Chicago Dermatological Society

Monthly Educational Conference

Program Information
CME Certification
and
Case Presentations

Wednesday, April 18, 2018
Gleacher Center – Chicago, IL

Conference Host:

COOK COUNTY HEALTH & HOSPITALS SYSTEM
CCHHS

Stroger Hospital of Cook County
Division of Dermatology
Chicago, Illinois

Program

Host: Stroger Hospital of Cook County
Wednesday, April 18, 2018
Gleacher Center, Chicago

8:00 a.m.	**Registration & Continental Breakfast with Exhibitors** *All activities will take place on the 6th Floor of the Gleacher Center*
8:30 a.m. - 10:15 a.m.	**Clinical Rounds** Slide viewing/posters
9:00 a.m. - 10:00 a.m.	**Basic Science/Residents Lecture** "Mast Cell Disease: What Every Resident Should Know" *Michael D. Tharp, MD*
10:00 a.m. - 10:30 a.m.	**Break and Visit with Exhibitors**
10:30 a.m. - 12:15 p.m.	**Resident Case Presentations & Discussion;** **MOC Self-Assessment Questions**
12:15 p.m. - 12:45 p.m.	**Box Lunches & visit with exhibitors**
12:55 p.m. - 1:00 p.m.	**CDS Business Meeting**
1:00 p.m. - 2:00 p.m.	**General Session** BARSKY LECTURE - "Treatment of Chronic Urticaria: A Recipe for Success When Antihistamines Don't Work"" *Michael D. Tharp, MD*
2:00 p.m.	**Meeting adjourns**

Mark the Date!

Next CDS monthly meeting – Hosted by Rush University
Wednesday, May 9th; Gleacher Center, Chicago

IDS/CDS Joint Conference & Awards Luncheon
Wednesday, June 6, 2018; Stephens Convention Center, Rosemont

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

Guest Speaker

MICHAEL D. THARP, MD

Chairman (retired)
Department of Dermatology
Rush University Medical Center
Chicago, IL

Michael D. Tharp, MD, was the Clark W. Finnerud, MD, Professor, chairman and residency program director at the Department of Dermatology, Rush Medical College. He also was senior attending physician at Rush University Medical Center, retiring in 2017.

Dr. Tharp received his medical degree, cum laude, from The Ohio State University College of Medicine, Columbus, OH. He completed an internship in medicine and a residency in internal medicine at Parkland Memorial Hospital, Dallas, TX. Dr. Tharp also completed a residency and fellowship in dermatology at Duke Medical Center, Durham, NC. He was an Assistant and Associate Professor in the Department of Dermatology at UT Southwestern Medical School, Dallas, TX, and Professor and Vice Chair in the Department of Dermatology at the University of Pittsburgh prior to moving to Chicago.

Dr. Tharp's research interests have focused on mast cells and mast cell-mediated disorders including urticaria, mastocytosis, mast cell activation syndrome and atopic dermatitis. His clinical interests include immune mediated connective tissue diseases and immune bullous diseases, as well as psoriasis and cutaneous T cell lymphoma. He has been the recipient of numerous grants for dermatological research and an invited speaker to numerous national and international societies and meetings. Dr. Tharp has authored more than 170 articles, books, book chapters and reviews. He is chief editor of Dermatologic Therapy and a reviewer for numerous research and clinical journals.

CME Information

April 2018

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 2017/18 series of meetings, the participant should be able to:

1. Discuss key factors in the diagnosis and treatment for allergic conditions, 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 4.5 *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.

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.

Neither the guest speaker, Michael Tharp, MD, nor any of the planning committee members have any conflicts of interest to disclose.

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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.

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*Protocol to be posted same-day on the CDS website

Key Location: full body **Case 1A**

Presented by Charles Vainder MD, Shilpa Mehta MD, and David C Reid MD

History of Present Illness

A 27-year-old man presented with pyrexia and an asymptomatic eruption of two days' duration. The lesions started on his face, then spread to involve the trunk, extremities, oral mucosa, and genitalia. One week prior, he experienced flu-like symptoms, including subjective fever, conjunctivitis, sore throat, generalized weakness, and myalgia. He denied recent travel or sick contacts, and was unsure of his previous vaccination history.

Past Medical History

None

Medications

None

Social History

Moved from Mexico ten years ago

Review of Systems

No itching, headache, rhinorrhea, abdominal pain, nausea, diarrhea

Physical Exam

Vitals: Tmax 101 HR 104 BP 122/76 RR 20 SaO_2 98%
Face, trunk, and extremities: scattered erythematous vesiculopustules in different stages of healing
Palms: few scattered erythematous papules

Laboratory data

Platelets	91	[161-369]
HIV screen	Negative	
Syphilis EIA	Negative	
HSV PCR	Negative	
VZV PCR	Positive	
VZV IgG	Negative	
VZV IgM	1.68	>1.1 = positive

Radiology

Chest radiography: no pulmonary infiltrate

Diagnosis

Varicella

Treatment and Course

He was treated with valacyclovir one gram three times daily for a seven-day course. At follow-up five days later, he reported feeling well and most skin lesions had encrusted.

Key location: full body **Case 1B**

History of Present Illness
A 37-year-old man presented with a pruritic eruption of two days' duration. The lesions began on his face and scalp, then spread to involve his entire body. One day prior to onset, he experienced subjective fever and a sore throat. He recalled that his girlfriend had similar-appearing lesions on her arm one month prior. He denied a previous history of varicella and was unvaccinated as a child.

Past Medical History
Denied history of varicella as a child

Medications
None

Social History
Moved from India two years ago

Review of Systems
No itching, headache, rhinorrhea, abdominal pain, nausea, diarrhea

Physical Exam
Vitals: Tmax 99.4 HR 99 BP 115/70 SaO_2 98%
Entire body sparing palms/soles: scattered and numerous erythematous papulovesicles on an erythematous base, many with hemorrhagic crust

Laboratory Data

ALT	44	[5-35]
LDH	238	[85-210]
Platelets	156	[161-369]
VZV PCR	Positive	
HSV1 PCR	Negative	
HSV2 PCR	Negative	
HIV antibodies	Negative	
Hepatitis B antigen	Negative	
Hepatitis B surface antibody	Positive	
Hepatitis B core antibody	Positive	
Hepatitis C antibody	Negative	

Radiology
Chest radiography: no pulmonary infiltrate

Diagnosis
Varicella

Treatment and Course
He was started on valcyclovir one gram three times daily for a seven-day course. At follow-up, he had clinical improvement of skin lesions and resolution of transaminitis.

Key location: full body **Case 1C**

History of Present Illness
A 55-year-old woman presented with a pruritic and painful eruption of ten days' duration. The lesions first appeared on her neck and then spread to the rest of her body. She had visited the emergency department and was started on clindamycin for presumed folliculitis. Subsequently, she noted that the lesions became fluid-filled and then eroded. She reported subjective fevers and diarrhea. She had returned from a vacation in Wisconsin one week prior to development of symptoms.

Past Medical History
None

Medications
Clindamycin, hydroxyzine

Social History
Noncontributory

Review of Systems
No headache, rhinorrhea, abdominal pain, nausea, vomiting

Physical Exam
Vitals: T 98.5 HR 88 BP 153/77 RR 16 SaO_2 95%
Left lateral neck, posterior left ear, upper back: scattered hemorrhagic crusted plaques
Posterior neck, back, arms, and legs: scattered 1-2 mm vesicles on an erythematous base

Laboratory Data

GGT	77	[3-60]
AST	40	[0-40]
ALT	88	[5-35]
Lipase	64	[5-55]
VZV PCR	Positive	
HSV1 PCR	Negative	
HSV2 PCR	Negative	
HIV screen	Negative	

Radiology
Chest radiography: no acute cardiopulmonary findings

Diagnosis
Varicella

Treatment and Course
She was admitted due to elevated liver enzymes and started on acyclovir 700 mg intravenously three times daily. Gastroenterology was consulted and concluded that her hepatic lab abnormalities were likely secondary to a chronic process. She clinically improved and was discharged on valacyclovir one gram three times daily for a seven-day course.

Discussion

Varicella zoster virus (VZV), or human herpesvirus 3, is a member of the alpha herpes virus family, which includes seven other viruses. It is a double-stranded DNA virus that is typically transmitted through the air in droplets, but can also spread via direct contact with active blisters. The virus has an incubation period ranging from 7-23 days, during which it replicates in lymph tissues and infects T-cells. Following primary VZV infection, the virus remains dormant in sensory ganglia and it can later reactivate, causing herpes zoster.

Primary varicella, colloquially known as chickenpox, usually presents with prodromal fever, malaise, headache, or abdominal pain. These symptoms precede cutaneous manifestations by one to two days. Characteristically, pruritic erythematous macules and papules first manifest on the head and then spread caudally to the rest of the body. As the lesions develop, they become vesicular and overlie an erythematous base, demonstrating the characteristic "dew drops on a rose petal" appearance. They can number in the hundreds and appear in different morphologies concomitantly. The disease is transmittable from one to two days prior to development of skin lesions until all lesions have encrusted.

Diagnosis of primary varicella is based on clinical presentation, history, and exposure. However, experience in diagnosing the disease has waned since the introduction of the VZV vaccine. Additionally, it can present with fewer manifestations in previously vaccinated individuals. Thus, laboratory testing remains an important tool for diagnosis. The most sensitive test is polymerase chain reaction (PCR), which has a sensitivity of 95-100% in unvaccinated individuals. Serologies are less sensitive than PCR for primary infections, as IgM can be positive in reactivated VZV, and false negatives are common. IgG serology can be a useful adjunct, but it cannot clearly define whether antibodies are from current or previous exposure.

Current CDC guidelines recommend that hospitalized patients should be placed on airborne and contact precautions, in addition to standard precautions, until lesions become encrusted. Patients should only be cared for by providers with evidence of immunity. Antiviral treatment should be considered in patients at high risk for complications. Patients with high-risk exposures, contraindications to the VZV vaccine, and no prior exposure can alternatively receive VZV immune globulin for prophylaxis.

Primary varicella is usually a self-limited disease; however, it can cause systemic complications including pneumonia, CNS involvement, bacterial superinfection resulting in sepsis, encephalitis, or hepatitis. All can be potentially fatal. Those at increased risk for complications include immunosuppressed patients, infants, elderly, and pregnant women.

Varicella classically has been considered a childhood disease. Historically, prior to the vaccination program, greater than 90% of cases were in children. However, despite the incidence being higher in children, adults had a 25 times greater risk of mortality than children 1-4 years old. Specifically, pneumonia was most frequently associated with mortality.

Perception has been that varicella among adults is frequently associated with severe systemic complications. Varicella complications can be severe; however, serious complications are infrequent. Data from the Varicella Active Surveillance Project found the relative risk of complications to be 2.3 times greater in patients 20 and over compared to those between 0 and 14 years of age. The most common adverse effects were diarrhea, otitis media, and pharyngitis. Pneumonia rate was only 60 in 10,000 cases. Only one case of viral meningitis was noted.

Varicella is preventable by vaccination. Prior to vaccination, there were approximately 11,000-13,500 hospitalizations and 100-150 deaths annually. Most deaths occurred in previously healthy individuals. Varivax, a live attenuated vaccine against VZV, was first introduced in 1995. The vaccine was initially administered as one dose at one-year of age, but studies demonstrated that it was only effective at preventing infection in 80-85% of individuals.

In 2006, the CDC began recommending a second dose at four to six years of age. Addition of the second dose reduced odds of developing infection by 95% as compared with the single dose schedule. Subsequently, annual VZV incidence declined 84.6% when comparing the years 2005-2006 to 2013-2014. Comparing the year 2012 to the pre-vaccination era, hospitalizations decreased by 93% and outpatient visits by 84%. Importantly, vaccination provided long-term protection over 14-year follow up, and possibly reduced the risk of herpes zoster development.

In vaccinated populations, cases of primary varicella are most likely secondary to vaccine failure. Breakthrough disease in vaccinated patients is typically milder, less likely to produce fever, and cases typically have fewer lesions with a shorter duration of illness. Further, the cutaneous presentation is predominantly macular and popular, rather than vesicular. Still, severe disease and systemic complications can occur in vaccinated individuals. As an additional complication, many adults and patients from foreign countries remain unvaccinated. Despite the success of the vaccination program, clinicians should remain vigilant for primary varicella and its varying presentations.

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13. Wang, L., L. Zhu, and H. Zhu, *Efficacy of varicella (VZV) vaccination: an update for the clinician.* Ther Adv Vaccines, 2016. 4(1-2): p. 20-31.

Key location: right lower extremity **CASE 2A**

Presented by Susan Hwang MD and Warren Piette MD

History of Present Illness

A 71-year-old man presented with a three-month history of a painful, draining, right lower extremity growth with associated swelling. It began as a solitary lesion, which was followed by the development of surrounding papules.

Past Medical History

Adenocarcinoma of prostate, non-insulin dependent diabetes, gout, hypertension, hyperlipidemia, obstructive sleep apnea, venous stasis ulcers

Medications

Albuterol, allopurinol, amlodipine, clopidogrel, flutamide, gabapentin, insulin, furosemide, loratadine, losartan, metformin, sildenafil, tamsulosin, metoprolol

Allergies

Penicillin

Social History

30 pack-years tobacco

Review of Systems

Negative

Physical Exam

Skin:	Solitary, circumscribed 4x3-cm exophytic, ulcerated, draining nodule, with several surrounding erythematous, circular plaques on the right medial leg in the setting of 2+ pitting edema
Lymph nodes:	No cervical, submental, submandibular or occipital lymphadenopathy

Histopathology

Shave biopsy, right leg: dense infiltrate of darkly staining cells extending from the base of the biopsy to the papillary dermis. Positive for synaptophysin, CD56, CAM 5.2, cytokeratin OSCAR. Negative for CD20, TTF-1, AE1/3, S100, MART-1, HMB45, prostatic specific antigen, prostatic specific acid phosphatase, Merkel cell polyomavirus.

Imaging

Chest, abdomen and pelvis computed tomography: retroperitoneal, right iliac chain and right inguinal adenopathy.

Diagnosis

Neuroendocrine tumor, unknown primary

Treatment and Course

He underwent an upper gastrointestinal endoscopy and colonoscopy, which did not reveal the location of the primary malignancy. He subsequently received one dose of cisplatin-etoposide, which decreased the size of the malignancy. Due to a national shortage of etoposide, he was switched to a regimen of cisplatin-irinotecan.

Key location: scalp **CASE 2B**

Presented by Susan Hwang MD and Warren Piette MD

History of Present Illness

A 52-year-old man presented with a two-month history of tender, non-draining nodules on the scalp, which were enlarging and increasing in number. Four months prior, he was diagnosed with metastatic stage IV high-grade prostate adenocarcinoma and was treated with androgen deprivation therapy and docetaxel.

Past Medical History

Stage IV prostate adenocarcinoma, seizure disorder, left leg deep venous thrombosis

Medications

Nifedipine, amitriptyline, pantoprazole, phenytoin, tamsulosin

Social History

30 pack-years tobacco
Four to five beers weekly

Review of Systems

Positive for flank pain, back pain, fatigue

Physical Exam

Skin:	Multiple, small, firm, minimally tender, erythematous papulonodules on the posterior scalp and right temple
Lymph nodes:	No cervical, submental, occipital, or submandibular lymphadenopathy

Laboratory Data

The following labs were abnormal:

WBC	14.3	[4.4-10.6 k/uL]
HGB	8.0	[12.9-16.8 g/dL]
BUN	77	[8-20 mg/dL]
Creatinine	5.6	[0.6-1.4 mg/dL]
Calcium	7.3	[8.5-10.2 mg/dL]
Albumin	3.3	[3.5 to 5.5 g/dL]
AST	151	[0-40 U/L]
ALT	73	[5-35 U/L]
Bilirubin (total)	10.4	[<0.3 mg/dL]
Bilirubin (direct)	6.6	[<1.2 mg/dL]
LDH	442	[85-220 U/L]

Histopathology

Punch biopsy, scalp: dense, poorly circumscribed, trabecular infiltrate of small to medium cells with amphophilic, finely granular cytoplasm in the deep dermis. Diffuse positivity for synaptophysin and CK20; patchy positivity for chromogranin and CK7, with perinuclear dot and cytoplasmic staining. Patchy weak-to-moderate positivity for PAX5. Negative TTF1, CDX2, Merkel cell polyomavirus, prostatic specific antigen and prostatic specific acid phosphatase.

Radiology
Chest, abdomen, pelvis computed tomography: pulmonary, hepatic, pancreatic, renal and adrenal masses, retroperitoneal and bilateral pelvic lymphadenopathy.

Diagnosis
Neuroendocrine tumor, poorly differentiated, unknown primary

Treatment and Course
He was treated with symptomatic biliary drainage and nephrostomy tube placement. His course was complicated by septic shock and tumor lysis syndrome requiring dialysis. He was started on carboplatin and etoposide. Due to the lack of a therapeutic response, the patient and his family elected for home hospice.

Discussion
Neuroendocrine tumors (NET) are a heterogeneous group of malignancies identified primarily by their common features: capability of secreting hormones, neurotransmitters, neuromodulators, and neuropeptides. Precursor neuroendocrine cells are found in all solid organs, skin, and mucosae, allowing for tumors to arise from varying locations; however, primary NET of the skin is extremely rare. An approximate incidence rate of 1-2 new cases per 100,000 person-years has been reported, representing 0.5% of all malignancies. The most common primary site is the gastrointestinal tract, followed by the appendix, lungs, and small intestine. Twelve percent of patients present with metastases from an unknown primary site. Detection of the primary site in metastatic NET poses a challenge to clinicians, and the recommended diagnostic work-up includes endoscopy, computed tomography, and scintigraphy.

As a group, NETs metastasize in 20-30% of cases, and most commonly travel to the lymph nodes, liver, or lung. Cutaneous metastases are rare, with only 31 cases previously reported. Mean age at diagnosis is 55 years and there is no predilection for sex. Clinically, NETs present as single or multiple, non-ulcerated, painless, slow growing nodules, ranging from 0.5- to 2.5-cm in diameter. The scalp and trunk are the most commonly affected sites. The overall prognosis for metastatic NET to any location is poor, with a five-year survival rate of 19%. However, resection of the primary site can increase disease-free survival and allow for appropriate chemotherapy.

References

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CASE 3

Presented by Evan Stokar MD and Warren Piette MD

A 39-year-old Hispanic man presented with hemorrhagic bullae on the lower left leg of two weeks' duration.

UNKNOWN

Key location: face **Case 4**

Presented by Jackelyn Tanios MD and Vidya Shivakumar MD

History of Present Illness
A 28-year-old healthy woman presented with asymptomatic papules on the face since age eight. She continued to develop new lesions and was bothered by their appearance. Her father, two paternal aunts, and sister have similar findings, as well as her son and daughter. She has one son and one sister who are unaffected. She is unaware of any family history of cancer.

Past Medical History
None

Medications
None

Social History
Noncontributory

Review of Systems
Denies fevers, chills, weight loss, cough, shortness of breath, chest pain, joint pain, dysuria, irregular menses

Physical Exam
Hundreds of 0.5-1cm dome-shaped, firm, skin colored papules on the central face, coalescing over the nasal bridge and nasolabial folds, and involving the hairline and lateral face

Laboratory Data
The following labs were remarkable:
CYLD gene positive for heterozygous mutation

Histopathology
Punch biopsy, right temple: basaloid cells in a fibroblast-rich stroma, consistent with trichoepithelioma

Diagnosis
Multiple familial trichoepithelioma

Discussion
Multiple familial trichoepithelioma (MFT) is an autosomal dominant condition caused by a mutation in the CYLD gene, a tumor suppressor gene, leading to multiple trichoepitheliomas, most concentrated over the central face. Mutations in the CYLD gene are also associated with Brooke-Spiegler syndrome (BSS) and familial cylindromatosis; these diseases are thought to represent a phenotypic spectrum, rather than distinct syndromes. Trichoepitheliomas show predilection for the nose, nasolabial folds, and upper lips. Cylindromas typically occur on the scalp, with less frequent involvement of the face, trunk, and extremities. While cylindromas and spiradenomas arise from sweat glands (apocrine or eccrine), trichoepitheliomas demonstrate hair follicle differentiation. A unique feature of BSS is a lack of genotype-phenotype correlation, and therefore different tumor combinations can be observed. Some patients present with cylindromas and trichoepitheliomas, whereas others present with trichoepitheliomas and spiradenomas, with cylindromas and spiradenomas, or with all three tumor types. Interestingly, individuals within a single family can exhibit different tumor phenotypes.

Given the multitude of lesions, conventional surgical excision is not recommended. Ablative therapies, including electrosurgery and CO_2 laser, have been reported to improve cosmetic outcome in some patients. A recent report described the utility of topical rapamycin, an mTOR inhibitor, both alone and in conjunction with CO_2 laser treatment, in reducing the development of new trichoepitheliomas and rapid growth progression, which would be most beneficial in the treatment of affected children. Secondary basal cell carcinomas have been reported, however, given the ubiquity of this neoplasm, it is unclear whether this is a true association or coincidental. To date, MFT has not been associated with internal malignancy, but patients should be periodically followed regardless.

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Key location: left breast **CASE 5**

Presented by Maria Yaldo MD and Shilpa Mehta MD

History of Present Illness
A 79-year-old black woman presented with a one-year history of an asymptomatic, ulcerated nodule on the left breast. It began as a pink papule that grew and subsequently ulcerated with intermittent bleeding. The lesion was treated with oral antibiotics by her primary care provider with no improvement. Review of systems was unremarkable.

Past Medical History
Type 2 diabetes mellitus, dyslipidemia, hypertension

Medications
Insulin, aspirin, simvastatin, hydrochlorothiazide, enalapril, atenolol

Family History
Relevant for bladder cancer in her brother and leukemia in her father

Social History
No tobacco, drug, or alcohol use

Physical Exam

Skin:	Left lateral breast with a well-circumscribed, red to violaceous, ulcerated, exophytic tumor with protuberant friable tissue approximately four centimeters in size
Lymph nodes:	No cervical, axillary, or inguinal lymphadenopathy

Histopathology
Punch biopsy, left breast: tumor composed of lobules and sheets of basaloid cells extending into the subcutaneous tissue with areas of sebaceous differentiation, prominent necrosis, epidermal pagetoid spread, and numerous mitotic figures. The tumor was poorly differentiated, however no lymphovascular or perineural invasion was identified. Immunohistochemistry revealed positive staining for epithelial membrane antigen (EMA) and androgen receptor (AR). Carcinoembryonic antigen (CEA), gross cystic disease fluid protein 15 (GCDFP-1), B-cell lymphoma 2 (bcl-2), and S100 protein (S-100) were negative.

Diagnosis
Extraocular sebaceous carcinoma

Treatment and Course
The patient was referred to surgical oncology for a wide-local excision. At the time of surgery, there were palpable axillary lymph nodes which were removed, but negative on biopsy. Screening for Muir-Torre syndrome revealed the presence of microsatellite instability of the tumor and loss of MSH2/MSH6 mismatch repair proteins on immunohistochemical staining. Colonoscopy five years ago was unremarkable. Patient was referred to genetics. Germline mutation analysis was negative for Muir-Torre syndrome.

Discussion

Sebaceous carcinoma (SC) is a rare malignant adnexal neoplasm, comprising 0.2% to 4.6% of all cutaneous malignancies. It often presents in the periocular area, whereas extraocular locations are infrequent, with the majority on the head and neck. Including our patient, to our knowledge, only two cases of extraocular sebaceous carcinoma occurring on the cutaneous breast have been reported to date, the other being on the nipple. Other reported cutaneous sites include scalp, face, salivary glands, neck, axilla, forearm, chest wall, scrotum, and vulva.

Regardless of location, SC is more common in elderly whites with no sex predilection. Clinically, sebaceous carcinoma can have a variable presentation. In the periocular location, it can present as a skin colored to erythematous papule or nodule often confused for chalazion or chronic blepharoconjunctivitis. However, in extraocular locations, it often presents as an ulcerative pink to yellow-red nodule mimicking non-melanoma skin cancers, pyogenic granulomas, abscesses and benign or malignant adnexal tumors. The vast range of clinical presentations along with slow, asymptomatic growth often leads to delay in diagnosis.

Histologically, SC features basaloid or squamoid lobules or sheets of cells that invade the dermis. The growth pattern may be nodular, multinodular, or diffuse. There is variable differentiation ranging from un-differentiated blue cells to cells with sebaceous differentiation, characterized by vacuolated cytoplasm and indented nuclei, though the latter may not always be seen and makes the diagnosis difficult. Extraocular tumors tend to be more ulcerated than periocular tumors, while periocular tumors tend to show more pagetoid spread. In one review, the majority of extraocular tumors were found to be moderately differentiated and exhibited a squamoid growth pattern. Cytologically, cells may also appear pleomorphic with variable degrees of atypia and mitoses. Features of SC that denote a worse prognosis include poor sebaceous differentiation, pagetoid spread, highly infiltrative growth pattern, and lymphovascular invasion.

Immunohistochemistry is often used to confirm the diagnosis of SC, as histology may mimic basal cell or squamous cell carcinoma. Adipophilin has been found to have a high sensitivity and specificity in recognizing sebaceous differentiation. Staining for SC is also often positive for EMA, cytokeratin 7 (CK7), and androgen receptor (AR), though not as specific. Nuclear factor XIIIa has recently been found to be a sensitive marker for sebaceous differentiation. Emerging antibodies targeting proteins involved in intracellular lipid metabolism including ABHD5 (alpha/beta hydrolase-domain containing protein 5), PGRMC1 (progesterone receptor membrane component 1) and squalene synthetase may be more sensitive and specific, however further studies are needed to confirm.

There are no specific staging or tumor management guidelines for extraocular SC, and surgery is the primary treatment modality. Surgical options include Mohs micrographic surgery (MMS) or wide local excision, with MMS being slightly more favorable due to lower reported recurrence rates. The role of adjuvant radiotherapy, sentinel lymph node biopsy and imaging is unclear. Radiation may be considered if the patient is not a surgical candidate. Recurrence rates for extraocular lesions ranges from 4% to 29%. The five and ten-year relative survival rates for all SC are 92.72% and 86.98%, respectively. Metastasis of extraocular SC is rare. If metastasis occurs, it most commonly involves the draining lymph node basin, though reports of liver, small bowel, urinary tract, lung, and brain involvement have been reported. Prognosis is similar among ocular and extraocular SC in previous reports, however, a recent review reported increased all-cause mortality associated with extraocular SC.

Screening for Muir-Torre syndrome (MTS) should be considered in all sebaceous neoplasms with immunohistochemical staining for mismatch repair proteins (MMR) or microsatellite instability testing. Muir-Torre syndrome is a rare autosomal dominant disorder characterized by at least one

sebaceous neoplasm and at least one visceral malignancy with colorectal cancer being the most common. MTS is due to mutations in DNA mismatch repair proteins which include MSH2, MSH6, MLH1, and rarely PMS2. About one-third of patients with abnormal immunohistochemical staining will have germline mutations.

Finally, we describe a rare case of an extraocular SC which presented as an asymptomatic, ulcerative, slow growing nodule on the left breast. We suggest including sebaceous carcinoma among other cutaneous tumors in the list of clinical differentials for an ulcerative, red-yellow nodule at any site.

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Key locations: upper extremities **CASE 6**

Presented by Jessika Davis MD and Shilpa Mehta MD

History of Present Illness
A 53-year-old woman with a history of rheumatoid arthritis (RA) presented with a one-year history of tender skin lesions on the upper extremities. The lesions initially appeared on her elbows and then progressed to involve her medial upper arms. She was diagnosed with RA greater than 10 years prior and had failed multiple treatments, including sulfasalazine, hydroxychloroquine, and methotrexate, before starting etanercept about one-year prior to presentation.

Past Medical History
Hypertension, nonalcoholic fatty liver disease

Medications
Etanercept, losartan

Social History
Noncontributory

Review of Systems
Positive for arthralgias
Negative for weight loss, night sweats, pyrexia

Physical Exam
Superomedial ventral arms and elbows: multiple, circumscribed, symmetrically clustered, 5-15mm, firm, skin-colored to erythematous papules

Histopathology
Punch biopsy, right medial arm: interstitial dermal infiltrate of histiocytes with scattered ill-defined dermal granulomas containing a central neutrophilic infiltrate, necrobiosis and amorphous material with peripheral epithelioid histiocytes

Diagnosis
Anti-TNF-α-associated interstitial granulomatous dermatitis

Treatment and Course
She was initially treated with topical corticosteroids, during which her RA failed to respond to etanercept and her rheumatologist transitioned her to adalimumab. Her skin improved about two months after discounting etanercept. However, after initiating adalimumab, the lesions worsened, with significant pruritus that was unresponsive to topical corticosteroids. All TNF-α inhibitors were subsequently discontinued and the lesions resolved spontaneously with residual atrophic papules. She remained clear at her three-month follow-up.

Discussion
Interstitial granulomatous dermatitis (IGD) belongs to a group of reactive granulomatous dermatoses, comprised of IGD, palisaded neutrophilic and granulomatous dermatitis (PNGD) and interstitial granulomatous drug reaction (IGDR). These entities represent cutaneous reaction patterns to an underlying systemic disorder (e.g., connective tissue disease, inflammatory arthritis, malignancy) or to medications. Given the variety of clinical and histopathologic findings with overlapping features, there are inconsistencies within the literature, hindering the ability to

establish a definitive diagnosis. These disorders have thus been viewed as a continuum or progression of a single disease process, a variant of granuloma annulare, or distinct conditions.

The prevalence of IGD is unknown, although it has a 3:1 female-to-male predominance and has been reported in adults of all ages and, less commonly, in children. Less than 10% of IGD presents as the classic subcutaneous, rope-like, linear cords on the proximal trunk. More commonly, IGD presents as asymptomatic, erythematous to violaceous patches, annular plaques, papules, or nodules, distributed symmetrically on the upper lateral trunk and proximal limbs. IGDR presents similarly, with erythematous to violaceous plaques, often annular, with a predilection for skin folds or photo-exposed areas. This contrasts with PNGD, which typically manifests as symmetric, umbilicated or crusted, violaceous papules and nodules along the extensor arms, particularly around the elbows.

Both IGD and PNGD are associated with connective tissue diseases, inflammatory arthritis, and hematologic disorders, with IGD demonstrating a stronger association with inflammatory arthritides. IGDR has been attributed to medications such as calcium channel blockers, beta-adrenergic blocking agents, angiotensin converting enzyme (ACE)-inhibitors, lipid lowering agents, and allopurinol, whereas IGD has been associated with anti-TNF-α inhibitors, ACE-inhibitors, and furosemide. When induced by anti-TNF-α inhibitors, skin lesions may develop within one to three months, or more than one year after initiation of therapy, and improve within two months after discontinuation of the medication. The result of an immune-mediated reaction with anti TNF-α therapy is considered a 'borderline' paradoxical adverse event given that anti-TNF therapy is also utilized as an effective treatment for granulomatous conditions.

Histology of IGD shows interstitial, necrotizing, granulomatous inflammation, with sparse palisading interstitial histiocytes. In two-thirds of cases, rosettes of histiocytes may surround degenerated collagen, leading to visible clefting, known as the "floating sign." Mucin, eosinophils, and neutrophils are usually minimal to absent, and vasculitis is not generally observed. IGDR is similar to IGD, with the addition of a vacuolar interface dermatitis, prominent dermal eosinophils, mild lymphoid atypia, and minimal collagen degeneration. PNGD findings vary as the lesion evolves, with early lesions demonstrating leukocytoclastic vasculitis and mature lesions exhibiting palisading granulomas with collagen trapping, neutrophilic infiltrate, and nuclear debris.

In a patient with suspected reactive granulomatous dermatitis, the initial evaluation should include a thorough review of medications and a workup for underlying systemic disease. Management includes cessation of the culprit medication when indicated or controlling of the underlying systemic disease. Successful use of medications, such as topical, intralesional or systemic corticosteroids, nonsteroidal anti-inflammatory drugs, dapsone, hydroxychloroquine, and TNF-α inhibitors have also been reported.

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CASE 7

Presented by Anand Haryani MD and Warren Piette MD

History of Present Illness

A 37-year-old otherwise healthy man presented with a pruritic eruption for three months and fever for two days.

UNKNOWN

Key location: full body **CASE 8**

Presented by Divya Sachdev MD and Jerry Feldman MD

History of Present Illness
A 44-year-old African-American man presented with a hypopigmented eruption on the body that started five months ago. Lesions initially appeared on his hands and spread to involve the rest of his body, sparing the oral and genital mucosae. They were asymptomatic and had not previously been treated. He had a history of hair loss on the scalp and eyebrows since an early age, as well as a family history of alopecia. A couple months prior to his cutaneous eruption, he experienced acute vision loss due to bilateral posterior uveitis and retinal inflammation, which prompted initiation of prednisone and atropine eye drops. Recently, he presented with acute worsening of his vision along with pain. Ophthalmologic evaluation found bilateral anterior uveitis and choroidal thickening.

Past Medical History
None

Social History
30 pack-years tobacco

Medications
None

Review of Systems
Positive for eye pain, vision loss, decreased hearing, and tinnitus

Physical Exam
Scalp, eyelids, arms, dorsal hands, back, buttocks, legs, dorsal feet: scattered, circumscribed hypopigmented, non-scaly white patches, some petaloid-appearing, with accentuation under Wood's lamp
Scalp and eyebrows: widespread alopecia

Laboratory Data
The following laboratory findings were negative:
CBC, CMP, ANA, ANCA, Syphilis EIA, RF, ACE, TSH/free T4, hepatitis serologies, quantiferon

Diagnosis
Vogt-Koyanagi-Harada (VKH) syndrome

Treatment and Course
He was started on prednisone 40 mg daily with improvement of his visual symptoms after one week of therapy. Triamcinolone 0.1% ointment twice daily was initiated for the affected areas on his body. Referrals to neurology and otorhinolaryngology were also placed.

Discussion
Vogt-Koyanagi-Harada syndrome, also known as uveomeningoencephalitic syndrome, is a rare multisystem disorder with cutaneous, ophthalmic, neurologic, and auditory manifestations. It is a T-cell mediated autoimmune disorder, in which melanocytes are targeted by the host immune system. The condition usually presents in the second to fifth decade, with a female predominance. There is a genetic predisposition noted mainly in Asian, Middle Eastern, Hispanic, and Native American populations. Several HLA associations have been reported, including HLA-

DR4, HLA-DR53, and HLADQ4. Specifically, HLA-DRB1*0405 has been suggested as the main susceptibility allele for VKH. In addition, IL-23 has been suggested to play a role in the development and maintenance of autoimmune inflammation seen in VKH disease by stimulating IL-17 producing CD4+ T cells.

The condition is typically characterized by four clinical stages: prodromal, uveitic, convalescent, and chronic recurrent. The prodromal stage persists for a few days and can include fever, nausea, tinnitus, hearing loss, meningismus, headache, and other central nervous system-related symptoms. The uveitic stage persists for several weeks and presents with acute bilateral blurring of vision. In this stage, posterior uveitis with retinal edema, diffuse choroiditis, optic disc edema and hyperemia, and exudative retinal detachments can be observed. The convalescent stage typically lasts several months to years and includes ocular manifestations, such as widespread depigmentation of the choroid, in addition to cutaneous manifestations, such as vitiligo. The chronic recurrent stage includes a variety of ocular manifestations, including anterior uveitis, choroidal inflammation and neovascularization, glaucoma, cataracts, and subretinal fibrosis. Cutaneous findings of VKH occur after the ocular and neurological manifestations, and include vitiligo, alopecia, and poliosis. Other associations include inflammatory vitiligo.

There are 5 diagnostic criteria for VKH:

1. No history of penetrating ocular trauma or surgery
2. No evidence of other ocular disease that could explain the presenting clinical features
3. Bilateral ocular involvement
4. History or presence of neurologic or auditory findings, such as meningismus, tinnitus, or CSF pleocytosis
5. Presence of alopecia, poliosis, or vitiligo that should not have preceded the CNS findings

For a diagnosis of complete VKH, all 5 diagnostic criteria are required, whereas incomplete VKH requires criteria 1-3 and either 4 or 5, and probable VKH requires criteria 1-3. The diagnosis of VKH is based on history and clinical examination. Ocular ultrasonography and enhanced-depth optical coherence tomography (OCT) can be used to demonstrate choroidal thickening. During the early phase of VKH, fluorescein angiography can show widespread pinpoint areas of leakage through the fundus, as well as subretinal pooling of fluorescein in areas of exudative retinal detachments. Indocyanine green angiography can help visualize choroidal circulation and is used to diagnose and monitor response to treatment. Lumbar puncture may also be useful, as greater than 80% of patients exhibit transient pleocytosis during the initial phase of VKH. Additional cerebrospinal fluid findings include increased protein, increased pressure, and the presence of melanin-laden macrophages. If auditory or neurological symptoms are reported, audiology testing and magnetic resonance imaging should be performed, respectively.

First line therapy is usually high-dose oral prednisone for at least six months. Given the potentially chronic nature of VKH and potential side effects of oral corticosteroids, other immunosuppressive medications can be considered, including cyclosporine, mycophenolate mofetil, and infliximab. Intravitreal triamcinolone has been also used for persistent or severe visual inflammation, or if there is no improvement in retinal detachment with systemic steroids. The prognosis for VKH is variable and depends on early identification, as well as response to immunosuppression. Generally, resolution of neurological signs, intraocular inflammation, and exudative retinal detachments is noted. Vitiligo can be treated with topical corticosteroids and topical calcineurin inhibitors, similar to isolated vitiligo.

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Key location: right foot **CASE 9**

Presented by Dorothy Rodenbeck MD and Warren Piette MD

History of Present Illness
A 44-year-old Mexican man presented with right lower extremity edema and nodules for the last 30 years. Skin changes initially started as a small nodule on his plantar foot, which gradually developed into skin swelling and multiple nodules. He had been previously treated in Mexico for similar symptoms, where he had had a nodule on the medial foot excised 11 years prior in addition to an unknown course of an unknown oral medication with improvement. However, he was unsure of the diagnosis and did not have records. He presented to our ED for development of new nodules with worsening pain and swelling in the recent weeks.

Past Medical History
Hypertension, asthma

Medications
None

Social History
Recently immigrated from Mexico, where he worked on farms for most of his life, often barefoot.

Review of Systems
Negative for fever, chills, arthralgias, or similar lesions elsewhere on the body

Physical Exam
Multiple tender scattered 1-2cm round draining nodules on right dorsal foot and lower leg on a background of substantial non-pitting edema

Histopathology
Incisional biopsy, right medial lower leg: subcutaneous granules composed of radiating gram-positive filamentous bacteria with Splendore–Hoeppli effect. PAS negative for fungus.

Microbiology
Tissue cultures, right foot:

Bacterial	No growth
Mycobacterial	No growth
Fungal	No growth

Radiology
X-ray, right foot and leg: periosteal reaction surrounding the distal fibula. No evidence of active osseous destruction.

Diagnosis
Actinomycetoma, presumed nocardiosis

Treatment and Course
To date, he has been treated with sulfamethoxazole-trimethoprim (SMX-TMP) 800/160 mg twice daily for 5 months. His foot swelling has decreased and sinus tracts are closing.

Discussion

Mycetoma is a chronic subcutaneous infection that is caused by inoculation of various saprophytic soil-dwelling species of either fungi (eumycetoma) or aerobic actinomycetes bacteria (actinomycetoma). It is a worldwide disease that is endemic in tropical and subtropical regions, predominating between latitudes 30°N and 15°S, also known as the "Mycetoma belt" (Sudan, Somalia, Senegal, India, Yemen, Mexico, Venezuela, Colombia, and Argentina). Although rare in developed countries, an understanding of the disease is important for dermatologists due to migration of patients from endemic areas.

Sudan is the most endemic country for mycetoma, with a majority of cases (70%) being eumycetomas due to the fungus *Madurella mycetomatis*. Worldwide, however, actinomycetomas predominate and comprise 60% of all mycetomas. Actinomycetomas are most common in Latin America, with the highest incidence reported in Mexico. Actinomycete species derive from *Nocardia, Streptomyces*, and *Actinomadura* genera. *Nocardia brasiliensis, Actinomadura madurae, Actinomadura pelletieri* and *Streptomyces somaliensis* are most common. It is important to recognize that the term actinomycetoma may cause confusion as *Actinomyces* genera are *not* implicated in pathogenesis. In our patient's native Mexico, 98% of all mycetomas are caused by actinomycetes, 86% of which are caused by *Nocardia brasiliensis*.

Mycetoma is a cutaneous disease localized by contact with soil, most commonly affecting the feet and legs, followed by the hands. Inoculation occurs from a penetrating injury via a thorn prick, a wood splinter, or a stone cut, often while working barefoot, or through pre-existing skin barrier defects. Disease occurs most commonly in males age 20-40, presumably due to occupational exposure with agricultural work.

Due to a long incubation period (ranging from 3-9 months), the inciting injury is often not remembered by patients. Regardless of the causative organism, clinical presentation of mycetoma is uniform, characterized by a pathognomonic triad of painless firm subcutaneous mass or swelling, multiple fistulae, and a purulent or serosanguinous exudate containing grains. Infections start as a small nodule at the site of inoculation that eventually ulcerates, with resultant discharge containing characteristic granules composed of colonies of the organism. The mycetoma then grows and invades locally to form woody induration with focal papules, pustules and nodules that coalesce to form sinus tracts. Infection may traverse fascial planes to invade bones and other subcutaneous structures; hematogenous dissemination is rare. Actinomycetoma differs from eumycetoma by its more rapid, aggressive and destructive nature, invading bones and lymphatics earlier. Imaging, either radiologic or ultrasonographic, is important in assessing disease extent and bony involvement.

Diagnosis of mycetoma may be made based on the presence of uniform clinical features. However, evaluation of grains via direct examination, microscopy, or culture must be performed to determine the causative species and proper treatment. It is important that grain specimens be collected via a deep source (sinus wall scraping, aspiration of unopened sinus tract, or deep punch or incisional biopsy) versus extruded superficial grains, as the latter are commonly not viable and contaminated. Direct examination of exudate of granules smeared on a slide allows one to quickly distinguish between eumycetoma and actinomycetoma. Mounting with normal saline, KOH, or lactophenol blue allows differentiation between the branching thin filaments of actinomycetoma and the thicker hyphae and spores of eumycetoma. The color of the grains may further aid in classification, as most eumycetoma causative organisms produce black or pale grains, whereas actinomycetoma organisms produce yellow, white, or red grains.

Grain color	***Causative organisms***
Eumycetoma	
Black grains	*Madurella* spp.
	Leptosphaeria spp.
	Curvularia spp.
	Exophiala spp.
	Phaeoacremonium spp.
	Phialophora verrucosa
	Pyrenochaeta mackinnonii
	Pyrenochaeta romeroi
Pale, white, yellow grains	*Pseudallescheria boydii (Scedosporium apiospermum)*
	Acremonium spp.
	Aspergillus spp.
Actinomycetoma	
Pale, white, yellow grains	*Actinomadura madurae*, *Nocardia* spp.
Yellow to brown grains	*Streptomyces* spp.
Red to pink grains	*Actinomadura pelletierii*

Hematoxylin and eosin stain shows sinus tracts of neutrophilic granulomas, resembling stellate abscesses, surrounding foci of grains. At the periphery of the grain, accumulations of immunoglobulin appear as the Splendore–Hoeppli phenomenon. The accumulations are often club-shaped in eumycetomas and smooth in actinomycetomas. Special stains help in speciation, including Gram, periodic acid–Schiff (PAS), Gomorimethamine silver (GMS), and Ziehl–Neelsen (ZN). Fungi will stain positively with PAS and GMS, whereas actinomycetes stain positively with Gram stain. Ziehl–Neelsen staining may be used to discriminate actinomycetes species, which is positive if *Nocardia* species are present.

Culture of grains requires a minimum of 4 weeks and identification can be difficult because of the large range of colony types and resemblance to one another. Newer molecular-based techniques are being developed for more accurate classification, including species-specific PCR analyses.

After confirmation of the causative organism, treatment may be initiated. Actinomycetoma without osseous involvement usually responds well to long-term medical treatment. Several antibiotics have been shown to be effective, including cotrimoxazole, dapsone, amikacin, streptomycin, trimethoprim (TMP), rifampicin, and amoxicillin-clavulanic acid. Treatment of choice for *N. brasiliensis* is sulfamethoxazole-trimethoprim (SMX-TMP) 400/80 to 800/160 mg daily, with or without dapsone 100 to 200 mg daily, for a minimum of 6 months. Often, 2 to 3 years of medication is required. Infections with *A. pelletieri, A. madurae*, and *S. somaliensis* have been successfully treated with streptomycin in combination with SMX-TMP or dapsone. Eumycetomas usually do not respond as well to drug therapy, therefore, surgical excision with a long course of azole antifungals is first line management.

The criteria used to discontinue therapy is not clearly defined, but end points include reduction in volume of the swelling and masses, healing of fistulae, lack of grains on cytology of aspirated fluid, negative cultures, and radiological evidence of bone regeneration with disappearance of soft tissue mass. Recurrence is common due to non-compliance or resistance. For actinomycetomas, some experts recommend continuing treatment with dapsone 100 to 300 mg daily for several years after cure to prevent recurrence.

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Key location: lower extremities **CASE 10**

Presented by Barry Ladizinski MD MPH MBA and Warren Piette MD

History of Present Illness
A 52-year-old lady with a history of systemic lupus erythematosus (SLE) presented with a three-day history of urticarial-like plaques on the anterosuperior legs. Four months prior to presentation, she developed upper extremity bullous lesions consistent with bullous SLE, which resolved with initiation of dapsone 50 mg daily. At this visit, she reported minimally pruritic skin lesions localized to the thighs, and denied recurrent blisters or other skin eruptions. She denied new medications or sick contacts.

Past Medical History
Systemic lupus erythematosus, bullous systemic lupus erythematosus

Medications
Prednisone, azathioprine, hydroxychloroquine, dapsone

Social History
Noncontributory

Review of Systems
Negative for pyrexia, weight loss, oral ulcers, arthralgias

Physical Exam
Vital signs: afebrile, hemodynamically stable
Anterosuperior legs: symmetrical, circumscribed, confluent, arcuate, edematous, erythematous, urticarial-like plaques

Laboratory Data
The following labs were remarkable:

WBC	3.2	[4.4-10.6]
ANA	1:160, homogenous	[<1:160]
Ds-DNA Ab	>300 IU/mL	[0-4]
Smith AB	>8 AI	[0.0-0.9]
Ribonucleoprotein	>8 AI	[0.0-0.9]
SSA-Ab	>8 AI	[0.0-0.9]
SSB-Ab	0.3 AI	[0.0-0.9]
C3 complement	<50 mg/dL	[88-201]
C4 complement	9 mg/dL	[16-47]
ESR	87 mm/hr	[0-31]
CRP	2.94 mg/dL	[0.0-0.5]

Histopathology
Punch biopsy, left thigh: early vacuolar interface dermatitis with nuclear debris (leukocytoclasia) and neutrophils lining the dermoepidermal junction, around small blood vessels and scattered within the stroma. Colloidal iron stain shows stromal mucin deposition.

Diagnosis
Neutrophilic urticarial dermatosis

Treatment and Course

Her prednisone was increased to 30 mg daily with rapid resolution of lesions. At two-week follow-up, she had no recurrence of skin lesions and prednisone was tapered back to her baseline dose of 20 mg daily.

Discussion

Neutrophilic urticarial dermatosis (NUD) is a novel, but likely under-recognized, nonbullous neutrophilic skin eruption. Most patients with NUD have an associated systemic inflammatory disorder (e.g., SLE, adult Still disease, Schnitzler syndrome), or cryopyrin-associated periodic syndrome. The condition was initially described by Kieffer et al. in 2009, as an acute or chronic, asymptomatic to minimally pruritic eruption, clinically characterized by red macules, papules or plaques, typically appearing on the trunk or extremities, and resolving within one to two days.

NUD typically presents with associated pyrexia and arthralgias, often resulting in an incorrect diagnosis of acute SLE exacerbation. However, unlike SLE flares, NUD typically does not respond to increased immunosuppression, and is more effectively treated with neutrophil migration inhibitors, such as dapsone or colchicine. Still, most patients with NUD treated with dapsone or colchicine are also on systemic immunosuppressants, thus, the efficacy of these anti-neutrophilic agents as monotherapy for NUD is unknown. This was the case with our patient, who responded rapidly to an increase in prednisone, while maintaining her previous dapsone dosage of 50 mg daily. Additionally, NUD has been described without systemic involvement, as well as the presenting manifestation of SLE.

Skin biopsy is necessary to establish the diagnosis of NUD, with histopathology demonstrating a dense perivascular and interstitial neutrophilic infiltrate, focally extending into the epithelia of epidermis, hair follicles, and sebaceous and sweat glands, a finding recently termed neutrophilic epitheliotropism. Edema and vasculitis are not usually present, excluding urticaria and urticarial vasculitis, respectively. In addition to the classically associated SLE laboratory findings (e.g., ANA positivity, Smith and dsDNA antibodies), anti-Ro/SSA and anti-La/SSB antibodies have also been observed with NUD, although the significance of this is unclear.

Several types of neutrophilic dermatoses have been described in association with SLE, including acute febrile neutrophilic dermatosis (Sweet syndrome), amicrobial pustulosis of the folds, bullous SLE, pyoderma gangrenosum, and palisaded neutrophilic granulomatous dermatitis. Recently, NUD has been elucidated, and is reported to develop in up to five percent of SLE cases. The condition should be considered in SLE patients presenting with a minimally symptomatic, urticarial-like eruption that is not typical of a classic SLE exacerbation. The prognostic implications of NUD on SLE are currently unknown, and further studies are necessary to clarify the clinical significance of this dermatosis.

References

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