Chicago Dermatological Society

April 2015
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, April 15, 2015
Stroger/Cook County Hospital
Sidney Barsky Lecture

Conference Host:
Division of Dermatology
Stroger Cook County Hospital
Chicago, Illinois

Program

Conference Locations

Stroger Cook County Hospital; 1900 W. Polk, Chicago
Main hospital – entrance corner of Ogden & Damen or through the CCH parking garage
Hektoen Institute – 627 S. Wood St., 1st Floor Lobby & Auditorium
Parking: Cook County Hospital Garage: entrance on Polk St.
Alternate Parking: Rush Medical Center - Harrison just west of Ashland

Registration Area – beginning at 8:00 a.m. (sign-in sheets, name badges, exhibitors)
Lobby area of the Hektoen Institute; 627 S. Wood

Please note: Protocol books will be distributed in the Dermatology Clinic, Main Hospital until 10:30 a.m., and then at the registration area. ***Registration will be located at the Hektoen Institute only.*** *You may proceed directly to the clinic and register later, if you prefer.*

Program Events

8:00 a.m.	**Registration begins for all attendees** Continental breakfast & visit with exhibitors *Hektoen Institute, 1st floor lobby*
9:00 a.m. - 10:00 a.m.	**Resident Lecture** *Hektoen Auditorium, 627 W. Wood, 1st Floor* "What's New in Therapy" *Kenneth Tomecki, MD, FAAD*
9:30 a.m. - 10:45 a.m.	**Clinical Rounds** - Patient and Slide Viewing Dermatology Clinic G, 2nd Floor (use Elevator #1) Stroger-Cook County Hospital, 1900 W. Polk
11:00 a.m. - 12:00 p.m.	**General Session** *Hektoen Institute Auditorium 627 S. Wood, 1st Floor* BARSKY LECTURE "Resurgent Diseases" *Kenneth Tomecki, MD, FAAD*
12:00 p.m. - 12:40 p.m.	Box Lunches - Hektoen Institute Auditorium
12:40 p.m. - 12:50 p.m.	**CDS Business Meeting** *Hektoen Institute Auditorium*
12:50 p.m. - 2:30 p.m.	**Case Discussions** *Hektoen Institute Auditorium*
2:30 p.m. - 3:00 p.m.	**Maintenance of Certification** Self-Assessment Questions
3:00 p.m.	**Meeting adjourns**

Mark the Date!

Next CDS monthly meeting – Wednesday, May 20, 2015; hosted by Rush University at the Stephens Convention Center in Rosemont.

Guest Speaker

KENNETH TOMECKI, MD FAAD
Vice Chairman
Dermatology at Cleveland Clinic
Cleveland, OH

Delivering the Sidney Barsky Lecture

Dr. Tomecki is a graduate of Columbia College and Columbia College of Physicians and Surgeons. He completed his medical and dermatologic training at SUNY at Buffalo, followed by fellowship at the National Cancer Institute, NIH. He is a Board-certified dermatologist practicing in Cleveland since 1980.

Dr. Tomecki is a clinician/educator whose areas of expertise cover the gamut of adult clinical dermatology. His main interests are infectious diseases and medical education. He lectures regularly, both nationally and internationally, including many stints as visiting professor. He's the author of more than a hundred primary and secondary publications, including more than forty book chapters. In addition, he has been an assistant editor of The JAAD. Dr. Tomecki is an active member of the American Academy of Dermatology. He was a member of the Academy's Board of Directors for four years and was recently elected Vice-President-elect.

CME Conflict of Interest Disclosure: Dr. Tomecki will make his conflict of interest disclosure at the meeting.

Table of Contents

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

CASE 1

Presented by Vidya Shivakumar, MD and Warren Piette, MD

Patient is an 81-year-old woman who presented with abrupt-onset "burning" scalp lesions.

UNKNOWN

Key location(s): Left lower extremity **CASE 2A**

Presented by Tarana Mohammadi, MD and Joerg Albrecht, MD

History of Present Illness

A 35-year-old man with a history of left hip congenital dysplasia and acute on chronic osteomyelitis was admitted for group B streptococcus septic arthritis of his left knee. Dermatology was consulted for evaluation of a large erythematous patch involving his left lower extremity. The patient had been diagnosed with chronic left-lower-extremity lymphedema in Mexico at a young age. Left leg enlargement had been present since birth. Skin color changes, first noticed on his ankle, began at age 13 and over the years continued to grow proximally.

Past Medical History

Left hip congenital dysplasia, acute on chronic osteomyelitis resulting in chronic hip pain, and palliative femoral head ostectomy

Medications

None

Review of Systems

Positive for fever, chills, and nausea

Physical Exam

Pelvic tilt while standing
Left lower extremity: hypertrophy, hyperpigmented to erythematous reticulated patches with sharply circumscribed borders on lateral aspect, many venous varicosities, no induration or edema

Laboratory Data

Significant abnormal labs:

WBC	11.4 k/µL	[4.4 - 10.6 k/µL]
Neutrophil #	10.3	[2.2 - 6.9]
Lymphocytes #	0.5	[1.2 - 3.4]
Prothrombin Time	15.9 sec	[12.1 - 14.7 sec] – after starting VTE prophylaxis

Histopathology

Punch biopsy from left lateral thigh, erythematous portion: Increased numbers of capillaries and thin-walled blood vessels traversing through the mid dermis and subcutaneous fat.

Radiology

CT of the pelvis and bilateral hips: Post-surgical changes consistent with the left femoral head resection and evidence of chronic infection.

CT angiogram of lower extremities: Congenital left hip dysplasia, left suprapatellar joint effusion suggestive of synovitis, hemihypertrophy of the lower extremity with multiple dilated venous channels/varicose veins.

Echocardiogram: Normal ejection fraction.

Diagnosis
Klippel–Trénaunay syndrome

Treatment and Course
The patient is followed by musculoskeletal medicine, physical therapy and the vascular service. He can walk without assistance and has continued with an at-home physical therapy regimen. He has been pain-free and is able to work full-time. The patient is awaiting fitting of vascular garments and orthopedic shoes.

Key location(s): Right lower extremity **CASE 2B**

History of Present Illness
A 31-year-old woman with a history of recurrent cellulitis presented to the emergency department with a two day history of worsening right lower extremity swelling, pain, and redness. She reported subjective fevers, chills, and headache, and was tachycardic. Deep venous thrombosis was ruled-out, and she was admitted for treatment of cellulitis. Further history revealed that the leg swelling began at age five and had worsened over the last ten years.

Past Medical History
Chronic lymphedema

Medication
Ibuprofen

Social History
No smoking, alcohol, or illicit drug use

Review of Systems
Negative for nausea, vomiting, diarrhea, chest pain, shortness of breath, cough, dizziness, neck pain, or photophobia

Physical Exam
Right lower extremity: hypertrophy, prominent varicosities, and an ill-defined, faint reticulated erythematous patch. Focal areas within the patch are fibrotic with overlying hyperkeratotic papules; remaining areas of swelling are pliable and soft.

Laboratory Data
The following labs were remarkable/abnormal:

WBC	16.0 k/μL	[4.4 – 10.6 k/μL]
Neutrophil #	13.9	[2.2 – 6.9]

Radiology
X-rays of the tibia/fibula: Soft tissue swelling with diffuse demineralization and mild degenerative changes of the medial knee joint compartment.

Venous duplex ultrasound of her right lower extremity: No DVT.

CT angiogram of the right lower extremity: Marked soft tissue swelling of the calf and ankle. Multiple venous collaterals in the right lower extremity. Normal primary vasculature with extensive tortuous branching. No arterio-venous fistulas.

Diagnosis
Klippel–Trénaunay syndrome

Treatment and Course
The patient was fitted for compression stockings and leg elevation was advised.

Key location(s): Right trunk/extremities **CASE 2C**

History of Present Illness
A 36-year-old woman with an extensive "birth mark" was admitted to the hospital for treatment of cellulitis and work-up of presyncopal event. Dermatology was consulted for evaluation of her "birth mark," which encompassed the right side of her body. The lesion had become more red and swollen over the last two years. Ambulation was difficult and she had recently developed finger contractures of the right hand over the course of months.

Past Medical History
None

Medication
Naproxen

Review of Systems
Negative for emesis, diarrhea, chest pain, shortness of breath, cough, or photophobia

Physical Exam
Right side of body involving shoulder, dorsal arm, forearm, palm, chest, back, and lower extremity: large geographic erythematous to violaceous patches
Right lower extremity: hypertrophy, multiple tortuous varicosities, and a soft compressible venous bundle
Flexion contracture of 5th digit, and mild involvement of 2nd digit

Laboratory Data
The following labs were remarkable/abnormal:

WBC	19.6 k/μL	[4.4 - 10.6 k/μL]
Neutrophil #	17.9	[2.2 - 6.9]
Lymphocytes #	1.1	[1.2 - 3.4]
Prothrombin Time	15 sec	[12.1 - 14.7 sec] – after starting VTE prophylaxis
D-Dimer	6.66	[0.27 - 0.49]

Radiology
Venous duplex ultrasound: No DVT.
MRA of the right upper extremity: Multiple high flow state arteriovenous malformations, predominating in the right hand (digital arteries and large draining vein along the ulnar side of the forearm), as well as the distal forearm and cubital fossa.
MRA of the right lower extremity and angiogram: Multiple, complex arteriovenous malformations from the mid right thigh to the distal lower leg. High flow vascular malformations of the right lower extremity predominate below the right knee joint. On arteriogram, these lower extremity arteriovenous fistulas were not amenable to embolization.

Diagnosis
Parkes-Weber syndrome

Treatment and Course
The treatment of this patient is ongoing and will continue to require a multidisciplinary approach. She has an upcoming follow-up visit with vascular surgery for further assessment of the upper extremity. Multifocal aterio-venous malformations such as those

discovered in this patient can eventually cause cardiac overload, and may well have been the cause of the presyncopal episode. Currently, the patient wears elastic support garments and has infrequent right lower extremity pain, controlled by over the counter nonsteroidal anti-inflammatory medications.

Discussion

Klippel–Trénaunay syndrome and Parkes Weber syndrome are clinically similar vascular malformations. After a brief overview of the two entities, the focus of this discussion will be on complications and management of patients presenting with these syndromes.

Klippel–Trénaunay syndrome	Parkes Weber syndrome
Slow-flow malformations (venous and lymphatic)	High-flow malformations (arterio-venous)
Varicosities	Varicosities uncommon
No arterio-venous fistulas	Characterized by arterio-venous fistulas (local temperature increase, palpable pulse, thrill and/or murmur)
Lymphedema	Lymphedema uncommon
Hypertrophy of soft-tissue and +/- bone	Hypertrophy of muscle and bone
No lytic lesions	+/- lytic bone lesions
Thrombophlebitis, microthrombi, and pulmonary embolism	Increased cardiac load may lead to high output heart failure, cutaneous ischemia, and +/- pre-syncopal or syncopal episodes
Port wine stains/capillary malformation Primarily with lower limb involvement Limb length discrepancy	

Klippel-Trénaunay syndrome is a rare, usually sporadic congenital syndrome consisting of the following triad: capillary malformation, underlying bony and soft tissue hypertrophy, and varicose veins and/or venous malformations. To make the diagnosis two of these three features must be present. Simple Klippel-Trénaunay syndrome involves a blotchy or segmental port wine stain in a haphazard distribution over the affected extremity. This type has less dissymmetry and less severe venous malformations. Complex Klippel-Trénaunay syndrome is characterized by sharply demarcated, geographic port wine stains that are usually seen over the lateral lower extremity. This type has a higher risk of associated lymphatic malformations, more severe deep venous malformations, and incurs more complications (GU/GI bleeding, hemothorax, heart failure, massive limb overgrowth, and cellulitis).

Lymphatic malformations in Klippel-Trénaunay syndrome may result from lymphatic hypoplasia, leading to lymphedema or lymphatic macrocysts. The varicosities in Klippel-Trénaunay may be noticeable around the time a child starts walking and are complex, extensive, and avalvular. A marginal venous system typically exists and stagnant flow may lead to thrombophlebitis, ulcers, pain and recurrent cellulitis. Venous malformations may trigger an intravascular coagulopathy suggested by an elevated D-dimer or low

fibrinogen level. Both thrombotic and hemorrhage complications may ensue. Calcified phleboliths on leg imaging correlates with microthrombi and patients are at risk for venous thrombosis, pulmonary embolism, and chronic thromboembolic pulmonary hypertension. Patients with a prolonged prothrombin time, associated with consumption of fibrinogen and factor V, are at increased risk of bleeding and can have painful hematomas, hemarthrosis, and hemorrhages in the GI tract or other sites.

Diagnostic tests have specific utilities. Doppler ultrasound evaluates velocity and direction of flow, MRI/MRA quantifies vascular and lymphatic malformation, extension and tissue hypertrophy and types it. Arterial and venous angiography allows detailed evaluation of vasculature. Angiography is invasive with potential complications, but can be diagnostic as well as therapeutic if arteriovenous fistulas are embolized. In those with vascular malformations, high-flow anomalies may not be evident on initial exam. Therefore, ongoing follow-up and repeat studies may be necessary in order to monitor evolution of the lesion. In Parkes Weber patients, an echocardiogram measures pulmonary arterial pressure and cardiac muscle thickness. D-dimer and fibrinogen levels may be helpful in both.

Treatment of vascular malformation syndromes is preferably conservative. Managing venous insufficiency is essential. Limb elevation and compression stockings decrease swelling and discomfort, prevent and heal ulcers and infection. Lymphedema is managed with manual drainage and compression wraps, exercise regimens, and compression garments. Prophylactic antibiotics may be needed for recurrent cellulitis. Low molecular weight heparin has improved pain and reduced thrombosis in patients with localized intravascular coagulation. Regional osteoporosis may need to be treated with bisphosphonates. Pulsed dye laser is useful for port-wine stains, but is generally less effective than on the face, requires many sessions, and lesional recurrence is common. Orthopedic surgery may be indicated in children with limb length discrepancies including procedures that halt cartilage growth or elongate/shorten bones. Correction is important in prevention of future pelvic tilt and scoliosis. In adults, orthotic shoes are utilized. Surgical excision of venous and lymphatic malformations should be carefully considered as these occasionally recur. When arteriovenous malformations are present, surgical removal of the nidus may be attempted after embolization (better bleeding control). In patients with severe pain, recurrent infections, necrosis, deformity, and worsening heart failure, partial amputations have been done.

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Key location(s): Face, trunk **CASE 3**

Presented by Mariam Mafee, MD, Nicole Joy, MD, and Jerry Feldman, MD

History of Present Illness
A 3-year-old boy with a history of asthma was referred by his pediatrician for eczema and acne management. He presented with many skin-colored facial papules and truncal plaques that had been persistent for two years despite treatment with hydrocortisone 1% ointment. Developmental milestones were notable for speech delay, a presumable complication of his conductive hearing loss.

Past Medical History
Recurrent otitis media, conductive hearing loss, speech delay, obesity, atopic dermatitis, asthma, seasonal allergies, disruptive behavior disorder

Medications/Allergies
Singulair, hydrocortisone 1% ointment
No known drug allergies

Social History
Negative

Review of Systems
Negative

Physical Exam
BP: 98/56
Face: scattered small shiny tan to dark-brown papules
Left lower back and torso: minimally elevated, grouped skin-colored to yellowish papules coalescing into ½ palm-sized plaques

Laboratory Data
The following labs were remarkable/abnormal:

TSC1 gene	Negative
TSC2 gene	Heterozygous for the c.826_827delAT pathogenic variant in exon 9

Electrocardiogram:
Normal sinus rhythm

Histopathology
Left lower back, punch biopsy:
Epidermis with basal melanosis, some collagen fibers are thickened and eosinophilic with haphazard arrangement. No inflammatory infiltrate.

Radiology
CT Head: Multiple calcified and noncalcified cortical and subependymal tubers

Diagnosis
Tuberous sclerosis

Treatment and Course

The patient was referred to genetics and testing revealed a heterozygous pathogenic mutation in *TSC2*, confirming the diagnosis. Systemic work-up included an abnormal head CT showing multiple cortical tubers and a normal renal ultrasound. Evaluation by cardiology, ophthalmology, and dentistry were unremarkable. He is followed by pediatric psychiatry and was diagnosed with disruptive behavioral disorder, for which he will receive therapy. Future evaluation with neurology is scheduled.

Discussion

Tuberous sclerosis (TSC) is an autosomal dominant disease that can affect nearly any organ system, often presenting with cutaneous lesions as the first sign. The incidence is estimated to be 1 in 5,800 births and about two-thirds of cases are sporadic. It is caused by pathogenic mutations in *TSC1* and *TSC2* genes, which encode tuberin and hamartin, respectively. These proteins inhibit the activity of mammalian target of rapamycin complex (mTORC1), which regulates cell growth and metabolism.

Although a majority of individuals with tuberous sclerosis have a pathogenic mutation in TSC1 or TSC2, genetic studies have reported that 10-25% of patients do not have a mutation that can be detected by conventional genetic testing. Of those patients with an identifiable mutation, TSC2 mutations are more common than TSC1. Additionally, individuals with a *TSC2* mutation tend to have more severe symptoms. *TSC2* mutations are more frequently seen in de novo cases compared to familial cases. However, amongst patients with *TSC2* mutations, familial cases tend to have a less severe phenotype.

The first sign of tuberous sclerosis is often hypopigmented macules, which are usually present at birth or within the first few months of life. Patients begin to develop angiofibromas as early as two years of age and most will have them by adolescence. The characteristic shagreen patch, which represents a connective tissue nevus, is commonly seen in the lumbosacral area at around two years of age. Finally, periungual papules usually develop later in childhood through adulthood. Extracutaneous manifestations include hamartomas of the eye, brain, kidneys, heart and lungs as well as seizures and mental retardation. Because clinical presentation varies greatly among affected patients, it is important to have clear diagnostic criteria and standardized recommendations for surveillance and management.

In 2012, the International Tuberous Sclerosis Complex Clinical Consensus Conference was held to update previously existing criteria. This case is presented to highlight the major changes in diagnostic criteria as well as the most recent management recommendations. Most importantly, the updated criteria now state that genetic testing for *TSC1* and *TSC2* is diagnostic. The new criteria also include numerical requirements for many features. The table below lists the 2012 revised criteria in comparison the 1998 criteria (changes depicted in bold, table modified from the figure in Teng et al., 2014). A diagnosis of TSC requires at least two major features or one major and two minor features.

1998 Diagnostic Criteria	2012 Diagnostic Criteria (changes in bold)
Genetic Criterion	
None	***TSC1* or *TSC2* mutation**
Major Features	
Facial angiofibromas or forehead plaque	**≥ 3 angiofibromas or fibrous cephalic plaque**
≥ 3 hypomelanotic macules	≥ 3 hypomelanotic macules, **at least 5mm in diameter**
Nontraumatic ungula or periungual fibroma	**≥2 ungual fibromas**
Shagreen patch (connective tissue nevus)	Shagreen patch
Multiple retinal hamartomas	Multiple retinal hamartomas
Cortical tuber	**Cortical dysplasias**
Subependymal nodule	Subependymal nodules
Subependymal giant cell astrocytoma	Subependymal giant cell astrocytoma
Cardiac rhabdomyoma, single or multiple	Cardiac rhabdomyoma
Lymphangioleiomyomatosis	Lymphangioleiomyomatosis
Renal angiomyolipoma	**≥2 angiomyolipomas**
Minor Features	
Multiple randomly distributed pits in dental enamel	**≥ 3 dental enamel pits**
Gingival fibromas	**≥2 intraoral fibromas**
"Confetti" skin lesions	"Confetti" skin lesions
Nonrenal hamartomas	Nonrenal hamartomas
Multiple renal cysts	Multiple renal cysts
Retinal achromic patch	Retinal achromic patch
Hamartomatous rectal polyps	
Bone cysts	
Cerebral white matter migration lines	

The updated surveillance and management recommendations state that every patient with suspected or confirmed TSC should undergo genetic counseling and testing, as well as full body skin, ophthalmologic and dental exams. Additional testing includes a brain MRI (to assess for tubers, subependymal nodules, and sub-ependymal giant cell astrocytomas), abdominal imaging (to assess for angiomyolipomas and renal cysts), neuropsychiatric evaluation, electroencephalogram, blood pressure monitoring and evaluation of renal function. If a rhabdomyoma is identified prenatally, cardiac status should be evaluated via electrocardiogram and echocardiogram (potentially with fetal echocardiography). High-risk patients should also undergo pulmonary function testing and chest CT.

Patients with this disorder require a multi-disciplinary approach and life- long monitoring given the complexity of the disease. It is important to be aware of the most recent guidelines so that we provide our patients with thorough evaluation and appropriate care.

References

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Key location: Face **CASE 4A**

Presented by Nicole Joy, MD, Mariam Mafee, MD, David Reid, MD

History of Present Illness
One-day-old female born at 38 weeks was transferred from an outside hospital for a prominent midline abdominal defect. On day six of life, she developed a red patch on the left jaw and chin, which gradually enlarged and thickened. There was no evidence of respiratory difficulty.

Past Medical History
None

Medications/Allergies
None/NKDA

Family History
Father born with cleft lip and bifid uvula

Physical Exam
Left cheek extending to the lateral posterior neck: ill-defined, erythematous plaque with overlying telangiectasias; similar lesions on the inferior lip and right cheek.

Superior to umbilicus: linear atrophic plaque with prominent vasculature and violaceous hue.

Inferior to umbilicus: soft, reducible mass.

Pertinent Labs

Hb/Hct	15.7 g/dL / 46.9%	[10.0-20.0 g/dL] / [31-55%]
Plt	166 k/μL	[200-400 k/μL]

Imaging
MRI Abdomen/Pelvis without IV contrast: Umbilical hernia defect associated with slow flow vascular malformation, predominantly venous, with extension to the anterior abdominal wall.

MRI/MRA Head/Neck: Unremarkable

Echocardiogram: Patent foramen ovale (PFO) with left to right shunt and mild tricuspid regurgitation. Otherwise, all structures unremarkable.

Diagnosis
PHACE(S) Syndrome

Treatment and Course

Pediatric surgery was consulted for the abdominal defect and determined that no surgical intervention was warranted. By week two of life, the facial vascular lesion had evolved, becoming more elevated and extensive. The patient underwent PHACE(S) workup and initiation of propranolol therapy.

Imaging studies, detailed above, were unremarkable. A multidisciplinary approach was implemented, with neurology, ophthalmology, cardiology, and ENT consulted. Facial, ocular and laryngoscopic exams revealed no abnormalities.

After cardiac clearance, propranolol was started and titrated up to 2 mg/kg/day. Treatment was well-tolerated and the patient was discharged after two days of monitoring. As an outpatient, she has remained on this treatment, with stable appearance of the hemangioma. She continues to follow-up with cardiology, ophthalmology, ENT, and pediatric surgery.

Key location: Face **CASE 4B**

History of Present Illness
Four-week-old extremely premature female born at 24 weeks presented with an enlarging red plaque on the left frontotemporal scalp and face. The lesion was first noted at day two of life, when it was documented as light red and flat by the primary team. During the first few weeks of life, the patient was being managed in the neonatal intensive care unit for multiple life threatening conditions, and it was not until these were stabilized that dermatology was asked to evaluate the patient one month later.

Past Medical History
Respiratory Distress Syndrome complicated by pulmonary hemorrhage s/p intubation
Patent ductus arteriosus (PDA) s/p indomethacin
Anemia at birth s/p red blood cell transfusion
Sepsis (+MSSA)
Hyperbilirubinemia
Left inguinal hernia s/p repair
Retinitis of prematurity s/p laser photocoagulation

Medications
Vancomycin, gentamicin, caffeine, fuconazole, albuterol nebulizer, budesonide nebulizer

Allergies
NKDA

Family History
No significant history

Physical Exam
Left frontotemporal scalp, forehead, upper eyelid, cheek, and ear: well-demarcated, deep red, elevated, rubbery plaque.

Pertinent Labs

Hb/Hct	12.8 g/dL / 40.8%	[10.0-20.0 g/dL] / [31-55%]
Plt	223 k/μL	[200-400 k/μL]

Imaging
Liver Ultrasound: No evidence of hemangioma

MRI/MRA Head: Large left facial and neck infantile hemangioma with extension into the left orbit, left cavernous sinus, inferior CP angle, prepontine and interpendicular cisterns, and inferior cerebellar vermis. No narrowing, stenosis, or aberrant course of vessels. Otherwise, unremarkable brain MRA.

MRI/MRA Neck: Recommended but not completed

Echocardiogram: PFO with left to right shunt. Small PDA with left to right shunt. Mild tricuspid regurgitation. Otherwise, all structures unremarkable.

Diagnosis
Likely PHACE(S) Syndrome

Treatment and Course
Again, a multidisciplinary approach, with neurology, ophthalmology, cardiology, and ENT input was recommended. Prednisolone and propranolol were started by the primary team, but ongoing dosing was disrupted by repeated episodes of hypoglycemia. Eventually, the primary team titrated propranolol up to 2mg/kg/day. While on this dose, the patient developed an ulceration of the left helix, and thus the propranolol dosage was decreased to 1mg/kg/day. The ulcer was treated with local wound care, becaplermin gel, metronidazole gel, and pain control. Once the lesion stabilized, propranolol was again increased to 1.5mg/kg/day, with complete healing of the helix after two and a half months. Prednisolone was tapered down and discontinued at five months of age. As an outpatient, the appearance of her facial hemangioma continues to improve on propranolol therapy. She continues to follow as an outpatient with ENT, ophthalmology, neurology, and cardiology.

Discussion
Infantile hemangiomas represent the most common benign tumors in infancy, with an estimated incidence of 4-5%. In the setting of a large infantile hemangioma, it is critical to rule out extracutaneous manifestations and PHACE(S) syndrome. The acronym PHACE(S) stands for posterior fossa malformations, hemangioma, arterial anomalies, cardiac anomalies and coarctation, eye abnormalities, sternal clefting and supraumbilical abdominal raphe. Although PHACE(S) syndrome is uncommon, it has been reported that up to 31% of infants with large (>22cm^2) head and neck hemangiomas meet criteria. These include facial hemangioma >5cm in diameter plus various cerebrovascular, structural brain, cardiovascular, ocular, and ventral anomalies.

Evaluation and treatment of PHACE(S) patients requires a multidisciplinary approach with evaluation by cardiology, neurology, otolaryngology, and ophthalmology. Imaging studies, including echocardiogram and MRI/MRA of the brain and neck, should be performed to evaluate for cardiac, vascular, and structural brain abnormalities. Lesions involving ocular or auricular segments warrant serial ophthalmologic and hearing exams, while hemangiomas involving the "beard" region are at risk of airway involvement.

In recent years, propranolol has become a standard treatment for infantile hemangiomas. Initial doses typically start at 0.5 mg/kg per day, with gradual titration up to 2 mg/kg per day, divided into two to three doses daily. Potential side-effects include hypotension, bradycardia, bronchospasm, hypoglycemia, and hypothermia. Treatment should be administered under close observation to ensure that the medication is well tolerated.

Though it is known that large, segmental, facial hemangiomas respond very well to propranolol, it is important to understand the unique risks of this therapy in patients with PHACE(S) syndrome. The most common extracutaneous finding in patients with PHACE(S) syndrome is cerebrovascular anomalies, which can lead to ischemic stroke. Given that systemic therapy with a beta-blocker can cause hypotension and decreased perfusion, there is concern of augmenting the risk of stroke in high risk patients. The potential benefit of therapy must therefore be weighed against the risks.

A retrospective study by Metry et al. of 32 infants with PHACE(S) syndrome with cervical or intracranial arterial anomalies undergoing treatment with propranolol found that only

one infant developed a neurologic deficit, which improved without cessation of treatment. Another retrospective review by Siegel et al. of 22 cases of acute ischemic stroke in patients with PHACE(S) syndrome reported that one of the patients was being treated with propranolol. This patient had underlying narrowing and non-visualization of cerebral arteries. Given limited data, it is unclear whether propranolol significantly increases the risk of stroke in this population. However, propranolol should be used with extreme caution given the potential risk. An echocardiogram and MRI/MRA of the head and neck should be obtained prior to initiating therapy to identify patients at increased risk for stroke. Risk factors include narrowing or non-visualization of cerebral or cervical arteries. Additionally, measures should be taken to minimize drastic changes in blood pressure. These include using the lowest possible dose of propranolol, slow upward titration, and TID dosing.

Merry et al. also reported worsening ulceration or tissue necrosis during treatment with propranolol in three of the 32 patients. All three patients improved after lowering the propranolol dose. This parallels our experience the patient in with Case B, who developed helical ulceration that subsequently improved after lowering propranolol dose.

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CASE 5

Presented by Christina Kranc, MD, Jerry Feldman, MD, and David Reid, MD

Patient A is a 39-year-old man who presented with four subcutaneous nodules on the upper legs.
Patient B is a 53-year-old woman who presented with large subcutaneous nodules on the lower abdomen.

UNKNOWN

Key location: Chest **CASE 6**

Presented by Shilpa Mehta, MD, Sumul Gandhi, MD and Kubinne Kim, MD

History of Present Illness
A 59-year-old woman from Mexico presented with a two-year history of asymptomatic red, raised lesions on her chest. The lesions had been stable in number and size over the last one and a half years.

Past Medical History
Diabetes and hypertension

Medications/Allergies
Metformin, omeprazole, hydrochlorothiazide
No known drug allergies

Social History
Lives with husband
No alcohol, tobacco or illicit drug abuse

Family History
Not contributory

Review of Systems
Negative for fever, malaise, weight loss, dyspnea, nausea, emesis, and abdominal pain

Physical Exam
Chest with few discrete and coalescent red-brown firm papules and plaques
Normal nails, hair and mucosa

Laboratory Data
CBC and CMP within normal limits

Histopathology
Chest, punch biopsy:
Vascular and histiocytic proliferation with giant cells in the dermis
Staining positive for CD 31, CD 34, and CD 163 and negative for HHV 8

Diagnosis
Multinucleate Cell Angiohistiocytoma

Treatment and Course
A three-month trial of low and medium potency topical corticosteroids did not alter appearance of the lesions. Given the asymptomatic and benign nature of the condition, the patient opted for active non-intervention. Lesions remained stable in size and number at her five-month follow-up appointment.

Discussion
Multinucleate cell angiohistiocytoma is a distinct, benign, reactive condition. While likely to be underreported due to its asymptomatic nature, 75 cases have been documented

since its initial description in 1985. This disease affects middle-aged and elderly women and presents with insidiously developing dome-shaped red-brown to violaceous papules on the extremities. Chest involvement was only described once by Väkevä L et al. Lesions are usually unilateral, but a few bilateral and generalized cases have been reported.

Some authors consider the condition to be a fibrohistiocytic disorder, while others view it as a vascular tumor. Puig et al proposed that the interaction between mast cells and factor XIIIa–positive fibrohistiocytic cells leads to a release of proangiogenic cytokines that then initiate vascular proliferation. On the other hand, mast cells may also be involved in the production of multinucleated cells, namely via IL-4 secretion. These cells are thought to be mitotically and functionally inactive due to chronic stimulation. Additionally, trauma and estrogen have been implicated in the pathogenesis.

A skin biopsy rules out more common entities such as Kaposi's sarcoma, insect bite, dermatofibroma, sarcoidosis, lymphocytoma cutis and acroangiodermatitis. Histology reveals a dermal proliferation of capillaries and post-capillary venules with prominent endothelial cells. There is a lymphohistiocytic infiltrate with multinucleated giant cells containing angulated cytoplasm and scalloped borders. Unlike Kaposi's sarcoma, the polymerase chain reaction analysis for human herpesvirus-8 is negative. The immunohistochemical profile is positive for the following antigenic markers: CD31, CD34 and von Willebrand factor for endothelial cells; CD3+/CD4+ for lymphocytes; and vimentin, Factor XIIIa, alpha-1-antitrypsin and CD68 for interstitial mononuclear cells. Interestingly, the characteristic multinucleated cells express vimentin, a fibroblastic marker, and not the markers typical of monocyte/macrophage lineage.

Multinucleate cell angiohistiocytoma has a benign course with a tendency to slowly progress, persist, or in rare cases, spontaneous involute. Treatment is therefore optional. Surgical excision, argon laser, intense pulsed light and cryosurgery have been successfully used in a few cases.

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Key location(s): Scalp **CASE 7**

Presented by Steven Nwe, DO and Warren Piette, MD

History of Present Illness
A 39-year-old otherwise healthy male presented with a four month history of multiple scalp lesions. The lesions began as red pruritic patches confined primarily to the scalp and forehead. He was treated at an outside facility with a course of topical corticosteroids followed by a topical antifungal. After initial modest improvement, the lesions returned prompting empiric treatment with oral clindamycin followed by a four week course of oral terbinafine. Initial punch biopsies and culture at the outside facility were inconclusive. During this interval, the lesions progressed into larger plaques, some eroded, though otherwise asymptomatic. Given the rapid progression of the lesions, the patient was referred to our facility for consultation.

Past Medical History
Environmental allergies

Medications/Allergies
Hydroxyzine and loratadine

Social History
No history of tobacco or illicit drug use
Drinks alcohol socially
Works as a real estate agent
No household pets

Review of Systems
The patient endorsed generalized fatigue but otherwise denied fever, chills, night sweats or weight loss.

Physical Exam
Skin: Central superior forehead, near hairline: 5 cm exophytic friable soft mass with superficial erosions on the central superior forehead at the hairline. Surrounding fine pink patches scattered on the forehead.
Temporal, parietal and crown of scalp: Numerous erythematous rounded plaques and soft nodules of various sizes with fine scale and superficial erosions.
Lymph node: No palpable lymphadenopathy noted.

Laboratory Data

CBC	No noted abnormalities	
CMP	No noted abnormalities	
LDH	296 U/L	[Reference range 85-210 U/L]

Peripheral flow cytometry:
No abnormal circulating lymphoid cells.

Histopathology

Midline forehead scalp biopsy:
Skin with focal ulceration and infiltration by dense sheets of small to medium sized atypical lymphoid cells with nuclear irregularity with numerous plasma cells, eosinophils, and occasional neutrophils. No epidermotropism noted. The atypical T-cells were positive for CD3, CD4, CD5, focally positive for CD7, while negative for CD8. Rare CD30-positive cells were noted in the background. CD20 highlights the admixed B-cells.

Bone Marrow Biopsy:
Normocellular bone marrow showing trilineage hematopoiesis with orderly maturation. No atypical infiltrates were seen. Flow cytometry did not identify abnormal populations.

Radiology

CT head, chest, abdomen and pelvis: bilateral cervical, axillary and inguinal lymphadenopathy

Diagnosis

Primary cutaneous small/medium CD4 positive T-cell lymphoma

Treatment and Course

Given the size of his largest lesion and the extent of involvement, the patient was treated with four cycles of cyclophosphamide, daunorubicin, vincristine, and prednisone (CHOP) by the hematology/oncology service with reduction in tumor size. Prior to planned consolidation with radiation therapy, the patient developed new pink plaques on his forehead. Biopsy of these lesions were again compatible with primary cutaneous small/medium CD 4 positive T-cell lymphoma. At this time the patient is receiving his second round of CHOP chemotherapy along with brentuximab.

Discussion

Cutaneous peripheral T-cell lymphoma, unspecified/not otherwise specified (PTL, NOS), represents a heterogeneous group of cutaneous T-cell lymphomas that do not fit into any of the well-defined cutaneous T-cell lymphoma (CTCL) subtypes. Primary cutaneous CD4-positive small/medium T-cell lymphoma is delineated as a provisional rare subtype of PTL based on characteristic clinicopathologic, immunophenotypic, and prognostic features.

Primary cutaneous CD4-positive small/medium T-cell lymphoma (PCSM-TCL) has a predominance of atypical small to medium-sized CD4+ pleomorphic T cells without the clinical or histologic features of mycosis fungoides (MF). A review of 232 patients with PCSM-TCL by Williams et al. showed various presentations, most often with a favorable clinical course. Patients generally present with solitary plaques or tumors, which commonly occur on the head and neck, followed by the trunk. Multifocal skin lesions may occur, but will usually lack the clinical progression from patches to tumors that is more typical of MF. Lesions are mostly asymptomatic, but can rarely be painful, pruritic, or ulcerated.

The definition of PCSM-TCL is somewhat problematic because it shares many histopathologic features with MF. Shared features include atypical lymphocytes, epidermotropism, and infiltration into the subcutaneous fat. In PCSM-TCL, however, there are predominantly small to medium-sized atypical lymphocytes with a lack of cerebriform nuclei. Focal or absent epidermotropism can also help distinguish it from MF, where epidermotropism is more extensive.

Overall, PCSM-TCL has a favorable prognosis with 5-year survival rates of 60–80%. The majority of patients need only conservative therapy. A more aggressive variant (defined as lesions requiring multiple or systemic treatments, systemic involvement, and progressive or fatal disease) occurs in up to 13.8% of patients. Factors predictive of an aggressive clinical course include multifocal disease, larger tumor size (>5cm), high T-cell proliferation rates, scarce CD8 + cells, and variable CD4 and/or loss of CD2 expression on T cells. Garcia-Herrera et al. followed five patients who met criteria for aggressive PCSM-TCL, all of whom had died of extracutaneous dissemination by 18-36 months.

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Key location: Right plantar foot **CASE 8**

Presented by Sangeetha Venkatarajan, MD, Warren Piette, MD, and David Reid, MD

History of Present Illness
A 29-year-old woman presented with a right plantar foot lesion that had developed four years earlier. Over the past year, the lesion had gradually increased in size and became pruritic. She noted irritation of the lesion with walking due to rubbing against the shoe, but was otherwise asymptomatic. She had no similar lesions elsewhere.

Past Medical History
History of psoriasis, self-reported

Medications/Allergies
None/NKDA

Social History
No tobacco, alcohol, or illicit drug use

Review of Systems
No fever, chills, nausea, vomiting, or diarrhea
Intermittent bilateral knee pain that occurs with cold weather and spontaneously resolves

Physical Exam
Right medial plantar foot with a 4.3cm x 4.2cm well-demarcated, scaly, erythematous plaque

Laboratory Data
CBC, CMP, and fasting lipid panel unremarkable

Histopathology
Right Medial Foot, Punch Biopsy:
Band-like lymphocytic infiltrate in the papillary dermis with epidermotropism, Pautrier microabscesses and parakeratosis. Immunohistochemical stains highlight atypical lymphocytes in the epidermis that are weakly positive for CD45 and strongly positive for CD3, CD5, and CD8. There is a loss of staining of CD4 and CD7. There was no immunoreactivity with CD68, CD20, AE1/3, EMA, S-100, mart-1, and HMB45. GMS and PAS stains are negative for fungus.

Diagnosis
Pagetoid reticulosis

Treatment and Course
The patient was initially treated with triamcinolone 0.1% ointment BID and calcipotriene 0.005% cream BID without improvement. Once biopsy confirmed cutaneous T-cell lymphoma, topical therapy was transitioned to clobetasol 0.05% ointment BID. After two weeks, topical treatment was discontinued due to lack of improvement and new-onset burning sensation that the patient attributed to clobetasol. She then received excimer laser therapy twice weekly for two months with mild improvement, but she was unable to commit to additional appointments. The lesion then worsened. The current plan is to begin treatment with localized radiation therapy.

Discussion

Pagetoid reticulosis is a rare, indolent variant of mycosis fungoides. The localized variant of pagetoid reticulosis, Woringer-Kolopp disease, was first reported by Woringer and Kolopp in 1939 when they described a case of a 13-year-old boy with a solitary, erythematous lesion on his arm. Histologically indistinguishable from Woringer-Kolopp disease, Ketron-Goodman disease was previously considered to be a generalized variant of pagetoid reticulosis. It is now instead considered to be a primary aggressive CD8+ form of cutaneous T-cell lymphoma.

Pagetoid reticulosis has a male predominance and typically occurs in middle-aged patients. It presents as a solitary, well-circumscribed, psoriasiform or hyperkeratotic plaque or tumor. It is usually localized to distal extremities but has presented on the trunk in a few cases. On histological exam, pagetoid reticulosis is characterized by epidermal hyperplasia with parakeratosis, prominent acanthosis, epidermotropism, and intraepidermal infiltrate of atypical lymphocytes. On immunohistochemical stains, pagetoid reticulosis lesions may be CD4+, CD8+, or CD4-/CD8-, though nearly half of cases have a CD8+ predominance.

Effective treatments include topical nitrogen mustard, high-potency topical steroids, electron beam therapy, phototherapy including PUVA and narrow-band UVB, and surgical excision. In severe or recalcitrant disease, localized radiation therapy has been used. While surgical excision typically results in an adequate response, non-invasive therapies are usually tried first.

Radiotherapy, including localized radiation therapy and electron beam therapy, is well-established as an effective treatment option for mycosis fungoides, but there is limited data regarding its use specifically for pagetoid reticulosis. In one study by Lee et al., four patients treated with radiation therapy achieved a rapid and complete response. Radiation doses ranged from six to 41 Gy and the median duration of complete response was 12 years with a range of two to 23 years.

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CASE 9

Presented by Donna Hart, MD, Nicole Joy, MD, and Warren Piette, MD

History of Present Illness

A 65-year-old man with past medical history of granulomatosis with polyangiitis (Wegener's granulomatosis) who presented with an asymptomatic purpuric rash of unknown duration.

UNKNOWN

Key locations: Extremities **CASE 10**

Presented by Katie Manno, MD, David Reid, MD, and Jerry Feldman, MD

History of Present Illness
A 40-year-old male presented with a one-year history of enlarging vegetative plaques on his right upper extremity. At his initial visit, the patient was evaluated with biopsies and tissue cultures for atypical mycobacterial and deep fungal infections. While awaiting these results, he developed fever, tachycardia, and significant pain and swelling of the lower legs. He subsequently was admitted for suspected cellulitis. A chest CT angiogram during that admission demonstrated bilateral hilar lymphadenopathy and a left upper lobe nodule. A bronchoscopy was performed, and tissue cultures were obtained.

Following his hospitalization, the patient developed hand swelling and new discrete, erythematous, indurated, tender nodules on his lower legs. The upper extremity plaques, as well as the lower extremity pain and swelling, persisted.

Past Medical History
Diverticulitis s/p Hartmann's (2004)

Medications/Allergies
None/NKDA

Social History
Occasional marijuana use, no tobacco or alcohol abuse
Works as a taxi driver

Review of Systems
As above

Physical Exam

Vitals:	Intermittent fevers up to 103F, persistently tachycardic (110-115 BPM).
Skin:	Right distal second digit with edema, erythema, and a large fungating, verrucous plaque extending over the top of the nail plate. Right arm with multiple discrete thick, crusted, verrucous plaques on violaceous bases in a sporotricoid-like distribution. Lower extremities with discrete, erythematous, tender, indurated nodules.
Musculoskeletal:	Edema of wrists, hands, ankles.
Neck/Axillae:	No lymphadenopathy.
Chest:	Clear to auscultation bilaterally.

Laboratory Data
The following labs were notable:

Hb/Hct	12.5 g/dL / 36.6%	[12.9 – 16.8 g/dL] / [38.1-49%]
WBC	13.8 k/μL	[4.4 – 10.6 k/μL]
Angiotensin Converting Enzyme	41μg/L	[8– 52 μg/L]
HIV Ab screen	Non-reactive	

Histopathology
Punch biopsy, right arm:
Superficial and deep chronic inflammatory infiltrates of plasma cells, eosinophils, and few neutrophils. One focus with a non-necrotizing granuloma. No organisms identified on GMS or AFB stains. No polarizable material seen.

Punch biopsy, left distal anterior thigh:
Predominantly septal panniculitis most consistent with erythema nodosum. PAS, GMS, AFB for fungus and acid fast bacilli negative.

Bronchiolalveolar lavage:
No malignancy; GMS for fungi and PCP negative.

Endoscopic ultrasound-guided transbronchial needle aspiration:
Non-caseating, non-necrotizing granulomas. Special stains for GMS, PAS, and AFB negative. No polarized foreign material identified.

Microbiology
Tissue/skin, bronchial fluid, and lymph node fungal and AFB cultures negative.

Urine culture, histoplasma antigen, and blastomyces antigen negative.

Radiology
Chest CT angiogram: Mediastinal and bilateral hilar lymphadenopathy with mild compression of the left main pulmonary artery. In the left upper lobe, there is a well-circumscribed pulmonary nodule with adjacent focal infiltrate.

Diagnosis
Atypical Löfgren's syndrome

Treatment and Course
The patient was treated with prednisone with a slow taper. Over a two-week course, the skin lesions, joint pain, and panniculitis improved. He was referred to ophthalmology but missed his appointment.

Discussion
Sarcoidosis is a multi-system disease that is characterized by non-caseating granulomas of unknown etiology. Cutaneous lesions are estimated to be present in at least 20% of sarcoid cases and can be the presenting sign nearly one-third of the time. The cutaneous manifestations of sarcoidosis are typically divided into two categories: discrete lesions with histopathologically evident non-caseating granulomas, and reactive lesions that do not form granulomas.

Löfgren's syndrome (LS), a clinical variant of sarcoidosis, is often acute in onset. LS has classically been defined by the triad of erythema nodosum, hilar lymphadenopathy, and migrating polyarthralgias. The presentation of erythema nodosum is typically associated with a good prognosis, indicating a transient disease course that generally resolves spontaneously without systemic corticosteroid treatment. In the majority of cases, no additional cutaneous manifestations are seen. When additional skin findings are appreciated, reports have included findings of macular papular rash, plaques, infiltrated scars, and subcutaneous nodules.

The diagnosis of LS can usually be proven with a skin or extracutaneous tissue biospy. However, several authors suggest that the diagnosis can be accepted without histologic confirmation. In a review by Winterbauer et al., it was concluded that the finding of bilateral hilar lymphadenopathy in either asymptomatic patients, or in patients with additional findings of erythema nodosum (or uveitis), was highly suggestive of sarcoidosis. In addition, review of cases that were not confirmed with histopathology never developed a diagnosis other than sarcoidosis. Thus, biopsy is not recommended for patients presenting with classic symptoms and signs (both clinical and radiologic) of LS in order to make a diagnosis. However, if clinical and radiologic findings are not typical, histologic confirmation is warranted.

In this atypical case of LS, we see the classic presentation of reactive erythema nodosum, hilar lymphadenopathy, and arthralgias, as well as a secondary finding of vegetative cutaneous plaques, all of which resolved with prednisone treatment. At this point, it is unclear whether these more indolent, vegetative cutaneous findings are a component of the patient's sarcoidosis. Because of this unusual presentation and lack of current data providing insight into this presentation, it is important for clinicians to be reminded of the heterogeneous presentations of sarcoidosis.

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