sought a second opinion from Otolaryngology who discovered an exophytic mass on his right tonsil. Due to persistence of symptoms, an excisional biopsy was performed on 2/13/17 which was complicated by excessive bleeding.

PAST MEDICAL HISTORY

Coronary artery disease
Hypertension
Transient ischemic attack

PAST SURGICAL HISTORY

Knee surgery

MEDICATIONS

Metoprolol
Pravastatin

ALLERGIES

None known

FAMILY HISTORY

No family history of melanoma or skin cancer

SOCIAL HISTORY

Retired teacher

PHYSICAL EXAMINATION

Right tonsil: 1 cm well demarcated white plaque
No palpable cervical, supraclavicular, axillary, or inguinal lymphadenopathy.

HISTOPATHOLOGY

REPORT DATE: 2/16/2017
FINAL DIAGNOSIS
A. (OS Case# S17-1089-Mass of right tonsil; excision): Malignant melanoma.

Sections contain an ulcerated nodule of malignant melanoma measuring at least 1.5 cm in maximum dimension. Small areas of intact squamous mucosa are present on the surface of the nodule but no convincing intraepithelial melanoma is identified raising the possibility of metastasis.

The neoplasm is positive for S100 protein, Mart-1 and HMB-45 and negative for cytokeratin AE1/3, cytokeratin 5/6 and P. 63 supporting the diagnosis of melanoma. Immunohistochemistry controls are examined and show appropriate reactivity.

REPORT DATE: 3/16/2017
FINAL DIAGNOSIS
A. (Right tonsil; tonsillectomy):
Malignant melanoma, nodular type, measuring 0.8 cm and extends to a depth of 2 mm, present 0.3 cm from the medial margin. Melanoma in-situ, extends to the lateral margin.
Prior biopsy site changes are identified.
Stage: pT3Nx

NOTE
Sections reveal a mucosal nodule composed of nests of epithelioid cells beneath the epithelium. Pagetoid extension of the melanocytes is identified and there is a lentiginous proliferation of melanocytes within the adjacent epithelium with extension along the tonsil crypts. The tumor cells are positive for S-100, Melan-A (4 tissue blocks) and HMB-45. A Melan-A immunostain also highlights the melanoma-in situ extending to the lateral margin.

Due to the presence of melanoma in-situ within the adjacent epithelium, this is favored to be a primary mucosal melanoma.

Melanoma Summary:

Procedure: Right tonsillectomy
Site: Right tonsil
Macroscopic Satellite nodule(s) (required for excision specimens only): not identified
Histologic type: Nodular type
Maximum tumor thickness (Breslow): 2 mm
Clark level: N/A
Ulceration: Absent
Margins: Peripheral: Positive for melanoma in-situ.
Deep: Free
Mitotic index: 10 per mm2
Microsatellitosis: Not identified
Lymphovascular invasion: Not identified
Tumor infiltrating lymphocytes: Not brisk
Regression: Absent

DIAGNOSIS
Primary tonsillar melanoma

TREATMENT AND COURSE
An excisional biopsy of the right tonsillar mass was performed on 2-13-17 which demonstrated an ulcerated nodule of malignant melanoma. Given that there were small areas of intact squamous mucosa overlying the nodule and no intraepithelial melanoma, there was initial concern for metastatic melanoma. The patient then underwent a radical right tonsillectomy on 3-9-17 with otolaryngology at Rush University Medical Center. Histopathology of this specimen demonstrated nodular melanoma extending to a depth of 2 mm with melanoma in-situ extending to the lateral edge. Melan-A immunostaining also highlighted the melanoma in-situ extending to the lateral edge. Due to the presence of melanoma in-situ within the adjacent epithelium, the patient was diagnosed with primary mucosal melanoma; pT3Nx. PET/CT and CT neck did not reveal clear disease outside of the tonsil. At the patient's most recent visit to oncology, samples were sent for Tempus Molecular Testing to evaluate for mutations including CKIT, BRAF,

NRAS, and others. The patient was also referred to dermatology clinic for a total skin exam and no cutaneous lesions were found to be suspicious for skin cancer or melanoma.

DISCUSSION

The patient's case was discussed in melanoma multi-disciplinary conference. Questions addressed included whether to perform a sentinel lymph node biopsy, which lymph nodes would drain from the right tonsil, and how to approach additional surgery given positive in-situ margins on re-excision. Also with the large amount of tissue excised during the tonsillectomy, it was not clear whether an accurate sentinel lymph node biopsy could be performed. Together with the patient's exceedingly high risk of distant disease, there is currently no plan for lymph node exploration. Management at this time includes close monitoring with oncology and otolaryngology with re-imaging in three months. Decision was made to defer further surgery until documented recurrence. With initial imaging negative for metastatic disease, chemotherapy was not initiated. Lastly, there was discussion of whether to perform local radiation to the area.

Studies evaluating radiation treatment for head and neck melanoma have demonstrated decreased local recurrence but worse survival benefit. A study of 28 patients with oral mucosa melanoma who received radiation therapy reported that the major factor in the failure of treatment was distant, metastatic dissemination. Given the high risk of metastasis, local radiation was not preferred in our patient's case.

Observational studies have reported that primary mucosal melanoma of the oral cavity represents approximately 0.5-2% of all head and neck melanomas. One study describes fifteen patients with primary malignant melanoma of the upper respiratory tract, of which, those with nasal neoplasms had an average survival of 3 ½ years, but those with tonsillar or nasopharyngeal primary melanomas died within one year. Another study reviewing 52 cases of mucous membrane melanoma reported a local recurrence rate of 25% for oral cavity melanoma, and a total cure rate of 15%. Over five years, 11% of patients were still living and 74% had died because of their melanoma. For primary mucosal melanoma, there is an absence of data supporting adjuvant immunotherapy.

REFERENCES

1. Henderson LT, Robbins KT, Weitzner S. (1986) Upper aerodigestive tract metastases in disseminated malign melanoma. Arch Otolaryngol Head Neck Surg. 112: 659-63.
2. Nicolaides A, Fisher C, Evans PHR. (1989) Metastatic melanoma of the tonsil. J Laryngol Otol. 103: 890-2.
3. Lin D, Franc BL, Kashani-Sabet M, Singer MI. (2006) Lymphatic drainage patterns of head and neck cutaneous melanoma observed on lymphoscintigraphy and sentinel lymph node biopsy. Head Neck. 28: 249-55.
4. Aydogan LB1, Myers JN, Myers EN, Kirkwood J. Laryngoscope. 1996 Mar;106(3 Pt 1):313-6. Malignant melanoma metastatic to the tonsil.
5. V. Svane-knudsen. Primary, Malignant Melanoma of the Tonsil: Report of a Case. Pages 364-368 | Received 18 Sep 1956, Published online: 08 Jul 2009
6. Shibuya, H. The efficacy of radiation therapy for a malignant melanoma in the mucosa of the upper jaw: an analytic study. 1993. International Journal of Radiation. 25: 35-39.
7. Ivo, Starek. Sentinel lymph node biopsy: a new perspective in head and neck mucosal melanoma. 2006. Melanoma Research. 16: 423-427.
8. Mesara, B. Primary malignant melanoma of the upper respiratory tract. 1968. Cancer. 21: 217-225
9. Conley, J. Melanoma of the Mucous Membrane of the Head and Neck. 1974. Arch Otolaryngol. 99(5):315-319.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 7**

Presented by Andrew Thompson, MD, and Sheetal Mehta, MD
Department of Dermatology, RUSH University Medical Center

Unknown

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 8**

Presented by Todd Rickett, MD, PhD, and Mark D. Hoffman, MD
Department of Dermatology, Rush University Medical Center

HISTORY OF PRESENT ILLNESS

A 39-year old black woman with treatment-resistant systemic lupus erythematosus (SLE) and antiphospholipid antibody syndrome (APLAS) presented to clinic for follow up of her chronic cutaneous lupus. She was first diagnosed with lupus in 1998, and has had a course of relapsing and remitting signs and symptoms including joint pain, cytopenia, hepatitis, photosensitivity, hair loss, discoid lesions, and a malar rash.

In addition to her typical discoid lesions, she reports a 3 month history of ulcerations on her arms, legs, and right breast. These begin as acne-like papules that then ulcerate with some associated burning pain. She notes that these are different from her typical discoid lesions as they have a depressed center.

Her treatment regimen consisted of prednisone 40 mg daily, hydroxychloroquine 200 mg twice daily, tacrolimus 0.1% ointment to facial rash twice daily, and clobetasol proprionate 0.05% ointment to rash of arms and legs twice daily. She has previously been treated with belimumab, mycophenolate mofetil, leflunomide, systemic tacrolimus, dapsone, rituximab, methotrexate, cyclophosphamide, ustekinumab, and quinacrine with intolerance and/or toxicity and/or inconsistent responses to therapy, and with questionable adherence.

REVIEW OF SYSTEMS

Notable positives:

Constitutional:	+ fatigue, loss of appetite, hair loss
Gastrointestinal:	+ heartburn, frequent and recurrent blood in stools
Musculoskeletal:	+ pain and stiffness in the small joints of the hands that is worst upon awakening
Psychiatric:	+ depression, problems sleeping

PHYSICAL EXAM

Bilateral arms, wrists, fingers, anterior legs, and ankles showed punched out, punctate ulcerations, some with overlying crust. Several of these lesions had atrophic, white centers with red-brown borders with fine telangiectasias. Diffuse, mild erythema was noted of the eyelids and malar regions of the face. Her bilateral upper arms and right breast had several hyper- and hypo- pigmented patches and plaques, some with underlying erythema.

LABORATORY DATA

2017 Labs:
Anti-dsDNA: > 180 IU/mL ..... **High** (Normal range is <27 IU/mL)
C3: 61 mg/dL ..... **Low** (Normal range is 88-203 mg/dL)
ESR-Westergren: 34 mm/hr ..... **High** (Normal range is 0-27 mm/hr)
Hemoglobin: 10 g/dL ..... **Low** (Normal range is 12-16 g/dL)
Hematocrit: 31.8% ..... **Low** (Normal range is 37-47%)
Normal/negative: antiphospholipid antibody panel (anti-cardiolipin IgA, IgG, IgM; anti-phosphatidylserine IgA, IgG, IgM; anti-beta-2-glycoprotein IgA, IgG, IgM), lupus anticoagulant assay, platelets

2012 Labs:
Antiphospholipid antibody panel and lupus anticoagulant assay: normal

2006 Labs:
Anti-Beta-2-Glycoprotein 1 IgA: 27 ..... **High** (Normal range is <10)
Remainder of antiphospholipid antibody panel and lupus anticoagulant assay: normal

PAST MEDICAL HISTORY

Pregnancy History

-Premature delivery of a female fetus at 28 weeks EGA (estimated gestational age) due to placenta abruption. Infant was 1 lb. 12 oz. (<10% percentile for EGA) and lived for 5 days before passing away due to fetal age
-Miscarriage at 6-8 weeks EGA
-Miscarriage at 6-8 weeks EGA
-Full term delivery of a male infant at 38 weeks EGA via caesarean section. Cerebral palsy but otherwise healthy.
-Elective abortion at 10 weeks EGA

HISTOPATHOLOGY

The epidermis is atrophic with thickening of the basement membrane, regions of basilar vacuolization, and follicular hyperkeratosis. The superficial dermis is hypocellular with hyalinized collagen bundles and vascular walls. A superficial to mid- dermal perivascular lymphocytic infiltrate is noted with occasional small vessel thrombosis and lymphocytic vasculitis. A PAS stain highlights the thickened basement membrane zone and fibrin deposition in the vascular wall.

DIAGNOSIS

Degos-like lesions arising in the setting of SLE and cutaneous LE

DISCUSSION

Degos disease (also known as malignant atrophic papulosis or Kohlmeir-Degos disease) is a rare condition characterized by stereotypical skin lesions consisting porcelain-white atrophic papules with telangiectatic rims. About 15% of cases have classical skin lesions without internal involvement (benign cutaneous Degos disease or benign atrophic papulosis). However, it has been believed that most patients will also develop vascular infarcts in other organ systems. The most commonly involved extra-cutaneous organ system is the GI tract, with ~ 60% of patients developing intestinal, gastric, or esophageal infarctions. The second most commonly involved extra-cutaneous organ system is the central nervous system, and neurologic symptoms occur in ~ 20% of Degos Disease patients and may include strokes, paresthesias, epilepsy, memory problems, or aphasia. Infarctions can also occur in the eyes, cardiopulmonary system, liver and kidneys.

The systemic or “malignant” form of the disease is associated with a 50% mortality rate generally within 2-3 years after onset of skin symptoms, with death most frequently occurring from perforation of the small intestine leading to. Even patients with seemingly skin-limited disease should be followed for potential development of systemic symptoms years or even decades after disease onset.

Though Degos disease was first described in 1941, there still exists significant controversy as to the disease etiology. With a common end point of vascular damage, the three most accepted theories of disease pathogenesis involve a systemic coagulopathy, vasculitis, and endothelial cell dysfunction. High et al postulated that Degos-disease may not be a distinct clinical entity, but rather a clinical and histological end point for multiple types of vascular insult. Ball, Newburger, and Ackerman reported that early lesions of Degos disease may show mucin

accumulation with perivascular lymphocytic infiltrates and vacuolization of the dermal-epidermal junction that is indistinguishable from lupus erythematosus; they suggested that Degos disease was not a distinct disease entity but rather a morphological presentation of vascular occlusion, usually caused by connective tissue diseases—most commonly lupus erythematosus. Others have contested this view, highlighting the lack of photosensitivity, variable findings on direct immunofluorescence, and poor response to immunosuppressive. More recent reports often refer to patients having "Degos-like" lesions when they occur in the setting of an autoimmune disease.

Anti-phospholipid antibody syndrome is a possible confounder or comorbidity in the diagnosis of Degos disease. Multiple case reports have described Degos type lesions in patients with lupus anticoagulant and anticardiolipin antibodies and the skin infarcts induced in anti-phospholipid antibody syndrome can closely resemble Degos lesions. However, Assier's 19995 review of 15 patients with Degos disease found that none had significant titers of antiphospholipid antibodies, though the authors did not report what proportion of these patients had primary malignant atrophic papulosis or Degos-like lesions associated with connective tissue disease.

Management of patients with primary Degos disease or Degos-like lesions is complicated by a general consistent lack of response to conventional treatments including anti-malarials, warfarin, corticosteroids, azathioprine, methotrexate, cyclosporine, tacrolimus, and mycophenolate mofetil. First line therapy is often a trial of antiplatelet therapies, anticoagulants, and treatments to improve perfusion—notably aspirin, dipyridamole, ticlodipine, heparin, and pentoxyfilline with many case reports showing a decrease in new cutaneous lesions and partial regression of existing lesions. Recent reports have reflected interest in treatment with eculizumab (recombinant humanized monoclonal Ab to C5) and treprostinil (a synthetic analog of prostacyclin PGI2) though data is still limited on their long term efficacy. Given the morbidity associated with multi-system disease, screening any patient exhibiting Degos-like lesions for systemic involvement is of paramount importance to medical therapy. This may involve stool guaiac, colonoscopy, endoscopy, brain MRI, chest x-rays, ocular fundus examination, abdominal ultrasounds, and an autoimmune panel including the common antiphospholipid syndrome antibodies. Our patient was started on aspirin 325 mg daily and pentoxifylline 800 mg TID and continued on her lupus medications. She was also referred to her primary care physician for work up of her hematochezia. We await follow up to assess her response to the new medications, and we are interested to learn from others with experience in treating malignant atrophic papulosis.

REFERENCES:

1. Farrell AM, Moss J, Costello C, Fearfield LA, Woodrow D, Bunker CB. Benign cutaneous Degos' disease. British Journal of Dermatology. 1998 Oct 1;139:708-12.
2. Harvell JD, Williford PL, White WL. Benign cutaneous Degos' disease: a case report with emphasis on histopathology as papules chronologically evolve. The American journal of dermatopathology. 2001 Apr 1;23(2):116-23.
3. Lankisch MR, Johst P, Scolapio JS, Fleming CR. Acute abdominal pain as a leading symptom for Degos' disease (malignant atrophic papulosis). The American journal of gastroenterology. 1999 Apr 30;94(4):1098-9.
4. Theodoridis A, Konstantinidou A, Makrantonaki E, Zouboulis CC. Malignant and benign forms of atrophic papulosis (Köhlmeier–Degos disease): systemic involvement determines the prognosis. British Journal of Dermatology. 2014 Jan 1;170(1):110-5.
5. Yoshikawa H, Maruta T, Yokoji H, Takamori M, Yachie A, Torii Y. Degos' disease: radiological and immunological aspects. Acta neurologica scandinavica. 1996 Nov 1;94(5):353-6.

6. Theodoridis A, Makrantonaki E, Zouboulis CC. Malignant atrophic papulosis (Köhlmeier-Degos disease)-A review. Orphanet journal of rare diseases. 2013 Jan 14;8(1):10.
7. Magrinat G, Kerwin KS, Gabriel DA. The clinical manifestations of Degos' syndrome. Archives of pathology & laboratory medicine. 1989 Apr;113(4):354-62.
8. Ball E, Newburger A, Ackerman AB. Degos' disease: a distinctive pattern of disease, chiefly of lupus erythematosus, and not a specific disease per se. The American journal of dermatopathology. 2003 Aug 1;25(4):308-20.
9. High WA, Aranda J, Patel SB, Cockerell CJ, Costner MI. Is Degos' disease a clinical and histological end point rather than a specific disease?. Journal of the American Academy of Dermatology. 2004 Jun 30;50(6):895-9.
10. Scheinfeld N. Degos' disease is probably a distinct entity: A review of clinical and laboratory evidence. Journal of the American Academy of Dermatology. 2005 Feb 28;52(2):375-6.
11. Mutizwa MM, Tang MB, Ng SK. Prominent Degos-like skin lesions in a patient with chronic cutaneous lupus erythematosus. Dermatology online journal. 2010 Jul 1;16(7).
12. Riyaz N, Saleem R, Shafeeq R. Degos disease-like presentation in systemic lupus erythematosus. Indian journal of dermatology, venereology and leprology. 2011 Mar 1;77(2):219-221.
13. Englert HJ, Hawkes CH, Boey ML, Derue GJ, Loizou S, Harris EN, Gharavi AE, Hull RG, Hughes GR. Degos' disease: association with anticardiolipin antibodies and the lupus anticoagulant. Br Med J (Clin Res Ed). 1984 Sep 8;289(6445):576-576.
14. Mauad T, De Fátima Lopes Calvo Tiberio I, Baba E, R DE ANDRADE JUNIOR D, Lichtenstein A, Capelozzi VL, Sotto MN, Saldiva PH. Malignant atrophic papulosis (Degos' disease) with extensive cardiopulmonary involvement. Histopathology. 1996 Jan 1;28(1):84-6.
15. Farrell AM, Moss J, Costello C, Fearfield LA, Woodrow D, Bunker CB. Benign cutaneous Degos' disease. British Journal of Dermatology. 1998 Oct 1;139:708-12.
16. Black MM, Hudson PM. Atrophie blanche lesions closely resembling malignant atrophic papulosis (Degos' disease) in systemic lupus erythematosus. British Journal of Dermatology. 1976 Dec 1;95(6):649-52.
17. Assier H, Chosidow O, Piette JC, Boffa MC, Youinou P, Thomas L, Caux F, Cribier B, Bonnet-Blanc JM, Guillet G, Plantin P. Absence of antiphospholipid and anti-endothelial cell antibodies in malignant atrophic papulosis: a study of 15 cases. Journal of the American Academy of Dermatology. 1995 Nov 1;33(5):831-3.
18. Magro CM, Wang X, Garrett-Bakelman F, Laurence J, Shapiro LS, DeSancho MT. The effects of Eculizumab on the pathology of malignant atrophic papulosis. Orphanet journal of rare diseases. 2013 Nov 26;8(1):185.
19. Shapiro LS, Toledo-Garcia AE, Farrell JF. Effective treatment of malignant atrophic papulosis (Köhlmeier-Degos disease) with treprostinil–early experience. Orphanet journal of rare diseases. 2013 Apr 4;8(1):52.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 9**

Presented by Stacie Clark, MD, and Arthur Rhodes, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 24-year old white female presented to the emergency department for evaluation of a rash of 2 days duration. The eruption started on her lower extremities and progressively spread to involve the abdomen, back, upper extremities and face. There was associated pruritus, particularly on the face. There was no burning or skin tenderness. She denied fever, chills or recent infection. One month prior to presentation, she had been diagnosed with membranous lupus nephritis and tubule-interstitial nephritis. She had been started on cyclosporine, high dose prednisone and hydroxychloroquine at that time. She had also started dapsone as prophylactic treatment for pneumocystis pneumonia one month prior to presentation. The patient was taking all of these medications at the time of first presentation.

PAST MEDICAL HISTORY

Systemic Lupus Erythematosus
Lupus Nephritis
Fibromyalgia
Gastroesophageal Reflux Disease
Fetal Demise x 2 secondary to Neonatal Lupus

MEDICATIONS

Prednisone 60 mg QAM
Cyclosporine 150 mg BID
Hydroxychloroquine 200 mg daily
Dapsone 100 mg daily

ALLERGIES

Sulfa antibiotics - Rash

FAMILY HISTORY

There is no known family history of autoimmune disease.

SOCIAL HISTORY

Current smoker, approximately 1-2 cigarettes per day

PHYSICAL EXAM

At the time of initial examination (day 3 of rash), there were diffuse erythematous, blanching and edematous papules coalescing into plaques on the bilateral upper and lower extremities, face, chest, abdomen, and back. The palms and soles were spared. The oral mucosa was clear. There were no pustules evident.

On repeat examination 4 days later (day 7 of rash), there were confluent, erythematous and edematous papules studded with pinpoint pustules on the bilateral upper and lower extremities, face, chest, abdomen, and back

HISTOPATHOLOGY

2/28/17 (day 3 of rash): Subcorneal pustules, mild epidermal spongiosis and superficial perivascular inflammatory cell infiltrate containing frequent neutrophils.

3/2/2017 (day 7 of rash): Subcorneal and intraepidermal pustules with epidermal spongiosis and dermal inflammatory cell infiltrate consisting of lymphocytes and neutrophils.

LABORATORY RESULTS

2/26/17:

AST and ALT	Within normal limits	
Blood Urea Nitrogen (BUN)	35 mg/dL	[8-21 mg/dL]
WBC	14.05 K/uL	[4.00-10.00 K/uL]
Hemoglobin	9.1 g/dL	[12.0-16.0 g/dL]
Hematocrit	28.3%	[37-47%]
Platelets	396 K/uL	[150-399 K/uL]
Neutrophil #	10.43 K/uL	[1.84-7.80 K/uL]
Neutrophil %	74.2%	[46-78%]
Throat Culture, Group A Strep	Negative	
Respiratory Viral Panel	Negative	

3/2/17:

AST and ALT	Within normal limits	
Blood Urea Nitrogen (BUN)	Within normal limits	
WBC	21.30 K/uL	[4.00-10.00 K/uL]
Hemoglobin	9.4 g/dL	[12.0-16.0 g/dL]
Hematocrit	29.4%	[37-47%]
Platelets	472 K/uL	[150-399 K/uL]
Neutrophil #	18.49 K/uL	[1.84-7.80 K/uL]
Neutrophil %	86.8%	[46-78%]

TREATMENT AND COURSE

Baseline labs were obtained to exclude a viral cause of the patient's eruption. Throat culture for Group A Strep and a respiratory viral panel were negative. An exanthematous drug eruption was suspected, so dapsone and cyclosporine were discontinued. Prednisone and hydroxychloroquine were continued. A biopsy of a red, edematous lesion on the right lower back was obtained. Four days after admission, the patient became acutely febrile and developed worsening, confluent erythema studded with pinpoint pustules. Initial biopsy results were still pending at this time. Hydroxychloroquine was discontinued and an additional biopsy of a pustular red plaque was obtained. Repeat laboratory studies demonstrated leukocytosis with marked neutrophilia. The patient was continued on prednisone, and her skin eruption resolved over the remainder of her hospital admission.

DIAGNOSIS

Acute generalized exanthematous pustulosis, striking for a histopathologically evident, but delayed clinically evident, pustular component

DISCUSSION

Acute generalized exanthematous pustulosis (AGEP) is a rare skin disorder that is generally classified as a drug reaction. It is characterized by acute onset of edematous erythema, followed by abrupt eruption of dozens to hundreds of non-follicular, sterile pustules. Classically, AGEP has a predilection for skin folds, but it can be widely distributed. The cutaneous findings are often accompanied by fever (>38^{o} C) and leukocytosis with a neutrophil count > 7000 neutrophils/µl. Histopathologic features include subcorneal and intraepidermal pustules, a mixed perivascular infiltrate and papillary dermal edema. Once the causative drug has been withdrawn, AGEP is generally self-limited, with the entire episode lasting up to 15 days.

Antibiotics, particularly macrolides and beta-lactams, are the most commonly reported trigger of AGEP. However, a wide range of drugs has been implicated. Hydroxychloroquine, calcium channel blockers, and terbinafine have also been strongly associated. Compared to other cutaneous drug reactions, AGEP is less commonly associated with sulfonamides. The time from drug intake to appearance of AGEP is generally 1-5 days. There are multiple reports of a prolonged latent period (approximately 20 days), particularly in cases where hydroxychloroquine was the suspected inciting agent.

The exact pathophysiology of AGEP remains unclear. However, drug-specific CD4+ and CD8+ T cells have been isolated from the blood in affected patients. It is hypothesized that upon re-exposure to a causative drug, memory T cells recruit neutrophils through production of cytokines such as IL3 and IL8. Because AGEP is classically accepted as a self-limited eruption, the necessity of treatment with immune suppressing agents, such as a systemic glucocorticoid, is debated. In rare refractory cases of AGEP, cyclosporine has reportedly been a successful treatment, likely owing to its inhibitory effects on T cells and resultant reduction of IL8.

Approximately 1 month prior to onset of her skin eruption, this patient had been started on cyclosporine, prednisone, hydroxychloroquine, and dapsone. Both hydroxychloroquine and dapsone have been associated with AGEP, making it difficult to accurately elucidate a causative agent. While the patient had a known allergy to sulfonamide medications, the cross reactivity between sulfonamide antibiotics and sulfonamide non-antibiotics, such as dapsone, is thought to be low. As such, hydroxychloroquine is favored as the inciting agent of AGEP in this patient, particularly given the prolonged latent period between drug administration and cutaneous findings.

We suspect that our patient's unique subclinical presentation of AGEP - erythema initially without pustulosis for 6 days, followed on day 7 with diffuse pustulosis - was possibly related to immune suppression by cyclosporine. It is postulated that elimination of this medication alleviated a T cell blockade, leading to increased levels of IL3 and IL8, with subsequent development of classic, acute pustulosis, likely related to hydroxychloroquine.

REFERENCES

1. Halevy, S. Acute generalized exanthematous pustulosis. *Current Opinion in Allergy and Clinical Immunology.* 2009; 9: 322-328.
2. Sidoroff A, Dunant A, Viboud C, et al. Risk factors for acute generalized exanthematous pustulosis (AGEP) – results of a multinational case-control study (EuroSCAR). *Br J Dermatol*. 2007; 157:989-996.
3. Sidoroff A, Halevy S, Bavinck JNB, Vaillant L, Roujeau JC. Acute generalized exanthematous pustulosis (AGEP) – a clinical reaction pattern. *J Cutan Pathol*. 2001; 28:113-119.
4. Paradisi A, Bugatti L, Sisto T, Filosa G, Amerio PL, Capizzi R. Acute generalized exanthematous pustulosis induced by hydroxychloroquine: three cases and a review of the literature. *Clin Ther*. 2008; 30(5):930-940.
5. Tresch S, Cozzio A, Kamarashev J, et al. T cell-mediated acute localized exanthematous pustulosis caused by finasteride. *J Allergy Clin Immunol*. 2012; 129(2):589-594.
6. Di Lernia V, Grenzi L, Guareschi E, Ricci C. Rapid clearing of acute generalized exanthematous pustulosis after administration of ciclosporin. *Clinical and Experimental Dermatology*. 2009; 34: e757-e759.
7. Strom BL, Schinnar R, Apter AJ, Margolis DJ, Lautenbach E, Hennessy S, et al. Absence of cross-reactivity between sulfonamide antibiotics and sulfonamide nonantibiotics. *N Engl J Med*. 2003; 349:1628-1635.
8. Holtzer CD, Flaherty JF Jr, Coleman RL. Cross-reactivity in HIV-infected patientsn switched

from trimethoprim-sulfamethoxazole to dapsone*. Pharmacotherapy* 1998; 18:831-835.
9. Razera F, Olm GS, Bonamigo RR. Neutrophilic dermatoses – part II. *An Bras Dermatol.* 2011; 86(2):195-211.
10. Gomez E, Torres MJ, Mayorga C, Blanca M. Immunologic evaluation of drug allergy. *Allergy Asthma Immunol Res.* 2012; 4(5):251-263.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 10**

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HISTORY OF PRESENT ILLNESS

This 68 year-old female presented to clinic for evaluation of a recurrent rash of 6 months duration. The eruption started on the distal lower extremities, then progressively spread to the thighs, back and bilateral forearms. Individual lesions would rapidly expand, then gradually become indurated and resolve over several weeks. Pruritus and mild "burning" pain were associated with the rash. The patient denied fever, night sweats, bruising, arthralgia, recent infection, travel, or new medications. Prior treatment included a two-week course of Prednisone 10 mg daily with dramatic improvement of the rash, followed by a flare after discontinuation of therapy.

PAST MEDICAL HISTORY

None

MEDICATIONS

Triamcinolone 0.025% ointment PRN
Zantac 150 mg BID
Doxepin 50 mg QHS

ALLERGIES

No Known Drug Allergies

FAMILY HISTORY

Unremarkable

SOCIAL HISTORY

No tobacco, alcohol, or recreational drug use

PHYSICAL EXAM

Clinical examination revealed multiple edematous red papules and large red-brown plaques on the ventral forearms, left medial thigh, and anterior lower legs. Many individual lesions were round, while others were annular or arciform with central clearing. No scaling, vesicles, bullae or pustules were identified.

HISTOPATHOLOGY

Histopathology revealed dermal edema with a superficial perivascular lymphocytic infiltrate, numerous eosinophils and some flame figures.

LABORATORY RESULTS

Normal CBC w Differential; normal CMP; normal urinalysis

RADIOLOGY

None

TREATMENT AND COURSE

The patient was initially seen by her PCP and completed a two-week course of Prednisone 10 mg daily with near resolution of the rash. She flared upon discontinuation of oral corticosteroids and was started on daily oral antihistamines and topical triamcinolone as needed when flaring. She presented to clinic 3 months later with new lesions on the extremities. Biopsy of a large, annular red-brown plaque with central clearing on the left arm was obtained. Allegra and Zyrtec were recommended for relief of pruritus as biopsy results were pending. After histopathologic examination of the biopsy suggested a diagnosis of Wells' syndrome, a repeat course of prednisone was discussed with the patient but she declined due to prior adverse side effects. Topical Clobetasol ointment was initiated for 1 month but she continued to experience weekly flares. Steroid-sparing therapies, such as hydroxychloroquine and Dapsone were discussed but the patient declined any new oral medications. At her two month follow-up appointment the patient had experienced one additional flare with the above regimen.

DIAGNOSIS

Eosinophilic annular erythema variant of Wells' syndrome

DISCUSSION

Eosinophilic annular erythema (EAE) was recently described as a clinical variant in the spectrum of Wells' syndrome (WS). Patients with EAE present with slowly expanding, arcuate or urticarial-like lesions. These lesions are usually asymptomatic or mildly pruritic. El-Khalawany et al performed a multicenter long-term follow-up study and reported that well-developed and longstanding lesions of EAE are highly compatible with WS characterized by eosinophilic degranulation, flame figures and a granulomatous reaction. Based on this clinicopathologic description, our patient fits this subset of WS presenting with an annular or figurate pattern.

Wells' syndrome (WS), also known as eosinophilic cellulitis, is a rare inflammatory skin disease of unknown etiology. The clinical eruption is highly variable and usually follows a relapsing remitting course. Classically, WS presents as pruritic or painful erythematous urticarial or granulomatous plaques. Less common presentations include annular or arciform lesions, papules, vesicles, and hemorrhagic bullae.

The diagnosis of WS is corroborated by histopathological findings. The characteristic histologic features include dermal edema with eosinophils and phagocytic histiocytes together with scattered flame figures which represent degranulated eosinophilic material adhered to normal collagen. Flame figures are a hallmark of WS but not pathognomic. Flame figures represent a histological cutaneous reaction pattern that can be seen in eosinophil-mediated dermatoses, such as bullous pemphigoid, herpes gestationis, eczematous dermatitides, arthropod bites and dermatophyte infections.

A range of diseases can share similar clinical or pathological profiles, therefore, correlation of clinical features, the course of skin lesions and histopathological examination of a skin biopsy is necessary to obtain a definitive diagnosis. Our differential diagnosis included urticarial vasculitis given the persistence of lesions beyond 24 hours, erythema annulare centrifugum, urticarial bullous pemphigoid, and eosinophilic annular erythema. Urticarial vasculitis lesions demonstrate histological findings of leukocytoclastic vasculitis, which was not seen in our case on histopathological examination. Erythema annulare centrifugum is a figurate erythema that can resemble our patient clinically, but lesions typically have a trailing scale and are not associated with flame figures histopathologically. Urticarial bullous pemphigoid (BP) can clinically resemble the annular or arciform variant of WS, however our patient's direct immunofluorescence tests were negative. Bullous pemphigoid can also be associated with flame figures on histopathological examination. One retrospective study identified flame figures in 3 of 34

patients with bullous pemphigoid, however, in all cases linear deposition of IgG was observed by direct immunofluorescence.

Systemic steroids are known as the most effective treatment in WS, while antimalarials (chloroquine and hydroxychloroquine) and systemic steroids have been reported as equally effective in treating EAE. Initial therapy for WS usually consists of low dose oral steroids (prednisone 10-80 mg daily) for one week, then tapered over two to three weeks. This typically results in dramatic improvement within a few days. For mild cases, potent topical corticosteroids have demonstrated efficacy. In persistent and frequently recurrent cases, Coldiron et al suggest a therapeutic approach of low-dose (5 mg) alternate-day oral prednisone. Cyclosporine (1.25-2.5 mg/kg/day) for 3-4 weeks resulted in clinical resolution in two cases of steroid-resistant WS, with no relapse during the following 10 months. Spontaneous resolution is also possible after weeks to years.

Our patient represents a rare case of eosinophilic annular erythema, a subset of Wells' syndrome. This uncommon condition is a cutaneous inflammatory syndrome that runs a benign course but has a high probability of recurrence even with appropriate therapy. While lesions usually resolve without sequelae, skin atrophy and hyperpigmentation may occasionally occur. The diagnosis and evaluation of this condition needs close monitoring with repeated clinical, histological and laboratory assessment.

REFERENCES

1. Wells GC. Recurrent granulomatous dermatitis with eosinophilia. Trans St Johns Hosp Dermatol Soc. 1971;57:46–56.
2. Gilliam AE, Bruckner AL, Howard RM, Lee BP, Wu S, Frieden IJ. Bullous "cellulitis" with eosinophilia: Case report and review of Wells' syndrome in childhood. *Pediatrics*. 2005;116:e149–55.
3. Sinno H, Lacroix J-P, Lee J, et al. Diagnosis and management of eosinophilic cellulitis (Wells' syndrome): A case series and literature review. *The Canadian Journal of Plastic Surgery*. 2012;20(2):91-97.
4. Mitchell AJ, Anderson TF, Headington JT, Rasmussen JE. Recurrent granulomatous dermatitis with eosinophilia. Wells' syndrome. *Int J Dermatol*. 1984;23:198–202.
5. Aberer W, Konrad K, Wolff K. Wells' syndrome is a distinctive disease entity and not a histologic diagnosis. *J Am Acad Dermatol*. 1988;18:105–114.
6. Coldiron BM, Robinson JK. Low-dose alternate-day prednisone for persistent Wells' syndrome. *Arch Dermatol.* 1989;125:1625–6.
7. Weiss G, Shemer A, Confino Y, Kaplan B, Trau H. Wells' syndrome: Report of a case and review of the literature. *Int J Dermatol*. 2001;40:148–52
8. El-Khalawany M, Al-Mutairi N, Sultan M, Shaaban D. Eosinophilic annular erythema is a peculiar subtype in the spectrum of Wells syndrome: a multicentre long-term follow-up study. *J Eur Acad Dermatol Venereol*. 2013;27:973–979.
9. Moossavi M, Mehregan DR. Wells' syndrome: A clinical and histopathologic review of seven cases. *Int J Dermatol*. 2003;42:62–7.