Chicago Dermatological Society

Monthly Educational Conference

Program Information
CME Certification
and
Case Presentations

Wednesday, December 5, 2018
Gleacher Center – Chicago, IL

Conference Host:
Section of Dermatology
University of Chicago Hospitals
Chicago, Illinois

Program

Host: University of Chicago
Wednesday, December 5, 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*
9:00 a.m. - 10:30 a.m.	**Clinical Rounds** Slide and Poster Viewing
9:00 a.m. - 10:00 a.m.	**Basic Science/Residents Lecture** "New Developments in Dermatomyositisy" *Victoria P. Werth, 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** • **Medical Student Mentoring Lunch** - Room 602 • **Plans & Policies Committee** - Room 620
12:45 p.m. - 1:00 p.m.	**CDS Business Meeting**
1:00 p.m. - 2:00 p.m.	**General Session** LORINCZ LECTURE - "Cutaneous Lupus Erythematosus: New Developments in Pathogenesis and Treatment" *Victoria P. Werth, MD*
2:00 p.m.	**Meeting adjourns**

Mark the Date!
Next CDS monthly meeting – Hosted by the Stroger/Cook County Hospital
Wednesday, April 3, 2019; Gleacher Center, Chicago

Illinois Dermatological Society Practice Management Workshop
Wednesday, January 30, 2019; Stephens Convention Center - Rosemont

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

Guest Speaker

VICTORIA P. WERTH, MD

Professor of Dermatology at the Hospital of the University of Pennsylvania and the Veteran's Administration Medical Center Philadelphia, PA

Dr. Victoria Werth is a Professor of Dermatology and Medicine at the University of Pennsylvania and Chief of Dermatology at the Philadelphia VA Hospital. She has a practice devoted to care of patients with autoimmune skin diseases. Recent studies have worked to develop a validated disease activity measure that can be used for systematic clinical studies in cutaneous lupus. This has been used in several ongoing or completed therapeutic trials. She is on the Medical Advisory Board of the Lupus Foundation of America and has been funded for her basic, translational and clinical studies related to lupus by the NIH, the Veterans Administration, the Lupus Foundation of America, the Lupus Research Institute and the Alliance for Lupus Research.

Dr. Werth earned her medical degree in 1980 at Johns Hopkins University, Baltimore, MD. Prior to that, she completed her undergraduate degree and an MS degree at Catholic University, Washington, DC. She completed a residency in Internal Medicine (1983) at Northwestern University, Chicago; and a dermatology residency (chief resident) at New York University in 1986. Dr. Werth also was an NYU research fellow from 1986-88, and a Dermatology Foundation Fellow from 1987-89.

CME Information

12.5.2018

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 1901 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 2018/19 series of meetings, the participant should be able to:

1. Discuss key factors in the diagnosis and treatment for various diseases and conditions of the skin, including use of new or emerging medication options.
2. Describe the surgical techniques for treatment of skin cancers and for cosmetic purposes.
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.

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.

The guest speaker, Victoria Werth, MD, has disclosed the following potential conflicts of interest: Grants/Research Support - Celgene, Janssen, Pfizer, Biogen, Corbus Pharmaceuticals, Genentech, Syntimmune, AstraZeneca; Consulting fees - Celgene, Medimmune, Resolve, Neovcs, ACI, Immune Pharmaceuticals, Genetech, Idera, Octapharma, BSL Behring, Janssen, Lilly, Pfizer, Biogen, BMS, Biostrategies, Gilead, Amgen, Medscape, Principia, Nektar, Syntimmune, Incyte, EMD Sorona. None of the planning committee members have any relevant 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.

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.

University of Chicago
Section of Dermatology

Dermatology Residents

Third Year
Stephanie Kazantsev, MD
Kathleen Kelley, MD
Larry Napolitano, MD

Second Year
Clifford Hsieh, MD
Emily Lund, MD
Jared Wishik, MD

First Year
Julia Dai, MD
Arjun Dayal, MD
Erin Dodd, MD
Esther Kim, MD

AT THE FOREFRONT
UChicago Medicine

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CASE 1

PRESENTERS
Stephanie Kazantsev MD; Vesna Petronic-Rosic MD MsC MBA; Sarah Stein MD

UNKNOWN

A 10-year-old girl with a complex past medical history was admitted with a urinary tract infection, new-onset ascites, and disseminated intravascular coagulation. Dermatology was consulted to evaluate new skin lesions on the hands and feet that developed within 2 days of admission.

PRESENTERS
Clifford Hsieh MD, Christopher Shea MD, Oluwakemi Onajin MD, Keyoumars Soltani MD, Diana Bolotin MD PhD

PATIENT A

HISTORY OF PRESENT ILLNESS
The patient is an 80-year-old African American female with history of stage IV non-small cell lung carcinoma, on treatment with pembrolizumab for the past fifteen months, presenting to Dermatology for a pruritic rash on the trunk and extremities. She was started on pembrolizumab in January 2017 and receives her pembrolizumab infusions every three weeks. She was previously seen by Dermatology in June 2017, approximately nine months before the current presentation, for a rash involving the same areas that started after her sixth pembrolizumab treatment in May 2017. This rash was treated as an eczematous dermatitis and resolved after treatment with topical clobetasol 0.05% ointment for three months. Nine months later, she presented for re-evaluation due to worsening rash and waning response to topical steroids. Patient reported that shortly after each pembrolizumab infusion, she would develop an itchy eruption on the trunk and extremities that would not completely resolve. She had been using topical clobetasol 0.05% and triamcinolone 0.01% ointment as needed without much improvement. No other medications were started in the past three months.

PAST MEDICAL HISTORY
Stage IV non-small cell lung carcinoma- diagnosed in October 2016 on pembrolizumab
Hypertension
Hyperlipidemia
Hypothyroidism
Dementia

MEDICATIONS
Aspirin 81 mg daily
Bromocriptine 2.5 mg BID
Camphor-menthol 0.5-0.5% lotion QID PRN
Clobetasol 0.05% ointment BID PRN
Levothyroxine 75 mcg daily
Memantine 10 mg daily
Nifedipine 60 mg daily
Pembrolizumab 200 mg infusion every 3 weeks
Simvastatin 20 mg daily
Trazodone 25 mg nightly
Triamcinolone 0.1% ointment BID PRN
Valsartan 160 mg BID

ALLERGIES
Penicillin

FAMILY HISTORY
Mother with history of lung cancer

SOCIAL HISTORY
The patient lives at home with her sons. She has a caretaker during the day who manages her medications. The patient smokes one pack of cigarettes a day and has a sixty-year smoking history.

PHYSICAL EXAM
Hypopigmented, lichenified, scaly plaques were noted on the right and left lower extremities. A violaceous, non-blanching, edematous papule was present on the right anterior shin, and a bulla was present on the right distal medial malleolus. There were numerous excoriated papules and erosions on the bilateral patella, shins, and elbows, as well as multiple hyperpigmented macules over the upper and lower extremities.

LABORATORY DATA
CBC and CMP prior to presentation were unremarkable.

HISTOPATHOLOGY
Two 4-mm punch biopsies were obtained from the right anterior shin and right forearm. Histopathology of an edematous papule on the right anterior shin showed a subepidermal blister containing a mixture of neutrophils and eosinophils with perivascular inflammation of eosinophils and neutrophils.

Direct immunofluorescence of a perilesional biopsy from the right forearm showed linear deposition of IgG, C3, fibrinogen, and minimal IgA at the epidermal basement membrane zone.

DIAGNOSIS
Bullous pemphigoid secondary to pembrolizumab

TREATMENT AND COURSE
After discussion with Oncology, the patient was started on prednisone 60 mg daily (1 mg/kg/day) with a two month taper. After two weeks of prednisone, the patient was started on doxycycline 100 mg BID and nicotinamide 500 mg TID, and has been on this regimen since with resolution of the rash and pruritus. The Oncology team continued the patient's pembrolizumab throughout the treatment, which she tolerated well. The patient's pembrolizumab infusions were eventually spaced out to every six weeks given stable disease, and she has been without recurrence of bullous pemphigoid or progression of her lung cancer.

PATIENT B

HISTORY OF PRESENT ILLNESS
The patient is a 94-year-old Caucasian male with history of metastatic melanoma, on treatment with pembrolizumab for the past three months, presenting to Dermatology with a three week history of a pruritic rash. He reported the initial development of itchy, red papules on the chest and upper extremities approximately fourteen days after completion of his fourth pembrolizumab infusion, with subsequent development of blisters on the abdomen and upper extremities four days later. The patient had been using triamcinolone 0.1% cream BID that was prescribed by his oncologist, with some relief of the itching but not resolution of his rash. No other medications were started in the past three months.

PAST MEDICAL HISTORY
Stage IV metastatic melanoma- invasive melanoma on the R anterior ankle diagnosed in 2015 s/p wide local excision with full thickness skin graft and negative sentinel lymph node biopsy. Metastatic melanoma to the skin and lymph nodes diagnosed in August 2017. Patient was started on pembrolizumab in October 2017.
Basal cell carcinoma
G6PD deficiency
Coronary artery disease s/p coronary artery bypass graft
Atrial fibrillation

MEDICATIONS
Alprazolam 0.25 mg TID
Amlodipine 2.5 mg daily
Atorvastatin 80 mg daily
Isosorbide mononitrate 30 mg BID
Pembrolizumab 200 mg infusion every 3 weeks
Warfarin 3 mg daily

ALLERGIES
Penicillin
Sulfa

FAMILY HISTORY
No significant family history

SOCIAL HISTORY
Non-smoker

PHYSICAL EXAM
Small monomorphic, pink and erythematous, non-scaly papules were noted diffusely on the chest, abdomen, back, bilateral arms and upper thighs. Large tense bullae, some filled with blood, present on the abdomen and upper arms interspersed with smaller, tense, clear fluid-filled vesicles.

LABORATORY DATA
CBC and CMP prior to presentation were unremarkable.

HISTOPATHOLOGY
Shave biopsy of a bulla on the right lower abdomen showed a subepidermal split containing eosinophils and areas of re-epithelialization of the epidermis at sites of the split.

Direct immunofluorescence of a perilesional 4-mm punch biopsy from the right lower abdomen showed linear deposition of IgG and C3 at the epidermal basement membrane zone.

DIAGNOSIS
Bullous pemphigoid secondary to pembrolizumab

TREATMENT AND COURSE
After discussion with Oncology, the patient was started on prednisone 80 mg daily (1 mg/kg/day) with a 3 week taper. He was also treated with triamcinolone 0.1% ointment BID as needed. Given the severity of his clinical presentation, Oncology decided to hold his pembrolizumab infusions. On the patient's last PET scan (two months after starting pembrolizumab), he was noted to have significant response to his pembrolizumab treatments with a decrease in uptake on the PET scan. The patient reported resolution of bullae and improvement of pruritus on systemic steroid treatment. A day after he finished the prednisone taper, he was admitted to the hospital for weakness and fatigue, and passed away a month later from sepsis.

PATIENT C

HISTORY OF PRESENT ILLNESS
The patient is an 84-year-old Caucasian male with history of mesothelioma on treatment with pembrolizumab for the past ten months, presenting to Dermatology with a pruritic rash on the trunk and

extremities. Two months prior to presentation, the patient developed a rash with erythematous itchy papules on the trunk and extremities that resolved with a two week course of prednisone 60 mg prescribed by his oncologist. In the past two weeks, the patient had developed a pruritic rash and blisters on the trunk, upper extremities, and lower extremities that became painful when ruptured. He had been developing new blisters daily over the two weeks prior to presentation. He had been using triamcinolone 0.1% ointment and prednisone 60 mg daily prescribed by his oncologist for the past ten days with minimal relief. No other medications were started in the past three months aside from the triamcinolone and prednisone.

PAST MEDICAL HISTORY
Mesothelioma- diagnosed in April 2015. Patient was started on pembrolizumab in October 2017.
Prostate cancer s/p prostatectomy
Hypothyroidism
Hypertension

MEDICATIONS
Aspirin 81 mg daily
Bisacodyl 5 mg daily
Esomeprazole 20 mg daily
Folic acid 1 mg daily
Ferrous sulfate 625 mg daily
Levothyroxine 25 mcg daily
Lisinopril 10 mg daily
Metoprolol 50 mg BID
Pembrolizumab 200 mg infusion every 3 weeks
Prednisone 60 mg daily for the past 10 days
Triamcinolone 0.1% ointment BID for the past 10 days

ALLERGIES
Iodine
Sulfa

FAMILY HISTORY
No significant family history

SOCIAL HISTORY
Non-smoker

PHYSICAL EXAM
Multiple erythematous, well-demarcated vesicles, bullae, and erosions were noted on the lower extremities, upper extremities, chest, and back.

LABORATORY DATA
CBC and CMP were unremarkable.

HISTOPATHOLOGY
Shave biopsy of a bulla on the left thigh showed a subepidermal split with dermal edema and a sparse inflammatory infiltrate, composed of neutrophils and eosinophils. Re-epithelialization was identified.

Direct immunofluorescence of a perilesional 4-mm punch biopsy from the left thigh showed linear deposition of IgG and C3 at the epidermal basement membrane zone.

DIAGNOSIS
Bullous pemphigoid secondary to pembrolizumab

TREATMENT AND COURSE
The patient was started on prednisone 100 mg, mycophenolate mofetil 1000 mg BID, and clobetasol 0.05% ointment BID. With the initiation of this regimen, he did not develop any new bullae, and the pruritus and pain resolved. Given the severity of his symptoms, Oncology decided to discontinue his pembrolizumab infusions. Prednisone was tapered to 20 mg daily over two months, with plans to continue to taper him off of prednisone after his next Dermatology follow up visit in four weeks. The patient's mesothelioma was responding well to pembrolizumab and is currently stable without progression of disease.

DISCUSSION
Immunotherapies using monoclonal antibodies, against programmed cell death protein-1 (PD-1), such as pembrolizumab, have shown efficacy and are increasingly used in the treatment of solid and hematologic malignancies.[1] Pembrolizumab is an antibody that binds to and blocks PD-1 on lymphocytes. Known as an immune checkpoint, the PD-1 pathway prevents the immune system from attacking its own tissues. Many malignant tumors overexpress programmed death ligand-1 (PD-L1), which binds to PD-1, activating the PD-1 pathway, allowing malignant cells to escape the immune system.[2] By using agents such as pembrolizumab to inhibit PD-1 on lymphocytes, T-cell suppression is reversed, and the antitumor effects of the immune system are potentiated. However, this activation of the immune system also leads to immune-related adverse events, such as cutaneous toxicities, arthritis, thyroiditis, pneumonitis, nephritis, colitis, and hepatitis.[2-4]

The most common anti-PD-1 immunotherapy-related adverse event is cutaneous toxicity, with a prevalence around 30-40%. Most commonly, pruritus, morbilliform eruptions, lichenoid dermatitis, eczema, and vitiligo are described.[3, 5-7] Patients are approximately two and a half times more likely to develop a rash after treatment with pembrolizumab than with standard chemotherapy.[2] Cutaneous adverse events can present with a delayed onset (median of 4.2 months after PD-1 inhibitor initiation) and even after discontinuation of the PD-1 inhibitors.[7] Increased use of PD-1 inhibitors in the treatment of various malignancies has recently led to more reports documenting development of bullous pemphigoid (BP) after the initiation of PD-1 inhibitors. There have also been documented cases of existing BP flaring with the initiation of pembrolizumab.[2]

The clinical presentation of immunotherapy-related BP is similar to classic bullous pemphigoid, which is the most common autoimmune subepidermal blistering disorder, most commonly seen in patients older than sixty years of age. Cutaneous manifestations are variable and include pruritus, urticarial eruptions, tense vesicles and bullae with a subepidermal split on histopathology. Non-specific cutaneous findings such as erythema, eczematous or papular lesions, and pruritus may be present for weeks to months during the non-bullous stage. In patients who progress to the bullous stage, tense bullae are observed most commonly on the lower trunk and flexural surfaces of the extremities. The skin manifestations are caused by a humoral and cellular response directed against BP antigen 180 and BP antigen 230, two components of hemidesmosomes, which are responsible for dermal-epidermal cohesion.[8]

The pathophysiology of immunotherapy-related BP is not clear, but is likely related to increased B-cell and T-cell activity due to immune stimulation caused by PD-1 inhibition.[3,5] It is also possible that PD-1 inhibitors act as a trigger in patients with underlying genetic susceptibility by immune response modification or alteration of antigenic properties of the epidermal basement membrane.[8] A review article examining documented cases of immunotherapy-related BP in the literature showed ten of twenty-one reported cases to be associated with pembrolizumab. Pruritus was a common feature in many cases,

and preceded or occurred simultaneously with the development of BP. Bullae typically developed within twenty-eight weeks (range of sixteen to eighty-four weeks) of initiation of PD-1 inhibitor treatments.[3]

Many of the reported cases of immunotherapy-related BP eventually required discontinuation of the immunotherapy. Intermittent development of new BP lesions has been seen even after one year of stopping the PD-1 inhibitor.[3] There are no established guidelines regarding treatment of immunotherapy-related BP. In most reported cases, immunotherapy-related BP has been successfully treated with treatments commonly used for classic BP, such as systemic steroids, and doxycycline and nicotinamide, when implemented quickly and aggressively.[1,3,5] There is a theoretical risk of oral steroids decreasing the efficacy of PD-1 inhibitors, however further studies are needed to investigate this hypothesis.[9,10] Other adjunctive therapies to supplement or to treat steroid-refractory classic BP cases include dapsone, azathioprine, mycophenolate mofetil, and methotrexate.[2,8]

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CASE 3

PRESENTERS
Erin Dodd MD; Diana Bolotin MD PhD; Dena Elkeeb MD

HISTORY OF PRESENT ILLNESS
A 63-year-old female with a 30-year history of Stage 3 hidradenitis suppurativa (HS) was admitted to the hospital with sepsis secondary to an infected chronic perineal wound. Dermatology was consulted to evaluate the wound. The patient's HS was managed at an outside facility. In 1987, the patient had multiple HS lesions excised in both the groin and axillae with subsequent quiescence of her disease for many years. Over the past 2 years her HS had flared, resulting in a large perineal ulcer. During this time, she was treated with adalimumab and doxycycline. She self-discontinued adalimumab after 5 months due to a perceived lack of clinical improvement. She underwent loop sigmoid colostomy for fecal diversion to facilitate perineal wound care five months prior to presentation. Since that time, she experienced increasing pain and foul-smelling discharge from the perineal wound with associated generalized weakness and an unintentional 50-pound weight loss. On admission, she was also found to have severe hypercalcemia with elevated parathyroid hormone-related peptide (PTHrP). Physical examination was limited by severe pain but revealed an extensive chronic perineal ulcer with a raised, verrucous, rock-hard border. The patient could not tolerate bedside biopsy due to severe, intractable pain. Therefore, dermatology recommendations included incisional biopsies in the operating room and imaging with CT of the chest, abdomen, and pelvis to evaluate for malignancy and metastasis.

PAST MEDICAL HISTORY
Hidradenitis suppurativa s/p excision – bilateral axilla and groin (1987)
Loop sigmoid colostomy for fecal diversion (6/2017)
Diabetes mellitus
Hypertension
Hypothyroidism

MEDICATIONS
Duloxetine
Levothyroxine
Fentanyl patch
Tramadol
Oxycodone
Gabapentin
Vancomycin
Meropenem
Dronabinol
Mirtazapine
Ketamine
Insulin aspart
Calcitonin

ALLERGIES
Penicillin

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
Married with 2 grown children, lives in Indiana. Former smoker.

PHYSICAL EXAM

The patient was chronically ill-appearing and in severe distress secondary to pain. She had limited ability to tolerate examination due to limited range of motion and guarding. Exam revealed a deep wound with friable ulcer bed extending from the perineum to the superior aspect of the gluteal cleft with a raised, rock-hard, verrucous plaque extending along the periphery.

DERMATOPATHOLOGY

Histopathology from incisional biopsies of the left buttock and wound edge demonstrated islands of atypical squamous cells with keratin pearls, mitotic figures and parakeratosis consistent with squamous cell carcinoma invading to the deep inked margin. Immunohistochemistry was negative for p16 expression with weak to moderate PD-L1 immunoreactivity in approximately 30% of lesional cells.

CT-guided aspiration of a presumed left pelvic abscess with cytology was performed. Pathology revealed keratinizing squamous cell carcinoma.

LABORATORY DATA

Relevant laboratory results on admission:

Laboratory Study	Patient's value	Reference range
Serum calcium	13.7 mg/dL (H)	8.4-10.2 mg/dL
Parathyroid hormone	12 pg/mL (L)	15-75 pg/mL
PTHrP	4.6 pmol/L (H)	<2.0 pmol/L
Hemoglobin	8.3 g/dL (L)	11.5-15.5 g/dL
Lactate	3.64 mmol/L (H)	0.56-2.10 mmol/L

In addition, blood cultures were positive for multiple coagulase-negative *Staphylococci* species susceptible only to vancomycin. Tissue culture from the ulcer edge grew >1,000,000 CFU/gram *Pseudomonas aeruginosa* susceptible to amikacin, meropenem and tobramycin.

IMAGING DATA

Magnetic Resonance Imaging (MRI) Pelvis/Bone – with and without contrast

Extensive hidradenitis with large perineal wound and inflammatory changes that extend along the posterior wall of the vagina and cervix and abut the lower margin of the remaining rectosigmoid colon. There are rounded foci of fluid signal intensity within the inflamed tissues to the right of the midline, which could represent small abscesses. Abnormal signal intensity in the remaining upper coccyx is compatible with osteomyelitis.

Computed Tomography (CT) Chest/Abdomen/Pelvis – with contrast

Large peritoneal wound/mass is stable to slightly enlarged compared to the prior MRI. Fluid attenuating mass in the left pelvis has reaccumulated and is slightly larger than on the CT before percutaneous drainage. Cortical irregularity of the sacrum likely represents osseous destruction by tumor involvement or osteomyelitis. A 9 mm nodule in the left upper lobe is present with moderate suspicion for metastatic disease.

Positron Emission Tomography/Computed Tomography (PET/CT) Whole Body

Large cutaneous posterior pelvic mass centered in the perineum and extending to the gluteal cleft consistent with known squamous cell carcinoma. Extensive bilateral hypermetabolic pelvic lymph node metastases. At least two hypermetabolic pulmonary nodules in the bilateral upper lobes, very suspicious for lung metastases.

DIAGNOSIS
Marjolin ulcer arising in a chronic hidradenitis suppurativa wound

TREATMENT AND COURSE
Surgical resection was deemed inappropriate given extensive involvement of the tumor and evidence of distant metastases on imaging studies. Enrollment in an immunotherapy clinical trial was considered but deferred due to ongoing systemic infection and osteomyelitis.

The patient was discharged to a long-term care facility on a six-week course of IV meropenem. Palliative radiotherapy was planned, but patient was lost to follow up. She ultimately died less than 10 months after diagnosis.

DISCUSSION
Hidradenitis suppurativa (HS) is a chronic, inflammatory skin disorder affecting the apocrine gland-bearing areas of the axillae, breasts, groin and buttocks. It is characterized by recurrent painful nodules, cysts and abscesses that suppurate and lead to ulceration, sinus tract formation, and progressive scarring.[1,2] The disease burden of HS includes intense pain, disfigurement, disability, and overall poor quality of life.[3] However, chronic inflammation in affected areas also predisposes to development of cutaneous squamous cell carcinoma (cSCC).[1,4]

Marjolin ulcer refers to a malignancy arising within a chronic wound or scar. While Marjolin ulcer was originally described in burns, it has been reported to arise in a variety of chronic inflammatory conditions including HS wounds.[4,5] cSCC is the most common histological type of cancer arising in this setting.[2,4,6] Malignant transformation of HS to cSCC is rare with approximately 80 cases reported in the literature to date.[6,7] The average duration of symptomatic HS preceding a diagnosis of cSCC is approximately 25 years.[4,6] These tumors are most commonly well-differentiated on histopathology;[2,6] however, they tend to be uncharacteristically aggressive with high morbidity and mortality rates exceeding 40%.[2,6,8,9]

Although HS involves multiple intertriginous sites, malignant degeneration occurs almost exclusively in the anogenital region.[4,6] While HS is more common in women, malignant transformation is more commonly observed in men.[1,2] This is thought to be related to increased prevalence of extra-axillary disease in men.[1,6] Lack of reports of malignant degeneration of axillary HS has led to the hypothesis that a regional cofactor, such as human papillomavirus, may be implicated in transformation.[2,6] Others postulate that chronic subclinical lymphedema in HS renders these regions immunologically vulnerable to malignancy, akin to the pathogenesis of angiosarcoma in Stewart-Treves syndrome.[10]

Assessing for malignancy in long-standing HS represents a significant clinical challenge, and diagnosis is often delayed. Physicians' low index of suspicion is frequently cited as a common reason for delayed diagnosis.[5,11] Differentiation of new HS lesions from malignant degeneration of a chronic wound, especially in the background of severe scarring, ulceration and deformity in severe long-standing HS is difficult.[4,6] In addition, malignant transformation has been reported to occur, and spread along subcutaneous sinus tracts which may go undetected with superficial biopsies.[2,6]

Once the diagnosis of cSCC is made, imaging via MRI or PET can help elucidate the true extent of disease and evaluate for metastases.[6] Aggressive surgical intervention is essential to prevent significant morbidity and mortality.[4,6,9] Wide surgical excision with a margin of at least 2 centimeters is recommended whenever feasible.[2,5] Sentinel lymph node biopsy is also recommended given the high prevalence of lymph node metastasis.[2,6] While there is no widely accepted standard of care for unresectable disease, conventional treatment has included chemotherapy and palliative radiation. Over the past few years, clinical trials have demonstrated a promising role for immunotherapy with checkpoint

inhibitors, and the PD-1 inhibitor cemiplimab recently became the first FDA-approved treatment of advanced cSCC.[12,13]

Dermatologists should be aware of the rare yet devastating complication of Marjolin ulcer arising in chronic HS wounds. The highly aggressive nature of this condition and its propensity for metastasis and recurrence indicate the need for early diagnosis and treatment. Currently no guidelines exist recommending increased surveillance for malignancy in HS. Thus, threshold to biopsy any suspicious non-healing HS lesions must be low, and multiple deep or incisional biopsies may be necessary to establish the diagnosis. All excised tissue obtained during HS debridement surgeries should be sent to pathology for evaluation, and wide local excision may be considered for longstanding or non-healing HS wounds to reduce the risk of Marjolin ulcer in this population.

This case emphasizes the importance of close follow-up, early histological diagnosis, and aggressive management of HS, particularly in patients with extra-axillary disease.

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CASE 4

PRESENTERS

Kathleen Kelley MD; Christopher Shea MD; Diana Bolotin MD PhD

UNKNOWN

A 20-year-old male presented with sore throat, fevers, and a diffuse cutaneous eruption of 2 weeks' duration.

CASE 5

PRESENTERS
Emily Lund MD; Sarah Stein MD

HISTORY OF PRESENT ILLNESS
A female infant with a prenatal diagnosis of trichothiodystrophy was born at 34 weeks by induced vaginal delivery performed for preeclampsia. Apgar scores at 1 and 5 minutes were 8 and 9, respectively. Birth weight was 1660 g (12^{th} percentile), length was 42 cm (23^{th} percentile), and head circumference was 28.5 cm (7.5^{th} percentile). The infant was encased in a collodion membrane. Dermatology was consulted for management of the collodion membrane.

PAST MEDICAL HISTORY
Prenatal amniocentesis had revealed two pathogenic mutations in the *ERCC2* gene. The mother is a carrier of mutation c.2164C>T (pArg722Trp), and the father is a carrier of mutation c.1480-1G>C. The prenatal diagnosis of trichothiodystrophy was confirmed at a relatively late stage of gestation, and the family opted to continue the pregnancy. In addition to preeclampsia, the pregnancy was complicated by gestational diabetes, gestational hypertension, and intrauterine growth restriction.

MEDICATIONS
Ampicillin 100mg/kg q12h
Gentamicin 4mg/kg q36h
Lacrilube q2h to eyes

ALLERGIES
No known drug allergies

FAMILY HISTORY
Brother with trichothiodystrophy associated with multi-system deficits (presented at CDS in 2014), who passed away at the age of 2 years due to respiratory failure in the setting of respiratory syncitial virus (RSV) infection complicated by pneumonia
Healthy older sister
No other family history of inherited skin conditions or ichthyosis

SOCIAL HISTORY
Parents are nonconsanguineous

PHYSICAL EXAM
The entire baby was encased in a tight, cellophane-like membrane with focal areas of desquamation on the palms and soles. There was bilateral moderate ectropion with absent eyelashes and scant eyebrows. Lips were prominent and moist, held in an "O," but not everted. Scalp hair was matted and short. Finger and toenails were normal. After shedding of the collodion membrane in the second week of life, the skin was generally soft and smooth, the scalp hair continued to demonstrate a matted twisted texture, and the eyebrows and eyelashes were scant.

HAIR MOUNT
Microscopy of hair clipped from the scalp at 2 weeks of age demonstrated light and dark banding under polarized light.

DIAGNOSIS
Trichothiodystrophy, *ERCC2* mutation

TREATMENT AND COURSE

During the first week of life, the infant was maintained in a humidified incubator with humidity settings of 40-60 percent. Petrolatum was applied 2-3 times daily. By the second week of life, parental skin-to-skin bonding was encouraged with short periods outside of the humidified incubator. Physical therapists provided caregivers instruction on passive movement exercises to perform throughout the day to prevent pseudocontractures. The collodion membrane shed over the first two weeks of life revealing soft, smooth skin and the infant was weaned out of the humidified environment. The infant transitioned to full nasogastric feeds over the first week of life, and then over the subsequent three weeks, she transitioned to oral feeds. At the time of discharge at 1 month of age, the infant was successfully maintaining oral feeds and demonstrating consistent weight gain.

The patient was seen in dermatology clinic for follow-up at 2 months of age. Her scalp hair was brittle and fine, but normal in density. Eyelashes and eyebrows were sparse. She had developed fine, peeling scale diffusely over her trunk and extremities, with focal areas of thicker, more plate-like ichthyotic scale on the scalp, lower back, and inguinal folds. Fluocinolone 0.01% oil was added to assist in removal of scaly buildup from the scalp. Continued frequent daily applications of Cerave moisturizing cream were maintained. The patient was referred to otolaryngology for removal of desquamating skin from her external ear canals.

By five months of age, the patient had developed nystagmus and significant reflux with feedings. Complete blood count was notable for neutropenia, for which the patient is being followed closely by hematology. Early Intervention services are being accessed for emerging evidence of developmental delay. Prophylactic vaccinations against influenza and RSV are planned.

The family has been referred to the National Institutes of Health (NIH) working group studying defective DNA repair disorders including trichothiodystrophy.

DISCUSSION

Vera Price and her colleagues first used the term “trichothiodystrophy” in 1980 to describe a heterogeneous group of neuroectodermal disorders with the unifying feature of sulfur-deficient hair, first described by Pollitt et al. a decade earlier (1,2). This multi-system disorder referred to under the umbrella term trichothiodystrophy (TTD) is rare, with an estimated worldwide incidence of 1 in one million births, with numerous and varied clinical presentations (3). It results from recessive mutations in genes *ERCC2 (XPD), ERCC3 (XPB)*, or *GTF2H5 (TTDA),* which encode subunits of transcription factor IIH (TFIIH). In addition to its roles in RNA transcription and cell cycle control, this large protein complex participates in nucleotide excision repair, the pathway by which photo-induced DNA damage is recognized and corrected (3,4). The *ERCC2* and *ERCC3* genes are also implicated in xeroderma pigmentosa (XP). It is hypothesized that the XP mutations impact the nucleotide excision repair pathway more profoundly than the trichothiodystrophy mutations, ultimately resulting in increased carcinogenesis. As a result, while photosensitivity is characteristic of both disorders, the increased skin cancer incidence seen in XP has not been reported in TTD (4). Of note, there are reports of trichothiodystrophy cases without photosensitivity caused by mutations in *C7ORF11 (TTDN1)*, which may play a role in regulating cell division. These patients usually do not have ichthyosis (4).

Individuals with TTD have heterogeneous clinical presentations, with varied expression of cutaneous, neurologic, developmental, and immune abnormalities. Acronyms like PIBIDS, IBIDS, and BIDS are traditionally used to describe the clinical features seen in TTD, including *P*hotosensitivity, *I*chthyosis, *B*rittle hair, *I*ntellectual impairment, *D*ecreased fertility, and *S*hort stature. A systematic review of 112 cases of TTD published by Faghri et al. in 2008 emphasizes that these may be inadequate and inaccurate descriptions of the TTD phenotype. They found that thirty-six percent of patients did not fit into one of these three categories, and almost all of those who did had additional features not described by the

acronyms. In addition, major clinical features like abnormal characteristics at birth, ocular abnormalities, and immune abnormalities, which were found to be more prevalent than photosensitivity and decreased fertility, are not captured by these acronyms (5).

The ubiquitous finding in TTD, and its diagnostic signature, is brittle, sulfur-deficient hair. Under light microscopy, multiple hair abnormalities may be seen, including trichorrhexis nodosa, trichoschisis, and pili torti, but the finding of alternating light and dark bands seen under polarizing light, termed "tiger tail banding," is most suggestive of this condition (4).

The multisystem abnormalities characteristic of this disease warrant multidisciplinary care. Specifically, due to their immunodeficiency and susceptibility to viral illnesses, pediatricians should ensure that children with TTD receive their vaccinations on schedule, and that they receive Synagis, the RSV vaccine, as well as the flu vaccine. Consultation with Hematology may be indicated if neutropenia or thalassemia are present, and with Neurology if seizures occur. Regular ophthalmology exams to monitor for cataracts are indicated, as well as regular dental exams, as these children often have poor dentition. Gastroenterology and Nutrition are important to help manage feeding difficulties and poor growth. Finally, developmental therapies are critical to help address the expected developmental delays (5,6).

In this case, the patient has compound heterozygous mutations in the *ERCC2* gene. The maternal mutation has been previously reported and described, but to our knowledge, the paternal mutation is novel (7-15). There have been twelve reported cases of TTD resulting from the maternal mutation, three homozygotes and nine compound heterozygotes. Based on these case reports, the individuals with this mutation seem to have a more severe phenotype, with all reporting neurologic abnormalities and ichthyosis, and most reporting frequent infections and photosensitivity. Four cases passed away before the age of 4, as did our patient's brother (15).

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CASE 6

PRESENTERS
Esther Kim MD, Christopher R. Shea MD

HISTORY OF PRESENT ILLNESS
A 26-year-old Caucasian man was admitted with complaints of nausea and headaches. Dermatology was consulted for evaluation of an erythematous rash involving the eyelids, cheeks, back, shoulders, and chest. It was not painful or pruritic. Review of systems was positive for myalgias of the legs and back, intermittent headaches, and nausea. The patient denied fevers, sun sensitivity, or new medications.

PAST MEDICAL HISTORY
Anxiety
Appendectomy

MEDICATIONS
None

ALLERGIES
Iodine

FAMILY HISTORY
No family history of autoimmune disorders

SOCIAL HISTORY
No recent travel
No new workplace exposures
Graduate student

REVIEW OF SYSTEMS
Positive for myalgias, headaches, nausea

PHYSICAL EXAM
Multiple coalescing erythematous to violaceous macules and patches on the eyelids and periorbital regions, cheeks, upper chest, bilateral shoulders, upper back, and posterior neck. There was mild periorbital edema.

DERMATOPATHOLOGY
Hematoxylin and eosin stained sections of a characteristic lesion from the right shoulder exhibited a vacuolar interface dermatitis at the dermal-epidermal junction, and a sparse superficial lymphocytic infiltrate. A colloidal iron stain demonstrated increased dermal mucin.

LABORATORY DATA
Abnormal
CK: 673 (9-185 U/L)

Negative or within normal limits:
CBC with differential, CMP, Aldolase, RF, SSA, SSB, and ANA
Immunoglobulin subclasses
Complete myomarker panel (including Anti-Jo-1 Ab, PL-7, PL-12, EJ, OJ, SRP, MI-2, TIF Gamma, MDA-5, NXP-2, Anti-PM/SCI Ab, Fibrillarin, U2 SNRNP, Anti-U1-RNP Ab, KU)
EEG

IMAGING AND OTHER STUDIES

Computed Tomography (CT) Head – without contrast
Cystic mass in the right insula

Stereotactic serial biopsy
Oligodendroglioma

DIAGNOSIS

Dermatomyositis in the setting of an oligodendroglioma

TREATMENT AND COURSE

The patient was given a one time dose of oral prednisone 60 mg. Topical therapy was initiated with triamcinolone 0.1% ointment and hydrocortisone 2.5% ointment. Within 10 days of initial presentation, the patient reported complete resolution of the rash. He underwent a craniotomy for tumor resection several weeks after initial presentation. At follow-up four months later, he reported no recurrence of the rash or myalgias.

DISCUSSION

Dermatomyositis (DM) is a multifactorial inflammatory myopathy characterized by cutaneous eruptions and systemic involvement. In adults with DM, an association with internal malignancies is now well-established, with a reported incidence ranging from 15-25% [1-2]. The temporal relationship varies, with cancer being diagnosed before, concurrently, or after the diagnosis of dermatomyositis is made.

DM has been reported with a variety of malignancies including carcinomas of the ovary, colon/rectum, breast, lung, stomach, and pancreas, as well as with lymphomas (including Hodgkin and non-Hodgkin) [1, 3-4]. In Western societies, the malignancies most frequently associated with DM are ovarian, lung, and colorectal cancers [5-6]. The risk of cancer is highest in patients over the age of 60 and in the first year after the diagnosis of DM. The risk remains elevated but progressively decreases to baseline at 5 years after the diagnosis [6-7]. Given the increased risk of malignancy in this patient population, cancer screening is recommended at the time of diagnosis and then annually for at least five years [1, 6-7]. Minimum recommendations for adult patients with DM include history and physical examination (including the rectum, pelvis, and breast), complete blood count, complete metabolic panel, urinalysis, stool hematest, and chest x-ray [7].

While patients with DM are at increased risk of internal malignancy, only recently have steps been made to stratify their overall malignancy risk. Refinements in assays for DM-associated autoantibodies have broadened the range of diagnostic tests available that may help identify patients likely to harbor internal malignancies [1, 8-9]. Transcription intermediary factor-1γ (TIF-1γ) antibody and nuclear matrix protein-2 (NXP-2) antibody have been associated with an increased risk for malignancy in DM patients over the age of 45 [9]. However, in one study of 213 patients with DM, only 55% of the patients tested positive to antibodies against TIF-1γ or NXP-2. A similar association has not yet been reported in children or young adult patients [9].

The mainstay of treatment centers on the use of systemic corticosteroids and strict sun protection. Topical treatments such as corticosteroids and calcineurin inhibitors are also effective in controlling the cutaneous manifestations as was demonstrated in our patient. Other immunosuppressive medications such as oral anti-malarial agents, dapsone, or methotrexate may be used. In paraneoplastic dermatomyositis, the treatment of the underlying malignancy may result in the disappearance of DM-related symptoms [10-12]. Additionally, cutaneous and muscle findings can recur when patients relapse to cancer, providing further

support that DM represents an autoimmune paraneoplastic process related to oncogenesis [6].

Dermatomyositis in the setting of intracranial neoplasms is rare. Two previous studies have reported paraneoplastic DM in association with intracranial masses – in a patient after completion of dendritic cell immunotherapy for an oligoastrocytoma and in a juvenile patient with a choroid plexus papilloma and cystic liver changes [13-14]. To our knowledge, this is the first report of dermatomyositis in the setting of an oligodendroglioma. It is imperative for clinicians to recognize the association of DM as a possible harbinger of malignancy.

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CASE 7

PRESENTERS
Julia Dai MD; Oluwakemi Onajin MD; Liborka Kos MD; Adena Rosenblatt MD PhD

UNKNOWN

A 16-year-old boy presented with painful ulcerations on the face, trunk and extremities.

CASE 8

PRESENTERS
Arjun Dayal MD; Jared Wishik MD; Adena Rosenblatt MD PhD

HISTORY OF PRESENT ILLNESS
A 17-year-old Chinese female with history of alopecia areata presented to the dermatology clinic for evaluation and management. Her hair loss began in March 2016, at which time she was seen by a physician in China who diagnosed her with alopecia areata. She was initially treated with intralesional Kenalog injections to the scalp and intramuscular betamethasone injections with some improvement, but she continued to develop new lesions. Her hair loss waxed and waned over the next few months despite additional intralesional, intramuscular, and oral steroids. The patient additionally noted patchy hair loss from her arms and legs. She also tried a Chinese herbal medication without improvement.

PAST MEDICAL HISTORY
Otherwise healthy

MEDICATIONS
None

ALLERGIES
No known drug allergies

FAMILY HISTORY
No family history of skin or autoimmune disease

SOCIAL HISTORY
Lives in China

PHYSICAL EXAM
Patchy, non-scarring alopecic patches throughout her scalp with few very short, black hairs. Scattered alopecic patches on the bilateral arms and legs.

LABORATORY DATA
Normal thyroid function, ferritin, LH, and FSH levels.
No vitamin deficiencies were noted.

DIAGNOSIS
Alopecia areata

TREATMENT AND COURSE
The patient was prescribed topical 2% tofacitinib cream twice daily for the scalp. She started noticing hair growth after one month of application and eventually experienced complete and durable hair regrowth. In August 2018, she was switched to topical 2% tofacitinib solution, as her hair was now too dense for the cream formulation and decreased the frequency to once daily.

DISCUSSION
Alopecia areata (AA) is an autoimmune mediated condition. Clinically, it presents as round to oval, smooth patches of non-scarring hair loss. Short, tapered hairs with a narrow proximal shaft, also known as “exclamation point hairs,” are frequently seen at the periphery of the patches. Other variants of this disease include alopecia totalis (complete loss of scalp hair), alopecia universalis (complete loss of all body hair), and an ophiasis variant (band-like alopecia along the periphery of the temporal and occipital

scalp) [1]. Nail pitting may be present as well [2].

The prevalence of AA in the United states is 0.1-0.2%, and the average lifetime risk of developing AA is estimated at 1.7%. Twin studies demonstrate a 55% concordance, suggesting an interplay of environmental triggers and genetics. Specifically, it is thought that T-lymphocyte interaction with follicular autoantigens is central to the pathophysiology of this disease [1]. In unaffected persons, the hair follicle is an immune priveleged site, possibly related to low levels of major histocompatibility complex (MHC) expression. In AA, the hair follicle is attacked by CD8+ T-lymphocytes [2].

Many investigations support this autoimmune hypothesis, including a study by Tobin et al. which demonstrated that autoantibody levels against several known hair follicle antigens were present in significantly higher quantities in patients with AA as compared to study controls [3].

AA has a chronic, relapsing, and unpredictable course. Limited, patchy AA may be treated with topical corticosteroids, intralesional triamcinalone acetonide injections, topical minoxidil, and a variety of other topical medications. However, these treatments are not always effective, particularly in patients with more extensive alopecia totalis or universalis [1]. Many patients with the extensive variants will respond to high dose intramuscular or oral corticosteroids, but many require maintanence therapy which increases the risk of developing side effects such as osteonecrosis, weight gain, hypertension, and immunosuppression [4], [5]. Steroid sparing agents such as methotrexate and azathioprine have been unreliable in extensive AA. Other treatment options include topical immunotherapy with squaric acid dibutyl ester or diphencyprone, which induce a contact dermatitis and aim to redirect the immune response [1], [5].

Recently, case reports and small open label studies have demonstrated that oral tofacitinib can be a promising therapeutic option for patients with extensive AA [6]–[8]. Tofacitinib is a small molecule that is thought to act as a Janus kinase (JAK) inhibitor. JAK enzymes play an important role in the JAK/STAT pathway, which is responsible for signal transduction of cytokines, interleukins, interferons, and other molecules from the cell surface to the nucleus, where they activate downstream gene expression. Specifically, it is thought that IFN-γ and IL-15 are implicated in AA, further explaining the putative therapeutic mechanism of tofacitinib [5]. Side effects of oral tofacitinib include infections, thrombocytopenia, hypercholesterolemia, and neutropenia, as well as a theoretical increased risk of malignancies given the decrease in immune surveillance that accompanies immunosupression [5], [9].

Topical application of tofacitinib aims to increase local concentrations of the drug at the hair follicle, while avoiding systemic side effects. However, the evidence for its efficacy is quite limited. A small, double-blinded, placebo-controlled study of patients with AA universalis showed that 6 out of 16 patients experienced partial regrowth of hair with 2% tofacitinib ointment applied twice daily, as compared to 10 out of 16 patients that applied 0.005% clobetasol dipropionate ointment twice daily [10]. An open label trial of 10 patients with AA showed significant scalp regrowth in one patient and partial regrowth in two patients [11].

Perhaps for a certain subset of patients with extensive AA, such as our patient, topical tofacitinib can be a safe and promising treatment modality. There are at least four clinical trials underway that further investigate the efficacy of topical JAK inhibitors for alopecia areata [5].

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CASE 9

PRESENTERS
Larry Napolitano MD; Christopher Shea MD; Keyoumars Soltani MD

UNKNOWN

An 84-year-old male presented with a pruritic patch on the left back of 8 months' duration.

CASE 10

PRESENTERS
Jared Wishik MD; Oluwakemi Onajin MD; Christopher Shea MD; Keyoumars Soltani, MD

HISTORY OF PRESENT ILLNESS
A 20-year-old female transitioning from male presented to the University of Chicago Emergency Department for facial and hip swelling. Roughly 5 days before presentation, our patient was in her usual state of health when she began developing painful swelling of both cheeks. Later that same day, she noticed similar changes on both hips. The pain then became intolerable to the point where she presented to an outside emergency department. She was given a 3-day course of oral prednisone with no improvement, prompting presentation to our hospital. Dermatology was consulted to assist with diagnosis and management.

She denied any new medications including supplements. She denied any associated swelling of her lips or tongue, abdominal pain, or difficulty breathing. She denied any other symptoms and otherwise felt well. Upon further questioning, she admitted to self-administering fish oil injections to these specific sites 2 months prior. She stated that she had found videos on YouTube depicting how to accentuate feminine features by aspirating fish oil from over the counter capsules into syringes and then injecting them as a sort of "filler." She reassured us that she had used the sterile equipment she was given for her gender transition hormonal therapy. After her initial injections, she was quite pleased with her results and had not experienced any adverse effects until this episode.

PAST MEDICAL HISTORY
Human immunodeficiency virus (HIV) infection, with undetectable viral load on highly active anti-retroviral therapy (HAART)

FAMILY HISTORY
No family history of autoimmune conditions or recurrent infections

SOCIAL HISTORY
Denies any recreational drug use.
Currently undergoing hormonal therapy for gender transition.

MEDICATIONS
Genvoya (HAART)
- Combination of Vitekta (elvitegravir), tenofovir alafenamide, Emtriva (emtricitabine), and Tybost (cobicistat)

Hormone replacement for gender transition
- Patient unaware of specifics other than that she was injecting this medication

ALLERGIES
No known drug allergies

PHYSICAL EXAMINATION
Both cheeks had indurated, erythematous, nodular plaques with significant underlying edema. There was minimal breakdown of skin in edematous areas, and scattered collarettes of scale. Both hips had similar, firm, indurated, ill-defined, tender nodular plaques covering the majority of lateral hips, without overlying epidermal changes. She had no oropharyngeal edema. She had no obvious ocular lesions, but the periorbital edema limited her ability to open her eyes.

LABORATORY RESULTS

Laboratory Study	Patient Result	Reference Range
White blood cell count	18.7 x 10^3 /µL	3.5 - 11.0 10^3 /µL
CD4 count	559 /µL	515 - 1642 /µL
HIV RNA (viral load)	Undetectable	Undetectable

Comprehensive metabolic panel and the rest of her complete blood count were within normal limits.
Blood cultures were negative x 3.
Tissues cultures grew only rare *Staphylococcus hominis*, and were negative for fungi and acid-fast bacilli.

IMAGING

Computed Tomography (CT) Maxillofacial
Diffuse soft tissue swelling with subcutaneous fat stranding of the bilateral face, without any evidence of fluid collection or abscess.

Computed Tomography (CT) Pelvis
Extensive fat stranding and edema in subcutaneous tissues, and some nodularity that could represent fat necrosis, without evidence of fluid collection or abscess.

3-view x-rays of bilateral hips
Unremarkable, without evidence of osteomyelitis.

DERMATOPATHOLOGY
Histopathologic analysis of punch biopsy specimens from the right cheek and right hip both showed a predominantly lobular neutrophilic panniculitis with suppurative and granulomatous inflammation involving the deep dermis and subcutis. There was no evidence of vasculitis. PAS, Fite, and Gram stains were negative for infectious organisms.

DIAGNOSIS
Lobular neutrophilic panniculitis secondary to self-administered fish oil injections

TREATMENT & COURSE
Her hospital course was complicated by a one-time fever of 101.3 ºF on Day 1 of hospitalization, but she was otherwise afebrile. The infectious disease service was consulted given her HIV history and concern for infection. She was started on vancomycin and ceftriaxone for empiric coverage. Before results of punch biopsies were received, the primary team was concerned that her exam had worsened. Plastic surgery was consulted for incision and drainage of her bilateral malar eminences and reported expression of whitish, granular, caseous material. The patient's swelling of the face and hips began improving by day 3 of antibiotic therapy. Her white blood cell count normalized at that time as well. She remained clinically stable without the development of any additional symptoms throughout her hospitalization and continued to improve. She was subsequently discharged on a 14-day course of cephalexin 500 mg q6h and 1 Bactrim DS tab BID.

At her follow-up appointment with dermatology 2 months after discharge, she reported complete resolution of her symptoms shortly after her finishing the course of oral antibiotics. She agreed to avoid any self-administered treatments not directly approved by her physicians moving forward.

DISCUSSION

Lobular neutrophilic panniculitis can be seen in a number of settings including infection, subcutaneous Sweet syndrome, pancreatitis, connective tissue disorders such as rheumatoid arthritis, alpha-1-antitrypsin deficiency, and injection of foreign material, as in our patient. Classically, these panniculitides present as a subcutaneous swelling with overlying erythema, or as fluctuant, ulcerating nodules in various locations and at different stages, depending on etiology.[1] While a number of oils have been implicated in factitial panniculitis, such as mineral oil (paraffin), camphor, cottonseed, sesame oils, as well as liquid silicone,[2] fish oil causing this reaction pattern has rarely been described in the literature. Of note, paraffin injections were used from ~1899-1914 for breast augmentation, often with appalling complications.[1] This practice has since been discontinued. However, as is the case with medical-grade silicone, certain contaminants are at times purposely added to enhance fibrosis and prevent migration, a desirable effect for cosmesis.[1] Most adverse reactions to these materials result in a delayed granulomatous reaction. A review of the relevant literature discloses only 2 reported cases of patients experiencing fat necrosis after self-administered fish oil injections.

In a 2013 case, a 37-year-old female presented with a 1-week history of swelling, pain, and erythema in both breasts.[3] She had injected the contents of oral fish oil capsules into the four quadrants of both breasts, an act which she had done previously on two other occasions. She was noted to have an elevated WBC count and was afebrile. Imaging did not show any discrete fluid collections. She was started on empiric ampicillin. A sample was aspirated from the most indurated region and the purulent-hemorrhagic material was sent for microbiologic and cytologic examination. Gram staining showed abundant leukocytes and cocci, and cultures grew *Staphylococcus chromogenes*. Cytologic examination revealed erythrocytes, fibrin webs, neutrophils, and histiocytes. Her mastitis continued to worsen, and she was taken to the operating room for debridement. Pathologic analysis revealed a foreign body granulomatous inflammation and fat necrosis. She eventually required a bilateral mastectomy and breast reconstruction.[3]

The other reported case was discussed in 2017 when a 33-year-old woman with a history of type-1 diabetes presented to the emergency room with pain in her bilateral buttocks and hips.[4] She had been using her insulin syringes to inject 100 units of material from fish oil soft-gel capsules into these areas daily for the previous month. She was also noted to have leukocytosis and a mild fever. The patient was subsequently admitted and treated with intravenous (IV) cefazolin and vancomycin. A skin biopsy showed a sclerotic dermis with thick collagen bundles and a perivascular and periadnexal lymphohistiocytic infiltrate along with fat necrosis. Tissue and blood cultures were negative, and no organisms were observed with the Gomori methenamine-silver nitrate (GMS), Fite, or Gram stains. She was discharged with a 10-day course of home IV vancomycin, and her symptoms resolved at a 2-month follow-up.[4]

One proposed mechanism for this presentation is a delayed-type hypersensitivity reaction as in Texier disease, a response to subcutaneous vitamin K1 injection.[4] The sclerodermoid histology of the second case was similar to that found in Texier disease, but this constellation was not seen in our patient. It is also possible that these patients were reacting to another material found within the fish oil supplements, for a number of additive ingredients are listed in these products, such as gelatin, glycerin, water, mixed natural tocopherols, and sunflower oil.[4]

Although no pathogenic organism was identified in our case, bacteria should also still be considered as possible culprits in this phenomenon. The development of a biofilm has been well described in the literature as an adverse effect of fillers. In these cases, bacteria are difficult to culture and detect. Many delayed reactions to hyaluronic acid fillers that were once attributed to allergies are now thought to be secondary to activation of these biofilms.[5] Biofilms are thought to live in a passive state until activation by a variety of factors such as decreased immunity, dental infections, or hemolytic contamination.[5] Our patient denied any recent illnesses, but her immune system is compromised at baseline given her HIV

infection, so this could certainly be a contributing factor. Our patient's tissue culture did grow *Staphyloccocus hominis*, an organism usually considered to be a contaminant from normal skin flora; however, *S. hominis* has been proven to have the ability to form biofilms in human specimens.[6] Both our patient and the 2017 case report showed rapid improvement with empiric antibiotic treatment, without isolation of a pathogenic organism, which could point to an etiology such as activation of a latent biofilm.

Given the rarity of this entity, no formal guidelines for treatment have been established. As demonstrated in these cases, early antibiotic intervention may prevent significant morbidity. In the case of the patient who required a mastectomy, we believe that source control was necessary as her course was complicated by infection with a pathogenic organism unlike the other cases.

In today's world, dominated by social media, patients have access to seemingly unlimited sources for medical advice and alternative options. A quick Google search reveals numerous blogs and videos of individuals using injectable oils in a variety of potentially harmful ways. Providers should be aware of this increasing epidemic so that appropriate counseling can be given to avoid these complications.

We present this case to raise awareness of a potentially dangerous adverse effect from self-administered injections of a commonly used over-the-counter supplement.

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