Chicago Dermatological Society

June 2016
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
Case Presentations

Wednesday, June 8, 2016
Stephens Convention Center – Rosemont, IL

Conference Host:
Division of Dermatology
Loyola University Medical Center

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Program

Host: Loyola University
Wednesday, June 8, 2016
Stephens Convention Center, Rosemont

8:00 a.m.	**Registration & Continental Breakfast with Exhibitors** *Foyer outside Ballroom #41*
8:30 a.m. - 10:30 a.m.	**Clinical Rounds** Slide viewing/posters – *Ballroom #41* Patient viewing – *Rooms 55-59*
9:00 a.m. - 10:00 a.m.	**Resident/Basic Science Lecture** – *Ballroom #42* *RESIDENT LECTURE:* "Vaccines and New Therapies for Viral Disease" *Stephen K. Tyring, MD, PhD, MBA*
10:00 a.m. - 10:30 a.m.	**Break and Visit with Exhibitors** – *Ballroom #41*
10:30 a.m. - 12:00 p.m.	**Resident Case Presentations & Discussion** *Ballroom #42*
12:00 p.m. - 12:15 p.m.	**MOC Self-Assessment Questions** *Ballroom #42*
12:15 p.m. - 12:45 p.m.	**Box Lunches & visit with exhibitors** *Ballroom #41*
12:55 p.m. - 1:00 p.m.	**CDS Business Meeting** *Ballrom #42*
1:00 p.m. - 2:00 p.m.	**General Session** – *Ballroom #42* “Emerging Infectious Diseases” *Stephen K. Tyring, MD, PhD, MBA*
2:00 p.m.	**Meeting adjourns**

Mark the Date!
Next CDS monthly meeting – NOTE CHANGE OF TRADITIONAL SCHEDULE!
Hosted by Loyola University - Wednesday, September 28
Stephens Convention Center, Rosemont

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

Guest Speaker

STEPHEN K. TYRING, MD, PHD, MBA

Medical Director, Center for Clinical Studies Clinical Professor, Department of Dermatology; University of Texas Health Science Center; Houston, TX

Dr. Tyring received his undergraduate degree from Indiana State University and a Master's Degree from Abilene Christian University. He was awarded an M.D. from the University of Texas Medical Branch, a PhD from Texas Tech University and an MBA from Rice University.

Dr. Tyring was President of the Texas Dermatological Society (2009-2010). He is board certified by the American Board of Dermatology, and he is a member of the Infectious Disease Society of America, as well as the American Federation for Clinical Research. Dr. Tyring sits on several editorial boards and serves as a reviewer for a number of journals including the New England Journal of Medicine, Lancet, Antiviral Research, Journal of the American Academy of Dermatology, Archives of Dermatology, Journal of Infectious Diseases and Annals of Internal Medicine. He is principal investigator for more than 200 successfully completed clinical trials. Dr. Tyring's research interests include the therapy and prevention of various mucocutaneous diseases, especially those disorders with an infectious and/or immunological basis.

Dr. Tyring is the author of more than 600 journal articles and book chapters, as well as seven books - Interferon: Principals and Medical Applications; Human Papillomaviruses: Clinical and Scientific Advances; Mucocutaneous Manifestations of Viral Diseases; Antiviral Agents, Vaccines and Immunotherapies; Mucosal Immunology and Virology; Tropical Dermatology and Clinical and Basic Immunodermatology.

CONTINUING MEDICAL EDUCATION CREDITS

Chicago Dermatological Society

Presents

"Chicago Dermatological Society Monthly Meeting Series"

June 8, 2016 *Rosemont, IL*

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

JOINT SPONSOR STATEMENT

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

GOAL / PURPOSE

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

EDUCATIONAL OBJECTIVES

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

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

Continued next page

CREDIT STATEMENTS

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

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

DISCLAIMER STATEMENTS

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DISCLOSURE STATEMENTS

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

Dr. Stephen Tyring has disclosed the following potential conflicts of interest: Grants/Research Support – Abbvie, Amgen, BI, Agenus, Genocea, Novartis, Merck, Agqa, Leo, Galderma, Bayer, Celgene, Janssen, Vical, Regeneron, Pfizer, Dermira, Tolmar, Sandoz, Allergan; Speakers' Bureau – Abbbvie, Novartis, Aqua, Leo.

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

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

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 1**

Presented by Jennifer Eyler, MD and Wendy Kim, DO
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

Dermatology was called to evaluate a 4-day-old female for multiple vascular stains. In addition, she had macrocephaly, congenital hip dysplasia, vascular malformation, and syndactyly of the 2nd and 3rd toes on the right foot. The baby was born at an outside hospital via Cesarean section to a 39-year-old G5P3013 female at 32 4/7 weeks gestation. Prenatal course was unremarkable. Labor and delivery were unremarkable other than preterm labor. Apgar scores were 9 and 9. The patient was admitted to the neonatal intensive care unit for prematurity, presumptive sepsis, respiratory distress, and multiple congenital anomalies. She was intubated and placed on a mechanical ventilator. She underwent a workup for sepsis and was treated empirically with ampicillin and gentamicin given unknown group B streptococcus status in the mother. Initial labs were within normal limits and blood cultures were drawn. Initial imaging included normal liver and renal ultrasounds. A brain ultrasound revealed an impressive midline shift toward the left as well as a dilated third ventricle. There was no gross intracranial hemorrhage. A karyotype with reflex microarray was sent, and the patient was transferred to the Loyola on day 1 of life for further care. Upon transfer, an MRI brain showed falx cerebri congenitally placed to the left of midline and a small left cerebral hemisphere.

PAST MEDICAL HISTORY

32 4/7 weeks gestation
Multiple congenital anomalies

PRENATAL HISTORY

Rubella immune
RPR nonreactive
HbSAg negative
HIV negative
GC/Chl negative
GBS unknown
Trisomy 21, 18, 13 negative
CF screen negative

MEDICATION

None

FAMILY HISTORY

None pertinent

SOCIAL HISTORY

None pertinent

PHYSICAL EXAM

Physical examination demonstrated macrocephaly. The baby's head measured > 99.9th percentile for adjusted dates. She had syndactyly of the 2nd and 3rd toes on her right foot with deep-set toenails and fingernails.

There was a large, vascular, erythematous patch with a marbled and reticulated appearance and irregular borders encompassing the majority of her body. It also extended from the central forehead over the nasal bridge and dorsum to the philtrum and upper and lower vermilion lips. She had a large subcutaneous, compressible, somewhat firm nodule of the nasal bridge with an overlying central violaceous to bluish patch. The baby was hypotonic.

DIAGNOSIS

Macrocephaly-Capillary Malformation (M-CM) syndrome

TREATMENT AND COURSE

The baby was monitored with serial brain MRIs while in the neonatal intensive care unit. She was noted to have an acute thrombosis of the sagittal sinus and right transverse sinus and an acute intraventricular hemorrhage on day 13 of life. She was noted to have asymmetric moderate dilation of the lateral ventricles and third ventricle on subsequent scans as well as hemimegalencephaly of the right hemisphere and possible periventricular leukomalacia of the right frontoparietal and periventricular region. She did not sustain seizures or require shunt placement during hospitalization.

The patient was extubated on day 7. She was placed in a Pavlik harness for congenital hip dislocation and dysplasia. The extensive capillary malformation gradually lightened over several weeks. She developed pronounced right-sided hemihypertrophy of the head. The nasal bridge mass was excised when the patient was 2 months old. Tissue was sent for genetic sequencing. An expert in pediatric vascular anomalies is reviewing the pathology specimen.

The patient was discharged home in stable condition at the age of 2 months. She will maintain close follow up as an outpatient with dermatology, orthopedic surgery, neurology, ophthalmology, and otolaryngology.

DISCUSSION

Macrocephaly-Capillary Malformation (M-CM) Syndrome is a rare congenital syndrome of unknown etiology characterized by macrocephaly and a patchy, reticulated capillary malformation. It was initially described in 1997 as macrocephaly-cutis marmorata telangiectatica congenita (CMTC). It has been subsequently shown that the vascular anomalies in these patients are not true CMTC as they lack ulceration, cutaneous atrophy, or ipsilateral limb atrophy. There is also a characteristic persistent midline facial capillary malformation in patients with M-CM syndrome.

The capillary malformations in M-CM syndrome tend to fade substantially during the first years of life, unlike typical port wine stains. The macrocephaly noted at birth is often associated with several neurologic structural anomalies and may be progressive. Other characteristic features of M-CM syndrome include neonatal hypotonia, developmental delay, hydrocephalus, partial or asymmetric overgrowth, syndactyly or polydactyly, asymmetry, and connective tissue defects. Neuroimaging abnormalities include cerebral asymmetry, white matter alterations, ventriculomegaly, cerebellar tonsillar herniation, and cortical dysplasia.

Four sets of diagnostic criteria for M-CM syndrome have been proposed. The recent diagnostic criteria by Wright *et al* in 2009 and Martinez Glez *et al.* in 2010 are the most widely accepted as they include capillary malformation rather than CMTC. The Martinez Glez criteria also include asymmetry and overgrowth as well as neuroimaging abnormalities. Diagnostic criteria together with modern genetic sequencing techniques can confirm the diagnosis.

M-CM syndrome is included in the group of segmental overgrowth disorders with PIK3CA mutations due to somatic mosaicism. All reported cases are sporadic. The prognosis depends on the development of hydrocephalus and extent of the cerebral abnormalities. Developmental delay in these children is typically mild to moderate. They should have clinic evaluations no less than every 6 months for the first 6 years of life and at least yearly thereafter. Baseline brain magnetic resonance imaging scans are performed at the time of diagnosis with follow up studies every 6 months until age 2 years with an interval assessment at 3 years. Evaluation by a pediatric cardiologist with a baseline electrocardiogram and echocardiogram is recommended to evaluate for cardiovascular malformations and arrhythmias. A baseline thrombophilia evaluation may be warranted as dural sinus stasis and enlargement are common, and thrombosis has been reported. Serial limb length measurements are followed given overgrowth potential. Patients with M-CM syndrome and generalized hemihypertrophy are at a significantly increased risk for Wilms tumor, and therefore serial abdominal ultrasounds are recommended.

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7) www.M-CM.net.

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 2**

Presented by Amanda Champlain, MD, Rebecca Rovner, MD, and Laura Winterfield, MD, MPH
Division of Dermatology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 68-year-old woman was referred to the dermatology clinic by her internist for evaluation and treatment of pretibial myxedema. The patient had a history of hyperthyroidism secondary to Graves' disease since 2002, complicated by severe pretibial myxedema and exophthalmos. Ten years prior, she had treated the condition with topical clobetasol ointment under occlusion, decongestive massage physiotherapy, and compression stockings, without improvement. She complained of dryness and cracking of the affected skin, numbness of the dorsal feet when sitting for prolonged periods, and the inability to wear shoes due to the enlarged size of her feet. Her hyperthyroidism had been effectively managed with radioactive iodine, propylthiouracil and methimazole, and she was euthyroid at the time of presentation.

PAST MEDICAL HISTORY

Graves' disease complicated by pretibial myxedema and exophthalmos
Diabetes mellitus, type 2 with diabetic retinopathy
Hypertension
Hyperlipidemia
Breast cancer s/p right breast lumpectomy, radiation therapy, and tamoxifen therapy

MEDICATIONS

Methimazole
Metformin
Glipizide
Losartan
Simvastatin
Aspirin
Fish oil
Multivitamin

ALLERGIES

None

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Born in Vietnam. Smokes 2 cigarettes per day for the past 25 years. No alcohol or illicit drug use.

PHYSICAL EXAMINATION

Bilateral pretibial lower extremities, anterior ankles, dorsal feet, and toes with confluent erythematous indurated nodules and plaques with overlying fissures and hypertrichosis.

DIAGNOSIS

Pretibial myxedema treated with serial intralesional triamcinolone injections, combined with pentoxifylline therapy with significant clinical improvement

TREATMENT AND COURSE

Treatment was initiated with pentoxifylline 400 mg PO BID and serial intralesional triamcinolone acetonide injections. She received 12 treatment sessions scheduled approximately every 4-5 weeks. Triamcinolone acetonide 10 mg/mL was used for the first 3 treatments, the concentration was then increased to 20 mg/mL for the remaining 9 treatments. At each session the amount injected ranged from 1-2 mL and injections were directed at areas most symptomatic to the patient. Injected skin lesions became smaller, softer, and thinner with each treatment, with an overall significant clinical improvement in her condition.

DISCUSSION

Pretibial myxedema, also called localized myxedema, is characterized by thickening of the skin of the pretibial area due to mucin deposition. 90% of cases are associated with hyperthyroidism due to Graves' disease, an autoimmune thyroid disorder. Pretibial myxedema occurs in 0.05 – 5% of patients with Graves' disease and almost always with concurrent exophthalmos. Onset is typically 12-24 months after the diagnosis of hyperthyroidism, though it may develop many years after thyrotoxicosis. The condition has infrequently been reported in association with Hashimoto's thyroiditis, hypothyroidism after treatment of Graves' disease, and in euthyroid patients.

The pathogenesis of pretibial myxedema is not completely understood. The primary pathologic process involves fibroblast activation resulting in excess mucin production, reportedly up to 6-16 times the amount found in normal dermis. Polymerase chain reaction studies have demonstrated elements of the thyroid stimulating hormone (TSH) receptor in cutaneous fibroblasts, which could serve as a common antigen between fibroblasts and thyroid follicular cells. It has been hypothesized that T lymphocytes sensitized to this shared antigen migrate to the dermis and produce cytokines that stimulate fibroblasts. Mechanical dependency, trauma, and insulin-like growth factor may additionally play a role.

Pretibial myxedema is most commonly localized to the anterolateral aspects of the lower legs in a bilateral and symmetric distribution. It occasionally involves the feet and toes. Four clinical forms have been described: 1) diffuse nonpitting edema, 2) plaque form, 3) nodular form, and 4) elephantiasic form (nodular form with significant lymphedema). Lesions are waxy, indurated nodules and plaques that are typically pink-to-flesh-colored but may be yellowish or purple-brown. Follicular prominence can impart a "peau d'orange" appearance to the lesions. Other variably present clinical features include hyperpigmentation, hyperkeratosis, hyperhidrosis, and hypertrichosis confined to the myxedematous skin. Lesions are cosmetically undesirable but otherwise asymptomatic, though large lesions can cause functional disability.

Histopathology of pretibial myxedema shows large amounts of mucin in the reticular dermis with separation of collagen fibrils and thickening of the dermis. There is a lack of mucin deposition in the papillary dermis. A perivascular and periadnexal lymphocytic infiltrate with increased numbers of mast cells is observed. Hyperkeratosis and/or papillomatosis of the epidermis may be present.

Successful treatment with intralesional corticosteroids was first reported by Dyke *et al.* as a small case series in 1959. A recent randomized trial of 110 patients receiving intralesional triamcinolone acetonide injections every 3 days or every 7 days for a total of 7 treatments achieved complete response rates of 83.7% and 90.9%, respectively. However, approximately 1/3rd of patients had disease recurrence by 3.5 years follow-up. A case report describing monthly intralesional triamcinolone acetonide injections combined with pentoxifylline therapy showed significant clinical improvement with no recurrence at short-term follow-up in a patient with severe disease. Chang *et al.* demonstrated *in vitro* that pentoxifylline, an analogue of methylxanthine theobromine, inhibits fibroblast proliferation and glycosaminoglycan synthesis in Graves' patients.

Other reported therapies for pretibial myxedema include topical corticosteroids, oral steroids, octreotide, intravenous immunoglobulin, plasmapheresis, decompressive physiotherapy, and surgical resection with skin grafting. It is difficult to assess the efficacy of these treatments due to small sample size and lack of controlled studies.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 3**

Presented by Kelly K. Park, MD, MSL[1], Monika Kaniszewska, MD, MS [2,3], Kelli Hutchens, MD [4], James Swan, MD [1,3], Rebecca Tung, MD [1]
[1]Division of Dermatology, Loyola University Medical Center
[2]Dermatology & Plastic Surgery Associates, SC
[3]Section of Dermatology, Edward Hines Jr. Veterans Affairs Hospital
[4]Department of Pathology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS
A healthy 31-year-old Hispanic female of 37 weeks gestation presented with complaint of a rash on her left thigh and right cheek that had been present for over one year. The lesions were pruritic, growing in size, and friable with intermittent bleeding. They were also tender to palpation. The patient denied recent travel or affected close contacts. She denied having fever, chills, respiratory symptoms, or other cutaneous complaints and the remainder of her review of systems was unremarkable.

PAST MEDICAL HISTORY
None

MEDICATIONS
None

ALLERGIES
NKDA

FAMILY HISTORY
Non-contributory

SOCIAL HISTORY
Married, immigrated from Mexico

PHYSICAL EXAM
On the right cheek, there was a 3.3 cm x 2.0 cm pink, annular, well-demarcated, verrucous plaque with surrounding erythema and overlying scale with hemorrhagic crusting. On the left distal thigh was a 3.0 cm x 1.5 cm pink, firm, oval nodule with hyperpigmented borders that was studded with pustules.

DERMATOPATHOLOGY
Histological analysis revealed pseudoepitheliomatous hyperplasia with underlying dense superficial and deep mixed cell infiltrate composed of neutrophils, lymphocytes, histiocytes, and multinucleated giant cells. Well-formed necrotizing granulomas and large neutrophilic abscesses were readily identifiable. Several scattered round-to-oval organisms with refractile cell walls in the cytoplasm of giant cells were noted. Grocott's methenamine silver (GMS) stain highlighted the organisms. These findings were consistent with *Blastomyces dermatitidis* infection.

LABORATORY DATA
Fungal tissue culture grew *Blastomyces dermatitidis*, which was confirmed by DNA probe.

DIAGNOSIS
Blastomycosis in Pregnancy with an Unusual Postpartum Course

TREATMENT AND COURSE

Due to potential teratogenicity of the azole antifungals, amphotericin B is the drug of choice for blastomycosis in pregnancy. However, the patient opted to defer systemic therapy until after delivery due to the proximity of her due date at the time of diagnosis and absence of systemic symptoms. The patient delivered a healthy, full-term infant with no evidence of *Blastomyces* infection.

Postpartum, the patient's facial plaque continued to progress and began draining purulent material at the lateral edges while the thigh nodule continued to enlarge. Evaluation for pulmonary infection with a chest radiograph was negative and the patient continued to deny systemic symptoms. Treatment with itraconazole was discussed; however, the patient was unable to proceed with therapy due to lack of insurance coverage. At approximately six weeks postpartum, itraconazole was obtained and the patient was started on a dose of 200 mg twice daily by mouth for 6 months. After five months of therapy, both the facial and thigh lesions demonstrated favorable signs of regression.

DISCUSSION

Blastomyces dermatitidis is a dimorphic fungus responsible for systemic mycoses predominantly caused by inhalation of spores. Infection may present as an acute or chronic pneumonia with potential dissemination via hematogenous or lymphatic spread, occasionally progressing to fatal disease. Overall, skin involvement has been reported in 40-80% of cases. Even in endemic regions, blastomycosis infection during pregnancy is exceedingly rare. A comprehensive review by Lemos *et al*. of records at the University of Mississippi Medical Center (located in an endemic region) as well as of a review of the medical literature revealed only 19 cases of blastomycosis infections during pregnancy over a span of 108 years.

It has been suggested that pregnancy results in a partial immunosuppressive state, which may predispose gravid women to infection with fungal organisms. Infection with a non-obligatory opportunistic fungus, such as *Blastomyces*, may be more severe in immunosuppressed individuals, making disseminated disease more likely. Therefore, blastomycosis during pregnancy is particularly concerning. Beyond the concern for maternal health, blastomycosis during pregnancy also carries a risk of potentially fatal congenital blastomycosis of the newborn. All of the published cases of blastomycosis during pregnancy describe postpartum regression even in the absence of treatment. This observed improvement likely results from postpartum immune reconstitution.

Our case represents a rare instance of cutaneous blastomycosis during pregnancy. In this patient, we suspect that pregnancy contributed to an exacerbation of a preexisting case of cutaneous blastomycosis. The patient's decision to forgo treatment until after delivery of her child was warranted due to lack of systemic symptoms. While the patient had progression of cutaneous blastomycosis during and after pregnancy, she fortunately had no pregnancy related complications and delivered a healthy infant with no signs of systemic *Blastomyces* infection. Further, the patient did not display the expected postpartum regression of blastomycosis symptoms as seen in previously reported cases. Rather, the patient's cutaneous blastomycosis continued to progress beyond delivery, but she did not develop additional cutaneous lesions or signs of dissemination to noncutaneous sites.

The treatment of choice for blastomycosis during pregnancy is lipid formulation amphotericin B, 3-5 mg/kg/day, which is deemed effective and safe. Lipid formulated preparations of amphotericin B are used more commonly given their greater tolerability and lesser toxicity. Systemic therapy may prevent fetal transmission although definitive evidence is lacking.

Itraconazole is the drug of choice among available azole antifungal drugs to treat mild-to-moderate blastomycosis without central nervous system involvement occurring in non-pregnant individuals. Cure rates of 90% have been reported after a 6-12 month regimen of 200-400 mg daily.

CONCLUSION

When *Blastomyces dermatitidis* during pregnancy is suspected, thorough evaluation is imperative to exclude systemic disease necessitating therapy. This case underscores the importance of disease recognition and prompt appropriate treatment of blastomycosis if disease progression or systemic involvement is suspected. Treatment, particularly in unique circumstances like pregnancy, can halt further progression and may prevent possible transplacental dissemination. This case also describes conservative management of multi-focal cutaneous blastomycosis in a gravid female lacking systemic symptoms but emphasizes the need to institute treatment in the postpartum period if cutaneous disease is progressive.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 4**

Presented by Patricia Todd, MD[1], Carly Webb, MD[1], Kumaran Mudaliar, MD[2], Kelli Hutchens, MD, MBA[2], Wendy Schumacher-Kim, DO[1], and Lily Uihlein, MD, JD[1]
[1]Division of Dermatology, Loyola University Medical Center
[2]Department of Pathology, Loyola University Medical Center

HISTORY OF PRESENT ILLNESS

A 10 year-old girl with thrombocytopenia with absent radii (TAR) syndrome presented with a non-healing perianal sore and worsening of chronic constipation. The lesion had developed three months prior and caused significant pain and pruritus, particularly with bowel movements. The patient noted a small amount of bleeding occasionally with bowel movements. She had developed perianal irritation in the past due to her limited ability to cleanse after bowel movements, but had no history of perianal ulcerations. She had no history of diarrhea, but did report mild abdominal pain from time to time. Initial treatment with topical corticosteroids, topical and oral antibiotics, and antifungal and antiviral agents resulted in only limited improvement.

PAST MEDICAL HISTORY

Thrombocytopenia with absent radii (TAR) syndrome
Hearing deficit
Gastroesophageal reflux disease

MEDICATIONS

Acetaminophen
Omeprazole
Odansetron
Ranitidine
Simethicone
Polyethylene glycol

ALLERGIES

Latex, Chlorhexidine, Soy, Milk, Tape

FAMILY HISTORY

The patient is adopted, so family history is largely unknown. The patient's father has diabetes mellitus.

SOCIAL HISTORY

She lives with adoptive parents and 7 unrelated siblings.

PHYSICAL EXAMINATION

The patient was well appearing. There was an erythematous, slightly indurated, thin plaque extending from the superior gluteal cleft to the perineal region. The plaque contained a large, tender ulceration with deeply erythematous granulation tissue at the base and several smaller round ulcerations. The labia majora and minora had a thin, pink plaque with a larger ulceration superiorly and several small erosions. There were no oral lesions and no cervical, retroauricular, supraclavicular, axillary, or inguinal lymphadenopathy.

DERMATOPATHOLOGY
Histopathology demonstrated a dermal infiltrate of Langerhans cells focally displaying epidermotropism surrounded by a mixed infiltrate of eosinophils, plasma cells and neutrophils. CD1a immunohistochemical stain highlighted an increase in Langerhans cells in this distribution.

LABORATORY STUDIES

Laboratory Study	Patient Result	Reference Range
Platelets (1000/μL)	78	150-300
Bacterial culture	E. coli, Actinomyces and Corynebacterium species	Negative
Fungal culture	Negative	Negative
Viral culture	Negative	Negative
EBV IgM	Negative	Negative
CMV IgM	Negative	Negative

ADDITIONAL STUDIES
Skeletal survey showed no evidence of bony involvement of Langerhans cell histiocytosis. Chest CT showed no infiltrates or lymphadenopathy.

DIAGNOSIS
Anogenital ulcerative Langerhans cell histiocytosis (LCH) in the setting of thrombocytopenia with absent radii (TAR) syndrome

TREATMENT AND COURSE
The patient was referred to hematology-oncology at Lurie Children's Hospital where she has been followed for TAR syndrome. She was treated with prednisone and vinblastine with improvement in her perianal ulcers within the first 2 weeks of therapy. Her course has been complicated by thrombocytopenia requiring interruption of therapy. Cessation of the chemotherapy has resulted in temporary worsening of her ulcerations.

DISCUSSION
Langerhans cell histiocytosis (LCH) is caused by clonal proliferation and accumulation of Langerhans cell precursors: myeloid dendritic cells that are immunohistochemically similar to the antigen-presenting Langerhans cells naturally found in the epidermis. LCH affects 4-5 per one million children and may involve multiple organs, including the skin, bone, lymph nodes, lung and central nervous system. Prognosis is generally good; skin limited disease has close to 100% overall survival, and multi-system disease has roughly 85% survival. However, recurrences are frequent and may occur after long periods of remission.

The skin is the second most commonly involved organ in childhood LCH (following bone) and occurs in 50-80% of patients. Cutaneous disease commonly presents as an eczematous or vesiculopustular eruption that does not respond to standard therapy. Often lesions have a red-brown or yellow-brown color and may have associated petechiae. Most commonly, lesions occur on the scalp, trunk, and groin. Diagnosis is made by histologic examination of involved tissue. Pathology will demonstrate a proliferation of dendritic cells with characteristic reniform nuclei at the dermoepidermal junction. There may also be an associated inflammatory infiltrate with lymphocytes, neutrophils and/or eosinophils. The tumor cells have a specific immunohistochemical staining pattern: S100, CD1a, and CD207 (Langerin).

Once a diagnosis of LCH is made, complete systemic evaluation is indicated to assess for other organ involvement. This is essential for determination of prognosis and selection of treatment. Mortality in single organ skin disease is ~ 2% while that in multi-system, low-risk patients is up to 10%. In addition to a thorough review of systems and complete physical exam, the following studies are recommended: full blood count, complete metabolic panel including gamma-glutyl transferase and ferritin, coagulation studies, urine specific gravity and osmolality, abdominal ultrasound, chest x-ray, and skeletal survey.

Skin-limited LCH generally does not require treatment, as it commonly resolves on its own. However, more severe multi-focal cutaneous involvement and multi-system disease generally requires systemic therapy. First-line systemic therapy consists of vinblastine and oral corticosteroid. A recent study demonstrated decreased frequency of recurrence or progression when vinblastine and prednisone were given concurrently over a 12-month period. Routine re-evaluation of patients to assess for progression is imperative as lack of response to treatment portends worse prognosis and warrants intensification of therapy.

LCH uncommonly presents with isolated anogenital involvement. Lesions may resemble skin tags or condyloma; alternatively, they may present as cutaneous ulcerations. Diagnosis is frequently delayed due to a broad differential diagnosis that includes far more common infectious and inflammatory alternatives. Work-up of perianal/perineal LCH is identical to that of other variants. Reported cases have not shown an increased risk of multi-system disease compared to other cutaneous presentations, though recurrences seem frequent. Surgical treatment or radiation therapy of perineal LCH is reported in the gynecologic literature, though it is not clear if it is superior to medical management.

LCH is rarely seen in patients with TAR syndrome. Of the cases reported, two were in adults, and one was in a 9 year-old child. All had multi-system disease. Management of LCH in the setting of TAR syndrome is challenging as vinblastine and other second-line chemotherapeutic regimens may cause further bone marrow suppression. Reduced-intensity allogenic hematopoietic stem cell transplant has been suggested as an alternative to conventional therapy.

BRAF V600E gain-of-function mutations have been identified in over half of LCH cases with recent reports of response to targeted therapy with vemurafinib. Long-term follow-up is necessary to evaluate for relapse, progression and sequelae in patients with LCH. Up to 25% of patients with single system disease have long-term sequelae.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 5**

Presented by Dana Griffin, MD[1], Amanda Champlain, MD[1], Kumaran Mudaliar, MD[2], Jodi Speiser, MD[2], and Lily Uihlein, MD, JD[1]
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UNKNOWN

CHICAGO DERMATOLOGICAL SOCIETY **CASE # 6**

Presented by Daniel Opel, MD[1], Kumaran Mudaliar, MD[2], Jodi Speiser, MD[2], and Laura Winterfield, MD, MPH[1]
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HISTORY OF PRESENT ILLNESS
A 45-year-old Caucasian female presented in August 2015 for a lesion on the anterior neck. It started over a year earlier, in March 2014, as a small pustule, which had slowly enlarged to the point of irritation. She was initially treated with clindamycin lotion, clobetasol cream, and mupirocin, which helped with pruritus and erythema. A biopsy performed near the time of onset had demonstrated a perforating dermatosis. Afterward, she developed pain, erythema, and poor wound healing at the biopsy site. Except for a mild tremor, her remaining review of systems was unremarkable.

PAST MEDICAL HISTORY
Wilson's disease

MEDICATIONS
Penicillamine
Trientine
Meclizine
Ferrous sulfate

ALLERGIES
Sulfa, penicillin, azithromycin, doxycycline, erythromycin, fexofenadine, vicodin

FAMILY HISTORY
Sister had Wilson's disease and subsequently died from complications

SOCIAL HISTORY
Currently married and has two daughters, one age 12 and one age 21. They both have been tested for Wilson's disease and have been negative. No smoking. No alcohol.

PHYSICAL EXAMINATION
The patient was well-appearing. On the anterior mid-neck were several erythematous papules coalescing into a plaque with yellow, superficial, punctate crusting. There was no active oozing or bleeding and no nodularity on palpation. There was no lymphadenopathy.

DERMATOPATHOLOGY
Low power demonstrated a column of keratotic debris forming a focal invagination through a hyperplastic epidermis. Higher power inspection identified large, brightly eosinophilic fibers within the extruded material, with keratinous debris and a mixed inflammatory cell infiltrate undergoing transepidermal elimination. Verhoeff-van Gieson tissue stain revealed increased, abnormal, thickened elastic fibers in the dermis in the vicinity of the channel. The altered elastic fibers had small lateral buds arranged perpendicularly to the primary elastic fiber, resembling the twigs on a "bramble bush."

LABORATORY RESULTS

Laboratory Study	Patient Result	Reference Range
CBC, CMP	wnl	---
Serum copper (MCG/DL)	15	70-175
24hr Urine copper (MCG/24HRS)	102	15-60

ADDITIONAL TESTS
Transthoracic echocardiogram showed normal ejection fraction of 65%, no systolic or diastolic dysfunction, and no valvular or large vessel abnormalities.

DIAGNOSIS
D-Penicillamine induced elastosis perforans serpiginosa in the setting of Wilson's Disease

TREATMENT AND COURSE
The patient was seen by both dermatology and hepatology for treatment. She was initially started on oral zinc, which was discontinued due to nausea, and her D-penicillamine was switched to trientine. Subsequently, the patient noted worsening of her Wilson's disease with stable laboratory results, resulting in her restarting penicillamine. Additionally she was prescribed tazarotene cream twice daily as tolerated, as well as topical clobetasol.

DISCUSSION
Elastosis perforans serpiginosa (EPS) was first described by Lutz in 1953 as a chronic papular keratotic eruption in an arciform shape located on the sides of the nape of the neck. The lesions may be serpiginous, horseshoe-shaped, or annular. Lesions are most commonly found on the neck, although other sites including the upper arms, face, lower extremities and flexural areas may be involved. The disease runs a variable course with spontaneous resolution often occurring from 6 months to 5 years from onset, although residual scarring may persist.

About 1/3 of EPS cases occur with associated diseases, with Down syndrome being the most commonly associated disorder. About 1% of patients with Down syndrome have EPS. Other associated disorders include Marfan syndrome, acrogeria, pseudoxanthoma elasticum, osteogenesis imperfecta, Rothmund-Thompson syndrome, Ehlers-Danlos syndrome, and scleroderma.

The D-penicillamine (DPA) pathogenic process affects the middle and deep dermal elastic fibers. Two mechanisms of action have been postulated and both are probably relevant to the final elastopathy. The first mechanism is related to copper deficiency secondary to DPA treatment, which subsequently impairs lysyl oxidase function on elastic fiber cross-linking, a crucial process to stabilize and compact the fibers. This usually occurs only with the very high dose and prolonged administration of the drug as is characteristically used in Wilson's disease. Copper deficiency alone is probably not sufficient, which is suggested by the observation that EPS has never been documented in Menkes disease, a severe genetic copper deficiency. The second mechanism is likely related to direct DPA post-translational inhibition of type I collagen synthesis, which further results in abnormal fiber deposition. The formation of complexes with the collagen cross-linked precursors additionally impairs normal maturation of the elastic fibers.

The abnormal dermal elastic fibers accumulate and promote a foreign body reaction. In 1968, Mehregan coined the term “transepithelial elimination” to describe the peculiar histopathology he observed in eleven cases of idiopathic EPS, characterized by the formation of epidermal perforating channels through which abnormal dermal elastic material was spontaneously eliminated.

Microscopic findings support the hypothesis that the abnormal elastin is produced later in the patient’s life, several years after the drug is started, and covers the normal elastic fibers. The coarse and loose elastic fibers resulting from the paucity of cross-linkages are unable to re-expand after contraction on their major axes, producing the lateral budding characteristic of DPA-induced EPS. A possible relationship between sun exposure and elastic fiber degeneration has not been investigated, but it is interesting to note that lesions of EPS tend to be located on visible, sun-exposed areas, such as the nape and lateral sides of the neck or the forearms.

Treatment for EPS is difficult. Topical retinoids and high potency corticosteroids have some benefit. Individual lesions may resolve following liquid nitrogen cryotherapy. Some cases have responded to CO_2, erbium-YAG, or Pulsed Dye Laser therapy.

To conclude, DPA may cause significant alterations of the elastic tissue, which are so peculiar that they are easy to distinguish histologically from idiopathic elastosis perforans serpiginosa. A decrease in lysyl oxidase activity and a direct drug interaction with collagen fiber precursors are both involved in this complex and interesting pathophysiology. Misdiagnosis and delayed intervention frequently allows skin atrophy and scarring to occur.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 7**

Presented by Carly Webb, MD[1], Dana Griffin, MD[1], Kumaran Mudaliar, MD[2], Kelli Hutchens, MD, MBA[2], and Lily Uihlein MD, JD[1]
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HISTORY OF PRESENT ILLNESS

A 57-year-old male presented with recurrent, painful, subcutaneous nodules on the arms and legs of two months' duration. The lesions first appeared on the legs and were few in number. The lesions gradually increased in number and spread to involve the arms. He had undergone multiple incision and drainage procedures of the lower extremity lesions, with a negative bacterial culture from a representative lesion. The patient denied fevers, chills, night sweats, or abdominal pain. Review of systems was significant for fatigue and an unintentional weight loss of 30 pounds.

PAST MEDICAL HISTORY

No known history of pancreatitis or malignancy
Appendicitis s/p appendectomy
Aortic occlusion at level of renal arteries
Hypertension
CVA
Anemia

MEDICATIONS

Aspirin
Diazepam
Norco
Temazepam

ALLERGIES

Naproxen

FAMILY HISTORY

No known history of pancreatic or colon cancer

SOCIAL HISTORY

Prior social alcohol use (no current consumption)
Prior tobacco use (1 pack per day for 35 years)

PHYSICAL EXAMINATION

The patient appeared older than his stated age and was ill-appearing. Cutaneous examination revealed numerous erythematous to violaceous subcutaneous nodules, largely confined to the bilateral posterior lower legs with a few similar nodules also present on the bilateral anterior lower legs. Some lesions contained foci of ulceration and were draining yellow material. On the bilateral upper arms, there were faintly erythematous subcutaneous nodules within a background of reticulate hyperpigmentation. All lesions were tender to palpation.

DERMATOPATHOLOGY

Histopathology of a representative lesion on the left lower leg demonstrated superficial dermal fibrosis with an underlying lobular and septal panniculitis. Focal areas of fluffy purple material, consistent with fat saponification, were identified. Infectious stains, including Grocott-Gomori Methenamine-silver (GMS), Periodic acid-Schiff (PAS), Acid-Fast Bacilli (AFB), and Fite were negative.

LABORATORY RESULTS

Laboratory Study	Patient Result	Reference Range
WBC (K/UL)	7.8	3.5-10.5
Hemoglobin (GM/DL)	10.7	13.0-17.5
Platelet (K/UL)	313	150-400
Eosinophil # (K/MM^3)	0.2	0.0-0.7
Eosinophil %	3	N/A
Calcium (MG/DL)	8.6	8.9-10.3
ALT (IU/L)	11	10-40
AST (IU/L)	28	15-45
Alkaline Phosphatase (IU/L)	111	30-110
Lipase (U/L)	1826	10-58
Cancer Antigen (CA)19-9 (U/ML)	260	0-37
Carcinoembryonic Antigen (CEA) (NG/ML)	1.2	0-2.5
Vasoactive Intestinal Peptide (VIP) (PG/ML)	31	<75
Glucagon (PG/ML)	<79	< or = 134
Chromogranin A (NG/ML)	7	< or = 15
Aerobic Culture (left foot lesion)	No organisms	Negative

ADDITIONAL TESTS

A CT angiogram revealed a superior mesenteric venous occlusion, an occlusive aortic thrombus at the level of the renal arteries, and a pancreatic head mass with surrounding lymphadenopathy. An MRI of the abdomen revealed a 2.7 cm x1.8 cm complex cystic lesion within the uncinate process of the pancreas. Pancreatic calcifications suggestive of chronic pancreatitis were also noted. Endoscopic ultrasound revealed a superior mesenteric venous aneurysm and findings consistent with chronic pancreatitis.

DIAGNOSIS

Pancreatic panniculitis in the setting of chronic pancreatitis

TREATMENT AND COURSE

The patient's SMV thrombus and aortic occlusion were treated with anticoagulation; his pancreatitis was treated with supportive care. He has been seen by hematology-oncology in the outpatient setting for further workup and management of his pancreatic mass. Serial imaging studies of the pancreas thus far have revealed shrinking of the pancreatic head mass, supporting its nature as a complication of chronic pancreatitis rather than a pancreatic malignancy. He will be undergoing workup for autoimmune pancreatitis at future clinic visits.

DISCUSSION

Pancreatic panniculitis is a rare form of panniculitis seen in 2-3% of patients with diseases or anomalies of the pancreas. It may affect individuals of any race or gender but appears to have a predilection for alcoholic males.

The most common pancreatic disorders associated with pancreatic panniculitis are pancreatic malignancies (the most common of which is acinar cell carcinoma) and acute or chronic pancreatitis. However, pancreatitis panniculitis may also be seen in patients with other pancreatic disorders including abdominal trauma (resulting in traumatic pancreatitis), pancreatic ischemia, pancreatic divisum, pancreatic pseudocysts, and pancreatic fistulas. There is also a reported case of pancreatic panniculitis in the setting of primary HIV infection and hemophagocytic syndrome. The appearance of panniculitic lesions may precede, occur concomitantly with, or follow the diagnosis of the underlying pancreatic disorder. When present, the subcutaneous lesions are the presenting feature of underlying pancreatic disease in 40% of cases.

The pathophysiology of pancreatic panniculitis remains incompletely understood, but a widely accepted theory, particularly in cases of acute or chronic pancreatitis, is that the skin lesions result from pancreatic enzyme-mediated subcutaneous fat destruction. Indeed, elevated levels of lipase, amylase, and tryptase have been found in the skin lesions, urine, and bloodstream of patients with pancreatic panniculitis. Of the laboratory abnormalities seen in pancreatic panniculitis, an elevated serum lipase level is the most prevalent.

Another proposed etiopathological mechanism, particularly in cases of malignancy-associated pancreatic panniculitis, is an immunologic or paraneoplastic phenomenon, whereby subcutaneous fat necrosis results from antibody-mediated tissue destruction. It is proposed that antibodies targeting malignant tissue aberrantly cross-react with self-tissue in the subcutis.

The clinical presentation of pancreatic panniculitis resembles that of other panniculitides. Patients classically present with erythematous, firm, sometimes tender, reddish-brown subcutaneous nodules, most commonly on the legs. The scalp, arms, abdomen, and chest may also be affected. Lesions may occur singly or in crops; they may remain localized to their initial area of appearance or may subsequently migrate. Clinical differentiation from other panniculitides is difficult and, therefore, diagnosis is typically reliant on histopathologic findings. However, one distinguishing clinical feature of pancreatic panniculitis is that lesions may become fluctuant, ulcerate, and express a brown oily substance as a result of liquefactive fat necrosis. Pancreatic panniculitis is often associated with other systemic symptoms and findings, including fevers, abdominal pain, arthritis (caused by periarticular fat necrosis), and pleural effusions. Schmid's triad is a term reserved for the triad of subcutaneous nodules, peripheral eosinophilia, and polyarthritis in the setting of pancreatic panniculitis, and portends a poor prognosis. The clinical course of the panniculitic lesions is highly variable but tends to parallel that of the underlying pancreatic disorder. Treatment of subcutaneous lesions is most challenging in cases of an underlying pancreatic malignancy.

The histologic findings of pancreatic panniculitis depend on the age of the cutaneous lesions. Early lesions may exhibit features of a septal panniculitis, and older lesions progress to a mixed septal/lobular panniculitis. There is no associated vasculitis. Histologic features that help distinguish pancreatic panniculitis from other panniculitides are ghost cells (aged lipocytes which have lost their nuclei but retain a shadowy cell membrane) and fat saponification (basophilic granular deposits of calcium salts).

Treatment of pancreatic panniculitis is best achieved through management of the underlying pancreatic disorder. For disorders that cannot be successfully treated, such as unresectable pancreatic malignancies, supportive care may be employed, including leg elevation, use of compression stockings, and administration of octreotide to inhibit pancreatic enzyme production.

If histopathologic findings are concerning for pancreatic panniculitis, further workup should include a complete medical history and review of systems, serum lipase levels, +/- serum amylase levels, and a liver panel. Depending on laboratory values and systemic symptoms, abdominal imaging including CT, MRI or EGD/EUS, as well as serological tumor markers, may be warranted to identify the underlying pancreatic pathology.

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CHICAGO DERAMATOLOGICAL SOCIETY **Case # 8**

Presented by Lori Asztalos, MD and Rebecca Tung, MD
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HISTORY OF PRESENT ILLNESS

A 52-year-old Caucasian male presented with a 10-year history of rosacea with progressive and deforming rhinophymatous change. His rosacea was refractory to minocycline, doxycycline, Plexion® (sodium sulfacetamide USP 10% and sulfur USP 5%), metronidazole gel, cryosurgery, and Pulsed Dye Laser therapy. Given the disfiguring nature of disease, the patient requested more aggressive therapy.

PAST MEDICAL HISTORY

Malignant melanoma
Squamous cell cancer
Atrial fibrillation
Non-ischemic cardiomyopathy

MEDICATIONS

Sulfamethoxazole trimethoprim
Amiodorone
Metoprolol
Rivaroxaban
Carvediol
Lisinopril

ALLERGIES

None

FAMILY HISTORY

Father with non-melanoma skin cancer

SOCIAL HISTORY

Farmer in central Illinois

PHYSICAL EXAMINATION

Cutaneous exam was notable for patchy central facial erythema, telangiectasias, and fibrotic exophytic enlargement of the nose.

DERMATOPATHOLOGY

Left lateral ala biopsy consistent with rhinophyma

DIAGNOSIS

Phymatous rosacea

TREATMENT AND COURSE

The patient was treated with combined excisional decortication and Pulsed Dye Laser (PDL). Local anesthesia was achieved with infiltration of 1% lidocaine with epinephrine. A dermablade was used for debulking excess phymatous tissue and contouring of the nose. Hemostasis was achieved with aluminum chloride and electrocautery.

The treated sites were subsequently treated with PDL; wavelength of 595-nm, 5-mm spot size, fluence ranging between 7.5-9 J/cm^2 and a pulse width ranging between 3-6 ms. The areas were dressed with petrolatum and DuoDERM®. The patient had 5 treatments ranging from 2 weeks to 2 months apart (11/24/15, 12/8/15, 12/21/15, 1/4/16 and 3/14/16) with marked clinical improvement after each procedure. Wounds were treated at home with dilute vinegar soaks and silver sulfadiazine cream until the sites were healed.

DISCUSSION

Phymatous change is a late deformity in some patients with rosacea that primarily affects Caucasian males in the fifth to seventh decade of life. It has rarely been reported in patients with primary lymphedema, infections, and other inflammatory conditions such as psoriasis and atopic dermatitis. It is characterized by sebaceous hyperplasia, fibrous tissue proliferation, and blood vessel overgrowth leading to erythema and thickened skin with an irregular bulbous surface. Complications include nare obstruction causing difficulty breathing and psychological effects. Phymas may be very disfiguring and lead to serious emotional distress, lack of confidence, and social isolation.

The pathogenesis of rosacea is unclear. One proposed mechanism includes dysregulation of the immune system combined with vascular hyperreactivity. Patients with rosacea often have increased baseline expression of cathelicidin and kallikrein-5, increased levels of toll-like receptor 2 (TLR-2) and matrix metalloproteinases (MMP), and altered immunologic mediators (vasoactive intestinal peptide, gastrin, serotonin, histamine, and prostaglandins). Microorganisms are also thought to contribute to the increased inflammatory reaction. TLR-2 is upregulated by *Demodex folliculorum* and *Staphylococcus epidermidis*. Production of MMP-9, tumor necrosis factor, and interleukin-8 may be induced by *Bacillus oleronius*. Ultraviolet radiation has been shown to increase reactive oxygen species and propagate the kallikrein 5-cathelicidin inflammatory cascade via TLR-2. Vasoactive influences (alcohol, caffeine, spicy foods, and climate) lead to damaged and leaky cutaneous vessels.

Therapeutic approaches include both non-surgical and surgical options. Non-surgical treatments including topical corticosteroids, antimicrobials, and retinoids are largely ineffective in treating phymatous change, and surgical management is often warranted. Surgical options include complete excision with skin grafting, hot loop excision, dermaplaning, dermabrasion, cryosurgery, electrosurgery, and sharp blade excision. A combination of tumescent local anesthesia, dermaplaning with a Weck blade, and hemostasis using an Argon Beam Coagulator (TWA technique) is commonly performed by plastic surgery, but requires the patient to be under monitored anesthesia care (MAC). Surgical options may have cosmetically satisfactory outcomes, however adverse events include excess bleeding and risk of scarring. Preservation of the deep sebaceous glands and adnexal structures is imperative in allowing for reepithelization and decreasing the risk of scarring.

Laser ablation is another option leading to good cosmetic results. Reported laser therapies include conventional and fractionated carbon dioxide (CO2), argon, neodymium-doped yttrium aluminium garnet (Nd:YAG), erbium:YAG, and 1450-nm diode lasers. Complications include scarring and hyperpigmentation due to thermal injury with Argon lasers, poor hemostasis with Er:YAG, and extensive downtime with conventional CO2. Fractionated CO2 is most effective in patients with mild phymatous changes. Additionally, non-surgical therapies include radiofrequency ablation, coblation, and photodynamic therapy. Despite the multitude of options available, there is no clear gold standard treatment.

Combination therapy is emerging as a superior treatment option for severe phymatous change. Case reports have demonstrated good results with bipolar electrocautery/CO2, scalpel excision/electrosurgery, and erbium:YAG/CO2. Patients treated with combination therapy experience marked cosmetic improvement when compared to patients receiving treatment with a single modality alone. To our knowledge, this is the first reported case using excisional decortication to debulk and sculpt, followed by PDL to promote wound healing and minimize erythema and scar formation. Although the patient was required to return for multiple clinic visits, advantages of this treatment regimen include the ability to be performed in an outpatient clinical setting, decreased recovery time, and decreased risk from anesthesia.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE # 9**

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HISTORY OF PRESENT ILLNESS
The inpatient dermatology service was consulted by the neonatal intensive care unit for a 2-day-old male newborn with excess skin on his back and scalp. This finding was present since birth.

PAST MEDICAL HISTORY
Born at 32 weeks via normal spontaneous vaginal delivery
Birth weight: 3lb 14oz
Pregnancy Complications: oligohydramnios, PPROM, multiple fetal anomalies
Labor/Delivery Complications: maternal chorioamnionitis
Lung hypoplasia, respiratory distress syndrome, Left sided pneumothorax s/p needle thoracentesis
Proximal jejunal atresia s/p exploratory laparotomy and resection with enteroenterostomy
Absence of cavum septum pellucidum
Retinopathy of prematurity
Bilateral club feet

MEDICATIONS
Ampicillin
Gentamicin
Cyclopentolate with phenylephrine ophthalmic solution
Caffeine citrate

ALLERGIES
None

FAMILY HISTORY
No family history of excess skin, hernias, diverticulae, vascular abnormalities, or emphysema.
Mother, G1P1, with history of microcytic anemia, hyperthyroidism, depression, and anxiety.

SOCIAL HISTORY
Discharge plan was to live at home with mother and maternal grandmother.

PHYSICAL EXAMINATION
The back and posterior scalp had pronounced loose, redundant, and pendulous skin with decreased recoil on stretching. To a lesser extent, the bilateral upper and lower extremities, abdomen, and chest demonstrated loose skin with reduced elasticity. The patient had subtle facial abnormalities including a flattened philtrum, small, low-set ears, and sagging skin on the inferior cheeks.

DERMATOPATHOLOGY
Two adjacent punch biopsies were performed on the left back. Hematoxylin-eosin staining showed an unremarkable epidermis and no significant changes were noted in the dermis. Verhoeff-van Gieson stain highlighted a diminished number of elastic fibers in the papillary and reticular dermis.

The second biopsy was performed for electron microscopy, which demonstrated near complete absence of elastic fibers. The few elastic fibers that were noted had an immature structure with an excess of microfibrils compared to elastin.

ADDITIONAL STUDIES

Head Ultrasound: Echogenic subcutaneous tissue overlying vertex, likely focal soft tissue growth, subcutaneous edema, or hemorrhage
Echocardiogram: patent foramen ovale versus small secundum atrial septal defect
Genetic Microarray: 1.6 Mb gain of 2p14p13.3

DIAGNOSIS

Congenital Cutis Laxa (Generalized elastolysis)

TREATMENT AND COURSE

The patient was discharged home from the hospital on day 34 of life. Since discharge, health issues have included muscular hypertonicity, torticollis, poor weight gain, and emesis. His mother is considering the possibility of genetic testing through the University of Pittsburgh Cutis Laxa Research Study once the patient reaches the minimum weight requirement.

DISCUSSION

Cutis laxa is a rare connective tissue disorder characterized by loose, redundant skin with loss of elasticity. Congenital cutis laxa has an incidence of 1-2 per 400,000 people. The disease results from defective synthesis of elastic fibers and other proteins of the extracellular matrix. In addition to comprising 2%-4% of the dry weight of the dermis, elastic fibers are found in relatively high concentration in other organs such as the lungs and arteries. Therefore, extracutaneous manifestations of cutis laxa are common, including emphysema, lung hypoplasia, bladder and GI diverticulae, hernias, hip dislocation, vocal cord laxity, aortic aneurysms, vessel stenosis, and arterial tortuosity.

Elastic fibers are composed of two distinct structural components: a central amorphous elastin core and elastin-associated microfibrils. Elastin is a well-characterized connective tissue protein, which is synthesized and secreted as tropoelastin by fibroblasts and smooth muscle cells. During elastin fibrillogenesis, tropoelastin is extensively cross-linked by the oxidation of lysyl residues, which is mediated by copper dependent lysyl-oxidase enzyme. The microfibrillar component of elastic fibers is comprised of multiple proteins including fibrillins 1 and 3 and fibulins 1, 2, 3 and 4.

Cutis laxa may be inherited or acquired. The inherited forms of cutis laxa are heterogeneous with respect to gene mutation, systemic involvement, and prognosis. Autosomal dominant cutis laxa (ADCL) is due to mutations in the elastin gene (ELN). ADCL is typically considered benign with a normal life span, although systemic manifestations have been frequently reported including aortic root dilation, emphysema, and inguinal hernias. Skin involvement often improves with aging; the phenotype may be unrecognized in older patients. Approximately 30% of the patients with ADCL have been found to carry de novo dominant mutations in ELN.

Autosomal recessive cutis laxa (ARCL) is divided into several subtypes. ARCL-I is due to mutations in fibulin-4, (FBLN4/EFEMP2), fibulin-5 (FBLN5), or latent transforming growth factor-beta-binding protein 4 (LTBP4). Unlike ADCL, ARCL-I is associated with severe, often lethal, early systemic manifestations including developmental emphysema, diaphragmatic defects, arterial tortuosity, and aneurysms. ARCL-IIa and ARCL-IIb are caused by mutations in ATP6V0A2 and PYCR1, respectively.

Distinguishing features of ARCL-IIa include microcephaly, delayed closure of the fontanelles and neurological features; ARCL-IIb is associated with progeroid appearance, triangular face, and osteoporosis. ARCL-III (DeBarsy syndrome) is characterized by bilateral corneal opacities, progeroid appearance, and athetoid movements. Identified mutations include ATP6V0A2 and PYCR1. X-linked recessive cutis laxa (XLCL), also referred to as Occipital Horn Syndrome and previously designated Ehlers-Danlos syndrome type IX, is considered a less severe form of Menkes disease. In XLCL, mutations in the ATP7A gene, which encodes a copper-transporting ATPase, lead to impairment of copper-dependent enzymes such as lysyl oxidase. Clinical manifestations include downward-pointing exostoses on the occipital bone, chronic diarrhea, malabsorption, congenital hydronephrosis, bladder diverticulae, inguinal hernias, and coarse, kinky hair.

Acquired cutis laxa is subdivided into two types. Acquired cutis laxa type I typically begins in adulthood. Cutaneous involvement, characterized by pendulous, wrinkled skin, typically begins on the face and spreads caudally. Some patients have systemic involvement with emphysema, diverticulae, hernias, and aneurysms. Most cases are associated with an inflammatory dermatosis (dermatitis herpetiformis, Celiac disease, sarcoidosis), connective tissue disease (lupus, rheumatoid arthritis), malignancy (multiple myeloma, lymphoma), infection, renal disease, medication (isoniazid, penicillin, penicillamine, SSRI), amyloidosis, mastocytosis, or alpha-1 antitrypsin deficiency. Acquired cutis laxa type II, known as Marshall syndrome, affects young children. It is characterized by postinflammatory elastolysis after a neutrophilic dermatosis. Systemic involvement is generally absent in these patients.

The diagnosis of cutis laxa is based on clinical findings and confirmed with histopathology. The microscopic findings in cutis laxa include a reduction in the number of elastic fibers and fragmentation of these fibers. Because normal elastic tissue is difficult to visualize with routine hematoxylin-eosin, special elastic fiber stains including Verhoeff-van Gieson, orcein-Giemsa, Weigert, and Hart elastic stains are frequently used. Electron microscopy has been reported to be helpful in identifying the subtype of inherited cutis laxa. Genetic testing is also recommended. For congenital forms, additional labs and imaging may be warranted, such as serum copper, serum ceruloplasmin, urine copper, lysyl oxidase, serum elastase, alpha1-antitrypsin, echocardiogram, and pulmonary function tests.

Treatment options for cutis laxa are limited. Periodic follow-up is advised to detect systemic manifestations. Associated internal organ involvement requires multidisciplinary care. Botulinum toxin injections, thread lifts, and plastic surgery (e.g. rhytidectomy, ear lobe reduction, and blepharoplasty) have been employed with variable degrees of success in improving cosmetic appearance.

Our patient was diagnosed with congenital cutis laxa based on clinical presentation and histopathology. Given the electron microscopy findings, clinical presentation, and collaboration with the University of Pittsburg Cutis Laxa Research Study, we favor a diagnosis of the autosomal dominant type.

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CHICAGO DERMATOLOGICAL SOCIETY **Case # 10**

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CASE # 1

HISTORY OF PRESENT ILLNESS
A 46-year-old female patient was admitted to the burn unit from an outside facility for a worsening skin rash of 1-week duration. She had recently been diagnosed with prodromal rheumatoid arthritis and had started taking hydroxychloroquine 10 days prior to the onset of the eruption. The rash began on the hands and groin and subsequently spread to include her trunk, arms, and face. The patient discontinued hydroxychloroquine on day 2 of her symptoms, however the eruption continued to spread and her pruritus worsened. A biopsy was performed on day 4, and the patient was prescribed prednisone 60 mg daily. Her symptoms continued to worsen, and she was admitted to an outside hospital where two additional skin biopsies were obtained and treatment with methylprednisolone was initiated. The patient was transferred the following day to our institution due to concern for Stevens-Johnson syndrome.

PAST MEDICAL HISTORY
Protein C deficiency
Bipolar disorder
Asthma
Substance abuse

FAMILY HISTORY
Mother with history of rheumatoid arthritis
Aunt with history of systemic lupus erythematosus

MEDICATIONS
Acetaminophen with codeine
Docusate sodium
Quetiapine
Hydroxychloroquine sulfate

ALLERGIES
Penicillin
Sulfonamides

SOCIAL HISTORY
Cigarette smoking (30 pack year history)

PHYSICAL EXAMINATION
In a generalized distribution there were erythematous superficial papules with desquamation, which coalesced into larger plaques. There was no conjunctival injection or mucosal erosion/ulceration.

DERMATOPATHOLOGY
Biopsy results demonstrated a subcorneal, pustular dermatitis with underlying mixed dermal inflammation and extravasated erythrocytes.

LABORATORY RESULTS

Laboratory Study	Patient Result	Reference Range
CMP	Wnl	--
WBC (K/UL)	13.5	3.5-10.5
RBC (M/UL)	3.64	3.80-5.70
Hemoglobin (GM/DL)	10.2	11.5-15.5
Hematocrit (%)	31.0	34.0-46.5
Absolute Monocyte Count (K/MM^3)	1.1	0.0-1.0
Absolute Granulocyte Count (K/MM^3)	11.1	1.5-7.0

DIAGNOSIS
Acute generalized exanthematous pustulosis (AGEP)

TREATMENT AND COURSE
At the time of transfer to our institution, methylprednisolone was discontinued and prednisone was initiated. In addition, the patient was treated with diphenhydramine and topical triamcinolone ointment. Her skin findings improved and she was discharged from the hospital 3 days later with a planned prednisone taper. Upon follow-up two weeks later, superficial erythema and desquamation was noted on the bilateral upper thighs and palms, and the patient complained of associated itching and joint stiffness. Prednisone was briefly increased followed by a slow taper over the following 2 weeks. At her subsequent visit the rash and symptoms had completely resolved and lab results were unremarkable.

CASE # 2

HISTORY OF PRESENT ILLNESS
An 83-year-old female was admitted to the burn unit from an outside hospital for worsening skin rash of 10 days duration. The patient had started hydroxychloroquine for polymyalgia rheumatica 19 days prior to the onset of her symptoms. The patient's son first observed the rash on her face. The eruption subsequently spread to involve the neck and upper trunk. She was started on a methylprednisolone (medrol) dose pack on day 3 of the rash. On the third day of treatment, the patient's rash worsened acutely, spreading to involve the upper and lower extremities including the digits. She was admitted to an outside hospital, and hydroxychloroquine was discontinued. Treatment with methylprednisolone and vancomycin was initiated. Her symptoms continued to worsen and she was transferred to our institution on day 29 of the rash due to concern for Stevens-Johnson syndrome.

PAST MEDICAL HISTORY
Hypertension
Osteoarthritis
Obesity
Atrial Fibrillation
Polymyalgia rheumatica

FAMILY HISTORY
No family history of cutaneous disorders

MEDICATIONS
Alendronate
Amiodarone
Amlodipine
Aspirin
Docusate sodium
Gemfibrozil
Hydrocodone with acetaminophen
Hydroxychloroquine
Isosorbide mononitrate
Prednisone
Warfarin

ALLERGIES
Sulfonamides

SOCIAL HISTORY
No tobacco use, no alcohol use, no illicit drug use

PHYSICAL EXAMINATION
On the face, shoulders, proximal upper extremities, chest, and back there were confluent, blanchable, erythematous plaques with overlying superficial desquamation. The bilateral forearms and dorsal and palmar surfaces of the hands had confluent, beefy-red eroded plaques and overlying pinpoint pustules on the ventral surfaces of her fingers. Her abdomen and thighs had wide spread erythematous and targetoid beefy-red plaques with overlying desquamation, many with central bullous collections of purulent fluid. On the folds of the abdominal pannus there were focal erythematous pinpoint pustules. The dorsal surfaces of her feet had confluent circinate erythematous macules and papules with few discrete purulent bullae. There was no oral, ocular, or genital involvement.

DERMATOPATHOLOGY
Biopsy demonstrated a subcorneal, pustular dermatitis with underlying dermal edema and perivascular mixed inflammation, with numerous neutrophils.

LABORATORY DATA

Laboratory Study	Patient Result	Reference Range
CMP	wnl	--
WBC (K/UL)	33	3.5-10.5
Absolute Promyelocyte Count (K/MM^3)	0.3	<0.1
Absolute Metamyelocyte Count (K/MM^3)	0.6	<0.1
Segmented Neutrophil Count (**(**K/MM^3)	28.0	1.5-7.0
Absolute Lymphocyte Count (K/MM^3)	0.6	1.0-4.0

DIAGNOSIS
Acute generalized exanthematous pustulosis (AGEP)

TREATMENT AND COURSE
Upon admission to our institution, two punch biopsies were obtained. Methylprednisolone and meticulous wound care were initiated. Over the following 4 days the patient's skin findings improved and methylprednisolone was transitioned to prednisone. The skin continued to improve, her WBC count normalized, and the patient was discharged on a slow prednisone taper. She was subsequently lost to follow up.

CASE # 3

HISTORY OF PRESENT ILLNESS
A 70-year-old female patient with long standing mucocutaneous lichen planus presented to clinic with a complaint of a worsening rash of 5 days duration. Therapy with hydroxychloroquine had been initiated16 days prior to presentation along with a 12-day prednisone taper for acute worsening of her lichen planus along with erythema nodosum. The eruption had started on her left flank the day after completing the prednisone, and subsequently spread to her back, chest, abdomen, groin, hands, arms, legs, and feet. The rash was bright red with some peeling, and felt "prickly and warm." She had discontinued the hydroxychloroqine on the first day of the eruption, but continued to notice new lesions arising on her arms, hands, and scalp.

PAST MEDICAL HISTORY
Atrial fibrillation
Erythema nodosum
Lichen planus

FAMILY HISTORY
No family history of cutaneous disorders

MEDICATIONS
Hydroxychloroquine
Diltiazem
Sertraline
Xarelto

ALLERGIES
Propylene glycol
Sulfonamides
Nickel

SOCIAL HISTORY
No tobacco use, no alcohol use, no illicit drug use

PHYSICAL EXAMINATION
On the chest, back, abdomen, and bilateral upper and lower extremities there were brightly erythematous, arcuate plaques with superficial desquamation and areas of pinpoint pustules. No oral, ocular, or genital involvement.

DIAGNOSIS
Acute Generalized exanthematous pustulosis (AGEP)

TREATMENT AND COURSE

Upon development of the rash, the patient discontinued hydroxychloroquine and began applying betamethasone to the affected areas. She noted minimal improvement of her skin findings and continued to develop new skin lesions. Upon presentation to our clinic on day 5 of the rash, she was started on cetirizine, diphenhydramine, and topical triamcinolone ointment. At follow-up, the patient noted slow but steady improvement, with less redness and pruritus but increased peeling of her skin. She continued on cetrizine and triamcinolone ointment, and one month later reported the rash had completely resolved with no residual complications or scarring.

DISCUSSION

Acute generalized exanthematous pustulosis (AGEP) is a cutaneous reaction characterized by rapid and widespread formation of nonfollicular, sterile pustules on an erythematous base, classically involving intertriginous skin. Associated findings may include facial edema, low-grade fever, and neutrophilic leukocytosis. Superficial desquamation followed by spontaneous resolution typically occurs within days to weeks of removing the suspected cause. In 2007, the European Study of Severe Cutaneous Adverse Reactions (EuroSCAR) published proposed diagnostic criteria for AGEP that included lesion morphology, disease course, and characteristic histopathologic features.

The incidence of AGEP is estimated to range from 1 to 5 cases per million per year, and has been associated with human leukocyte antigens B51, DR11, and DQ3. The reaction pattern is medication-induced in the vast majority of cases, with beta-lactam antibiotics, anti-epileptics, and calcium channel blockers as the most commonly reported causes. Although relatively rare, antimalarial medications have also been linked to AGEP. Since an initial case in 1963, there have been 26 reported cases in the English literature describing hydroxychloroquine (HCQ)-induced AGEP and in 2000, the US Food and Drug Administration required a change to the labeling of HCQ to include the addition of AGEP as a potential adverse reaction.

HCQ is a synthetic analogue of quinine (a basic amine) derived from the bark of the cinchona tree. It was originally used exclusively in the treatment and prophylaxis of malaria. Its exact mechanism of action is unknown, however subsequent discovery of its immunosuppressive and anti-inflammatory effects have since dramatically expanded its clinical usage. It is now routinely utilized as first line treatment in a number of rheumatologic, dermatologic, and vasculitic conditions.

Adverse cutaneous effects due to HCQ are characterized as hypersensitivity reactions and include alopecia, hair bleaching, hyperpigmentation, exacerbation of psoriasis, and skin eruptions (urticarial, morbilliform, lichenoid, Stevens-Johnson, and AGEP). Interestingly, between 2000 and 2001 one institution reported a 100-fold increase in the number of cutaneous adverse events in patients treated with HCQ. This steep rise coincided with a change in formulation (a tablet coloring agent) by the manufacturer.

There are two onset patterns that have been described for AGEP. A median time to onset of 1-3 days occurs for antibiotic-induced AGEP. For all other medication-induced AGEP, including HCQ-induced, the mean time to onset is slightly longer and occurs approximately 11 days after initiating the medication. It has been suggested that the rapid onset of AGEP in patients treated with antibiotics is likely due to prior sensitization. The increased latency period in cases of HCQ-induced AGEP may be related to immunologic dysregulation secondary to the underlying disease, but is more likely due to a lack of prior sensitization.

The pathogenesis of AGEP is not completely understood, however studies suggest drug-specific T cells may play a critical role. Drug-specific cytotoxic CD4+ and CD8+ T-cells produce large

amounts of interleukin (IL)-8, a potent neutrophil-attracting chemokine that leads to neutrophil accumulation within vesicles. Interferon gamma and granulocyte/macrophage colony-stimulating factor levels are also increased, which aid in the survival of neutrophils and augment neutrophil response. While drug-specific T cell studies have been performed on a number of AGEP implicated medications, HCQ was not among those studied, therefore the pathogenesis as it relates to HCQ can only be hypothesized.

The cases discussed today are unique in their clinical presentations. While blister formation, facial edema, and targetoid lesions may be seen with AGEP, they are less commonly observed clinical features. Each of the three patients in this series initially presented with targetoid macules, patches, and/or bullae, suggestive of erythema multiforme (EM) or other bullous disorders; however, the histology and clinical course in all cases were consistent with AGEP. Interestingly, severe cases of AGEP simulating toxic epidermal necrolysis (TEN) have been reported. These cases were likely due to a confluence of pustules causing extensive desquamation and a falsely positive Nikolsky sign. A review of the literature yielded one case of AGEP progressing to TEN that could be specifically attributed to HCQ. Interestingly, the initial presentation clinically and histologically was that of AGEP, however progression to targetoid lesions, full thickness sloughing, and significant oral involvement developed. None of the three patients presented today had mucosal involvement and no keratinocyte necrosis was noted histologically when biopsy results were available.

In the majority of cases, AGEP is benign and self-limited. It typically resolves within 15 days of stopping the implicated medication. Treatment is therefore usually unnecessary; however, in order to limit the extent of cutaneous involvement and to relieve symptoms, patients may be treated with systemic and topical corticosteroids and anti-histamines, with expected gradual improvement over a 2-3 week period.

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