Chicago Dermatological Society

April 2014
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, April 9, 2014
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* "Psoriasis: Treatment Approaches for Moderate to Severe Psoriasis and Its Relationship to Cardiovascular Implications" *Erin Boh, MD, PhD, 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 "Biologics: Use in Dermatologic Diseases Other Than Psoriasis" *Erin Boh, MD, PhD, 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 21, 2014 at the Rush University

Guest Speaker

ERIN BOH, MD, PHD, FAAD

Joseph Chastain Professor and Chair of Dermatology; Tulane University Health Sciences Center; New Orleans, LA

Delivering the Sidney Barsky Lecture

Dr. Boh trained at Tulane University School of Medicine and completed her residency at the University of Texas Southwestern Medical Center, Parkland Hospital. She joined the faculty at Tulane University School of Medicine in 1990 and is currently a Professor of Dermatology. Dr. Boh has a strong interest in photobiology and chronic diseases such as psoriasis and skin cancers such as lymphoma. She also has a strong interest in psoriasis, cutaneous T-cell lymphomas, graft vs. host disease and cutaneous manifestations of internal disease, both in the pediatric and adult populations. She participates in a number of clinical research projects involving psoriasis, psoriatic arthritis and lymphoma. Dr. Boh is certified by the American Board of Dermatology.

CME Financial Disclosure: Dr. Boh has reported the following disclosures: Grant/research support - Janssen, Amgen, Eisai, Regeneron; Speakers bureau - Janssen, Abbvie, Amgen

Chicago Dermatological Society

"Chicago Dermatological Society Monthly Meeting Series"

April 9, 2014 Chicago, IL

OBTAINING YOUR CERTIFICATE OF CREDIT

Participants must attend the entire session to receive credit. Please be sure to sign the attendance list at the registration table before you leave the conference. Also, we ask that you complete the evaluation form and return it to the registration table. A certificate will be sent to you upon conclusion of the meeting. The information collected as part of this process represents an important part of the CME planning process. CFMC will retain a record of attendance on file for six years.

JOINT SPONSORSHIP STATEMENT

This educational activity is jointly sponsored by CFMC and the Chicago Dermatological Society.

GOAL/PURPOSE

To broaden the clinical knowledge of dermatologists.

TARGET AUDIENCE

This activity has been designed to meet the educational needs of physicians and other healthcare professionals.

FACULTY

Erin E. Boh, MD, PHD, FAAD

EDUCATIONAL OBJECTIVES

Upon completion of this series, participants should be able to:

1. Discuss key factors in the diagnosis and treatment for a variety of dermatologic diseases and conditions, including psoriasis, hair disorders, and dermatological symptoms of systemic diseases.

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

PHYSICIAN ACCREDITATION STATEMENT

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of CFMC and the Chicago Ophthalmological Society. CFMC is accredited by the ACCME to provide continuing medical education for physicians.

CFMC 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.

OTHER HEALTHCARE PROFESSIONALS STATEMENT

This educational activity has been planned and implemented following the administrative and educational design criteria required for certification of health care professions continuing education credits. Registrants attending this activity may submit their certificate along with a copy of the course content to their professional organizations or state licensing agencies for recognition for 4.5 hours.

DISCLOSURE STATEMENT

It is the policy of CFMC and the Chicago Dermatological Society that the faculty discloses real or apparent conflicts of interest relating to the topics of the educational activity.

Erin Boh, MD, PhD, FAAD: Grant/Research Support – Janssen, Amgen, Eisai, Regeneron; Speakers Bureau – Janssen, Abbvie, Amgen

All other members of the faculty and planning team have nothing to disclose nor do they have any vested interests or affiliations.

CHICAGO DERMATOLOGIC SOCIETY

We extend our sincere thanks to
our Pathology Department and Dr. Jordan Carqueville
for their review of the histopathology
from these cases.

Key locations: Right arm, left thigh, bilateral legs CASE 1

Presented by Shilpa Mehta, MD and Warren Piette, MD

History of Present Illness

A 40 year-old African-American man with no significant past medical history was admitted to the trauma service with right lower extremity ulcerations after sustaining a motor vehicle accident three weeks prior to admission. The patient had recently received antibiotics at an outside hospital with minimal improvement. On physical exam, he was observed to have asymptomatic nodules on the right arm, which he stated had been present for 6 months. Similar lesions were also present on the left thigh and shins.

Past Medical History

None

Medications/Allergies

None/NKDA

Social History

No tobacco or drug use. Drinks 1-2 beers weekly.

Review of Systems

The patient complained of subjective fevers but denied night sweats, weight loss, or anorexia.

Physical Exam

Skin — Right arm, left thigh: 5 cm firm indurated nodules (3 total) with overlying hyperpigmentation
Left thigh: overlying the indurated nodules are 2 superficial areas of ulceration, each 1.5 cm in size
Right anteromedial leg: 8 cm purulent ulcer with rim of surrounding hyperpigmentation
Left anteromedial leg: 1.5 cm ulcer with hyperpigmented crusted margin

Laboratory Data

The following labs were remarkable/abnormal:

ESR	32	[0 - 20 mm/hr]
CRP	3.01	[0 - 0.50 mg/dl]

The following labs were negative/within normal limits:
CBC with differential, CMP

Histopathology
RIGHT UPPER ARM, PUNCH BIOPSY:
Non-necrotizing granulomas in papillary and reticular dermis composed of epithelioid histiocytes, giant cells, and scattered lymphocytes. Special stains: GMS, PAS, AFB and Fite were negative. No polarizable material was seen.

Radiology
Negative chest x-ray.

Diagnosis
Cutaneous Ulcerative Sarcoidosis

Treatment and Course
The patient was started on treatment with systemic corticosteroids and hydroxychloroquine with some improvement noted. The patient was subsequently lost to follow up.

Discussion
Sarcoidosis is a multisystem granulomatous disorder of unknown etiology. It has an estimated prevalence of 10 to 20 per 100,000 individuals. Boeck, who described a case of multiple benign "sarcoid" lesions that resembled sarcoma, coined the term 1899. It has a prevalence of about 10-20 per 100,000 population, with lung being the most frequently involved organ.

Cutaneous involvement has been described in about 20-35% of patients with sarcoidosis. Various presentations include papules, plaques, nodules, lupus pernio, erythema nodosum, hypo- or hyper-pigmented patches, and scar sarcoid. Because lesions can exhibit multiple morphologies, cutaneous sarcoidosis is also known as a "great imitator" in dermatology. Ulcerated sarcoidosis has an incidence of just 1.1% in patients with cutaneous sarcoidosis. In a review of the literature conducted by Schwartz et al in 1982, only 26 patients with sarcoidosis exhibited cutaneous ulceration; 9 other cases were reported through 1997.

Ulcerative sarcoidosis has been described mostly in African American and Japanese women under the age of 40 years. Ulcers may arise on previously normal skin or in pre-existing papulonodules, most commonly on lower extremities. Albertini et al found that cutaneous sarcoidosis, including those lesions with ulcers, was the presenting feature in 26 of 35 patients with sarcoidosis. Clinical evidence of multisystem involvement was identified in most of these patients, specifically hepatosplenomegaly, pulmonary and ocular involvement. Local trauma, as the presented patient experienced, has been suggested as a possible cause of ulcerative sarcoidosis of the lower extremities, indicating that pathergy may be a notable feature. Treatment of ulcerated sarcoidosis is with corticosteroid therapy, with methotrexate reserved for refractory cases.

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Key locations: Scalp, Trunk CASE 2

Donna Sadowski, MD, Paula Kovarik, MD, and Warren Piette, MD

History of Present Illness

A 29 year-old man with no significant past medical history presented with a diffuse nodular eruption for the past 6 months. He first sought medical attention for this condition 2 months ago when he noted a burning sensation and intermittent clear drainage from a firm plaque on the scalp. He was admitted to an outside hospital and empirically treated with intravenous vancomycin, ceftriaxone, and fluconazole. Review of printed medical records revealed a normal general laboratory evaluation, peripheral blood cultures, and urine cultures. No tissue cultures or skin biopsies were performed. He was discharged on a short-course of doxycycline. After no improvement, he was seen by an ambulatory infectious disease physician, who changed his antibiotic regimen to sulfamethoxazole/trimethoprim and referred him to our clinic for further evaluation of the skin lesions.

Past Medical History

None

Medications/Allergies

None/NKDA

Social History

No tobacco, alcohol, or drug use. Works as truck driver.

Review of Systems

The patient denied fever, chills, dyspnea, weight loss, malaise, night sweats, cough, hemoptysis, or hematemesis.

Physical Exam

Skin	Scalp: Large, firm, lightly erythematous to gray colored plaques and nodules encompassing the entire frontal, midscalp, and vertex areas with several overlying round erosions, some brown crusting, and minimal serous drainage; associated extensive alopecia; focal tenderness to palpation Forehead, lateral cheeks, chest, back: Multiple firm non-tender slate gray nodules, several with central areas of light erythema
HEENT	Left-sided proptosis noted
Neck	Right postauricular lymphadenopathy and left submandibular and postauricular lymphadenopathy present

Laboratory Data

The following labs were negative/within normal limits:
CBC with differential, CMP, HIV, LDH, flow cytometry

Histopathology

LEFT VERTEX SCALP AND LEFT UPPER ABDOMEN, PUNCH BIOPSY:
Sections of skin show sheets of medium-sized, round to oval immature monocytoid cells with a high nuclear to cytoplasmic ratio in the superficial and deep dermis beneath a Grenz zone. On higher power, the nuclei are irregular with lacy chromatin and predominant nucleoli. Many nuclei are cleaved.

Immunohistochemical stains: Positive for myeloperoxidase, CD68, CD4, and CD43.

Bone Marrow Studies

Normocellular bone marrow showing trilineage hematopoiesis with orderly maturation. No abnormal cell populations identified on flow cytometry.

Radiology

CT NECK, CHEST, ABDOMEN, AND PELVIS (IV CONTRAST): Submandibular, parotid, posterior triangle, occipital, and retroauricular lymphadenopathy. Medial orbit soft tissue nodules. On the left side, lesion extends into the lacrimal duct and displaces the globe laterally.

Diagnosis

Aleukemic Leukemia Cutis (Type: Acute Myelomonocytic Leukemia)

Treatment and Course

Chemotherapy was initiated with cytarabine and idarubicin (7 + 3) regimen. After induction chemotherapy, the patient transferred his care to another institution where he received post-remission treatment with high-dose cytarabine (HiDAC) followed by allogeneic hematopoietic stem cell transplantation. The skin lesions have since completely resolved. Peripheral blood, bone marrow, and cerebrospinal fluid studies continue to be unaffected to date.

Discussion

Aleukemic leukemia cutis (ALC) is defined as leukemic cell infiltration into the epidermis, the dermis, or the subcutis in the absence of disease in the bone marrow or peripheral blood. This entity is extremely rare. Leukemia cutis (LC) is seen in 2-13% of leukemia patients (except in adult T-cell leukemia/lymphoma which has a disproportionate percentage of patients who develop LC). Of these patients, only 2-7% demonstrate primary LC without bone marrow infiltration or systemic symptoms.

Primary extramedullary leukemia (EML), which refers to the leukemic infiltration of any organ beyond the blood and bone marrow, is sometimes used synonymously with ALC. The skin is the most frequently involved site of EML. As many as 90% of patients with LC have other areas of extramedullary involvement, most commonly the lymph nodes. Additional sites include the spleen, bone, nasal sinuses, orbits, central nervous system, gingiva, and gonads. ALC typically portends a poor prognosis. The vast majority of patients go on to develop bone marrow and peripheral blood disease. In the literature, there have been five documented cases of patients with ALC who did not develop bone marrow involvement. Disease-free survival was documented in just two of these five cases, at 16 months and 30 months.

LC presents variably as red-brown to violaceous papules and nodules, indurated or hemorrhagic plaques, perifollicular acneiform papules, macules, ulcers, bullae, or palpable purpura. Aleukemic involvement is usually diffuse and papulonodular in presentation. Our case is particularly unique for both the degree of scalp involvement and the striking slate gray color of the subcutaneous nodules. To our knowledge, there are only two other reported individuals with ALC involving the scalp. Both of these were acute myelogenous leukemia (AML) cases, similar to our patient.

There is no consensus regarding the treatment for ALC because of the low incidence of this disease. Previous case reports have demonstrated that radiation alone is ineffective in preventing subsequent development of overt leukemia. Currently oncologists treat ALC with the same intensive remission-induction chemotherapy as is used in traditional acute leukemias. The

post-remission chemotherapy regimen and the role of allogeneic hematopoietic cell transplantation have not been well defined for ALC.

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Key location: Anterior neck CASE 3A

Presented by Christina Kranc, MD and Joerg Albrecht, MD

Unknown #1

Fast Break #1

Key location: Breasts CASE 4A

Presented by Nicole Joy, MD and Warren Piette, MD

History of Present Illness

A 51 year-old African American woman with HIV and end-stage renal disease on hemodialysis presented to the emergency room with altered mental status in the setting of painful necrotic breast ulcers and non-necrotic ulcers on the buttocks. The breast ulcers had been present for about a month prior to presentation. She had been admitted to an outside hospital a few weeks prior, where she was treated with antibiotics. During that hospitalization, a skin biopsy demonstrated significant clot in the deep vessels. She was in her usual state of health prior to onset of the lesions.

Past Medical History

HIV (CD4 count 710, viral load undetectable)
End stage renal disease on hemodialysis
Hypertension

Medications

IV acyclovir, ceftriaxone, piperacillin-tazobactam, vancomycin, tenofovir, emtricitabine, efavirenz

Allergies

NKDA

Social History

No history of tobacco, alcohol, or drug use.

Review of Systems

The patient reported right-sided headache and non-bloody diarrhea. She denied chest pain, dizziness, syncope, palpitations, diaphoresis, headache, urinary symptoms, rectal bleeding, chills, night sweats, nausea, vomiting, diarrhea, or any other systemic symptoms.

Physical Exam

General	In pain, drowsy but arousable.
Skin	Right breast, inferior aspect: Ulcerated necrotic plaque with multiple punched out shallow ulcers Left breast: Large necrotic plaque with surrounding dark red retiform purpura Buttocks and perianal skin: Multiple shallow, punched out ulcers with scalloped borders

Laboratory Data

The following labs were remarkable/abnormal:

Hemoglobin	6.5 g/dL	[12.9 – 16.8 g/dL]
Hematocrit	21.2%	[38.1 - 49%]
WBC	17.4 k/μL	[4.4 – 10.6 k/μL]
Creatinine	5.6 mg/mL	[0.6 – 1.4 mg/dl]
BUN	43 mg/dL	[8 – 20 mg/dL]

The following labs were negative/unremarkable:
CD4 count, calcium, phosphorus, parathyroid hormone, ANA, p-ANCA, c-ANCA, cardiolipin Ab, β2-glycoprotein I Ab

Histopathology

LEFT AND RIGHT BREAST, SIMPLE MASTECTOMY:
Breast tissue with necrosis and acute and chronic inflammation. Arterioles showing luminal narrowing and mural calcification consistent with calciphylaxis.

ANTRAL STOMACH, PARTIAL GASTRECTOMY:
Stomach with ulcer and perforation through serosal surface. Prominent calcification focally seen in the muscularis propria. Focally polarizable and nonpolarizable (calcium) material deposition within lymphovascular spaces in subserosa associated with the perforation and vascular obstruction. Von Kossa stain demonstrates that there is calcium deposition in small to medium-sized blood vessels. The above findings are suggestive of calciphylaxis. Immunohistochemical studies for CD68 and S-100 support the above interpretation.

Microbiology

WOUND CULTURE:
Cultures for herpes virus, CMV, varicella zoster were negative.
H. pylori IgG and antigen negative.

Radiology

CT head: No evidence of acute intracranial hemorrhage.

Diagnosis

Calciphylaxis

Treatment and Course

Initial differential diagnosis for the necrotic ulcerations included small vessel vasculitis, *Herpesvirus* infection, and calciphylaxis. She was empirically treated with IV acyclovir and antibiotics, however, viral cultures showed no growth and wound cultures showed only multiple fecal colonizers. Additionally, a thorough autoimmune workup was negative. Because of the continued spread of necrotic ulcers and significant amount of pain, the patient elected to undergo bilateral mastectomy with debridement of affected tissue. Microscopic evaluation of excised breast tissue demonstrated calciphylaxis. The chest wound was closed with a split-thickness skin graft. During month 2 of admission, the patient was discovered to have a slow GI bleed requiring multiple blood transfusions. Upper endoscopy demonstrated ulcerations in the distal esophagus, two large duodenal ulcers, and multiple small ulcerations in the stomach. *H. pylori* immunostains were negative. About three weeks after the upper endoscopy, the patient acutely developed abdominal pain and vomiting. Emergent exploratory laparotomy demonstrated perforated gastric ulcers. The patient underwent distal gastrectomy. Ten days after the second surgery, she decompensated and underwent PEA arrest, requiring ventilator and pressor support. Given her poor prognosis, the family elected to withdraw support, and she passed away shortly thereafter. The biopsy results of the gastric ulcers, reported after her death, were consistent with calciphylaxis of the stomach.

Key locations: Abdomen, thighs CASE 4B

Presented by Nicole M. Joy, MD and Warren Piette, MD

History of Present Illness

A 49 year-old Caucasian man presented to the emergency room with shortness of breath, abdominal pain, fever, and lethargy. On admission, physical exam was notable for pitting edema of the lower abdomen with malodorous, erythematous, and necrotic plaques that extended to the suprapubic area, groin, and inner thighs. He was admitted for treatment of septic shock thought to be secondary to obesity-related pressure ulcers. He underwent extensive surgical debridement on three separate occasions and was treated with multiple antibiotic courses resulting in minimal improvement. He was also intubated several times given worsening respiratory acidosis and altered mental status with airway compromise. Dermatology was consulted on day 25 of admission for evaluation of new purpuric skin lesions on the abdomen.

Past Medical History

Hypertension
NASH-related cirrhosis
Chronic kidney disease (baseline GFR 29 mL/min/1.73 m^2)
Diabetes mellitus, type 2
Morbid obesity (Body mass index 55)
Glaucoma
Osteoarthritis

Medications

Imipenem, caspofungin, fentanyl, lorazepam, heparin subcutaneous injection, famotidine

Allergies

Ceftriaxone

Social History

No history of tobacco or drug use. Drinks 2-3 drinks per month.

Review of Systems

On admission, he reported shortness of breath, abdominal pain, fatigue for the past two weeks and recent fever. He denied chest pain, dizziness, syncope, palpitations, diaphoresis, headache, urinary symptoms, rectal bleeding, chills, night sweats, nausea, vomiting, diarrhea or any other systemic symptoms.

Physical Exam

General	Intubated
Skin	Abdomen extending to anterior thighs: Large open surgical wound; surrounding skin with induration and focal non-inflammatory retiform purpuric plaque with central necrosis and areas of hemorrhage Lower legs: Purpuric retiform patches

Laboratory Data

The following labs were remarkable/abnormal:

Hemoglobin	8.9 g/dL	[12.9 – 16.8 g/dL]

Hematocrit	27.3%	[38.1 - 49%]
WBC	11.2	[4.4 – 10.6 k/μL]
Creatinine	3.7 mg/dL	[0.6 – 1.4 mg/dl]
BUN	52 mg/dL	[8 – 20 mg/dL]
Calcium	7.2 mg/dL	[8.5 – 10.5 mg/dL]
Phosphorous	5.1 mg/dL	[2.5 – 4.5 mg/dL]
PTH	383.0 pg/mL	[6.0 – 65.0 pg/mL]

Histopathology

ABDOMINAL SKIN AND FAT, DEBRIDEMENT OF WOUND:
Skin and subcutis with ulcer, marked acute inflammation and abscess formation extending to the subcutaneous fat. Calcification is seen in the stroma and within the media and intima of small to relatively large sized blood vessels, some of which are associated with thrombosis. Immunostains for CD31, CD34 and SMA support this interpretation. Special stains of PAS and GMS for fungus are negative.

Radiology

CT scan of abdomen and pelvis (day of admission): Significant amount of inflammation in the soft tissues of the mid abdomen extending inferiorly to the pelvis. There is no air within the soft tissues. There are multiple enlarged bilateral inguinal lymph nodes.

Diagnosis

Calciphylaxis

Treatment and Course

The diagnosis of calciphylaxis was based on multiple biopsies, calcium and phosphorous levels and the classic appearance of retiform purpuric skin lesions. The patient remained in the Burn ICU for ten weeks while receiving aggressive wound care and multiple extensive surgical debridements of the abdominal wall and anterior thighs. His hospital course was complicated by multiple infections, and he was found to have clinically significant *Aspergillus* and multi-drug-resistant *Pseudomonas* wound infections. Multiple episodes of respiratory failure required tracheostomy. Once the diagnosis of calciphylaxis was established, the patient was treated with sevelamir with a goal phosphorous level of less than 3.5 mg/dl. After a prolonged hospital course, his medical condition eventually stabilized, and he underwent successful split thickness graft of the debrided wound on the abdomen. He was discharged to a long-term acute care center with wound care consisting of xeroform and Eucerin to the abdomen, sulfamyelon to the peripheries of the skin graft, and xeroform to the lower extremity lesions. The patient was lost to follow up

Discussion

Calciphylaxis, also known as calcific uremic arteriolopathy, is a vasculopathy with calcification and ischemic necrosis of the skin and soft tissues. It is most commonly seen in patients with end-stage renal disease (ESRD), with an incidence of 1-4% in patients on hemodialysis. It is associated with a mortality rate of 60-80%, often secondary to sepsis or gangrene.

Risk factors for calciphylaxis include obesity, liver disease, systemic corticosteroid use, calcium-phosphate product of more than 70 mg^2/dl^2, serum aluminum greater than 25 ng/mL, and calcium ingestion. Additionally, women and diabetics are also at increased risk. Rarely, calciphylaxis occurs in patients in the absence of ESRD. A systematic review by Nigwekar et al.

found 36 reported cases of nonuremic calciphylaxis. This study found that risk factors in the absence of renal failure include primary hyperparathyroidism, malignancy, alcoholic liver disease, connective tissue disease, preceding corticosteroid use, and protein C and S deficiencies.

Clinically, calciphylaxis presents with extremely painful reticulated violaceous patches that can develop bullae, ulceration, and necrosis. The most commonly affected sites are areas with increased amounts of adipose tissue such as the abdomen, buttocks and thighs.

There have been only three reported cases of gastric calciphylaxis. Of these, only one case was correlated with histopathology. Breast calciphylaxis is rare and has been associated with coronary artery bypass grafting and internal mammary artery (IMA) harvest. A review of three cases of breast necrosis following IMA harvest identified obesity, macromastia, diabetes, hypertension, and ESRD as risk factors.

To date, there are no randomized control trials examining treatment options for calciphylaxis. Sodium thiosulfate (STS), which is thought to act via anti-oxidation, vasodilation and chelation, has been associated with favorable outcomes. In a study by Nigwekar et al., calciphylaxis completely resolved, markedly improved, or improved in 75% of patients. Other therapies that have been studied include cinacalcet and corticosteroids. Therapeutic parathyroidectomy has been attempted, but its role in patients without hyperparathyroidism is controversial. Finally, wound management with modalities including hyperbaric oxygen therapy, surgical debridement, and non-surgical debridement is commonly performed. Wound care should focus on pain control, minimizing trauma, and preventing infection.

Given the high mortality of calciphylaxis and the lack of evidence-based data, a focus on prevention is preferred. The National Kidney Foundation now recommends lower target values for serum phosphate (3.5-5.5 mg/dL), calcium (8.4-9.5 mg/dL), and PTH (150-300 pg/mL) for patients on hemodialysis. Additionally, use of low-calcium diasylate, close monitoring of calcium, phosphorous, PTH and nutritional status can be helpful in preventing calciphylaxis. In addition, minimizing modifiable risk factors such as diabetes and obesity can be helpful in preventing calciphylaxis.

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Key location: Posterior neck CASE 5

Presented by Stephanie St. Pierre, MD and David Reid, MD

History of Present Illness

A 10 month-old African-American male presented with a posterior neck plaque that reportedly had been present since birth. Per the patient's mother, the lesion started as a slightly firm, red area at birth that gradually thickened and enlarged. There was no apparent pain, tenderness, or itching.

Over the past 2 months, he had also developed hypopigmented macules on the trunk, arms, and left leg.

Past Medical History

NSVD to 20 year-old primigravid mother at 40 weeks gestation. Weight and height: 25th percentile, head circumference: 75-90th percentile. Newborn screen notable for borderline abnormal congenital hypothyroidism.

Medications/Allergies

None/NKDA

Social History

Lives with mother and father.

Family History

Mother has short 4th metacarpal.

Review of Systems

Negative for fussiness, difficulties eating, seizures, hair loss, constipation, lethargy, sleep difficulty. Normal vision and hearing.

Physical Exam

Skin	Forehead and upper eyelids: 4x9cm symmetric, ill-defined, erythematous patch Inferior right posterior neck: 2.5x3cm indurated, skin-colored, firm plaque with several overlying 2mm whitish papules Right mid-abdomen: hyperpigmented macule Shoulders, abdomen, back, arms: approximately 35 2mm confetti-shaped macules, some discrete while others clustered Right buttock fold, right leg: multiple 2mm ovoid hyperpigmented macules Left medial leg: 1.5cm hypopigmented patch with satellite pinpoint macules Nails normal
HEENT	Broad nasal root Depressed nasal bridge
Mouth	Several teeth present, no dental pits
GI	Umbilical hernia
Musculoskeletal	Short 4th metatarsals

Laboratory Data

The following labs were remarkable/abnormal:

Phosphorus (serum)	6.3 mg/dL	[2.5 – 4.5 mg/dL]
Fractional excretion of phosphate	6.7%	[10 – 20%]
TSH	10.4 μIU/mL (7 μIU/mL at 1 month of age)	[0.34 – 5.6 μIU/mL]
Parathyroid hormone	102.6 pg/mL	[6 – 65 pg/mL]
Alkaline phosphatase	596 U/L	[80 – 250 U/L]

The following labs were negative/within normal limits:
CBC, serum creatinine, free T4, calcium, Vitamin D, urine calcium/creatinine/sodium

Histopathology

POSTERIOR NECK, PUNCH BIOPSY:
Skin with dermal ossification/metaplastic bone formation.

Radiology

Cervical spine radiograph: C1 through T1 vertebral bodies visualized. No obvious misalignment. No calcification of the soft tissue.

Diagnosis

Albright Hereditary Osteodystrophy (Pseudohypoparathyroidism Type 1a) associated with Osteoma Cutis

Treatment and Course

Upon presentation to the Dermatology clinic, the patient had no known past medical history, save concern for congenital hypothyroidism. TSH had been elevated across multiple time points since birth but was not treated because his free T4 was within the normal limit. When skin biopsy revealed dermal bone formation, an evaluation for Albright hereditary osteodystrophy (AHO) was undertaken. He demonstrated elevated pseudoparathyroid hormone level with normocalcemia and hyperphosphatemia, consistent with pseudohypoparathyroidism. Urinary phosphorus excretion was low, consistent with parathyroid resistance. No treatment has been required to date.

Plastic Surgery, consulted for evaluation of excision, recommended against surgical intervention, as there was no functional deficit or cosmetic deformity related to the plaque.

Discussion

Primary osteoma cutis is rare, and its presence without known cutaneous or systemic disease mandates evaluation for several genetic conditions, including progressive osseous heteroplasia, fibrodysplasia ossificans progressiva, and AHO. The phenotypic presentation of pseudohypoparathyroidism (PHP), AHO is characterized by specific endocrine abnormalities, as well as distinct physical characteristics, including osteoma cutis in infancy or early childhood.

AHO is due to a mutation affecting the alpha subunit of a stimulatory G protein of adenylate cyclase, which is obligatory for proper functioning of parathyroid hormone (PTH). In AHO, i.e., PHP type 1a, there is a maternally inherited mutation of *GNAS*. Metabolic testing shows PHP in patients with PHP type 1a; however, in pseudo-PHP, the physical findings of AHO are present without the biochemical abnormalities. Patients with PHP type 1b show hypocalcemia without the physical features of AHO.

In PHP, there is an abnormal response of hormone receptors in skeletal muscle and the kidneys to PTH. For unknown reasons, hypocalcemia and hyperphosphatemia occur despite elevated PTH levels. Complications of PHP include tetany, muscle cramping, paresthesias, and seizures due to hypocalcemia, which may become evident in early childhood, around 2 to 3 years of age. Hypothyroidism, possibly from decreased sensitivity to thyrotropic-releasing hormone as well as to TSH, and decreased fertility may occur. Some patients may have osteopenia and rickets as a result of decreased osteoclast responsiveness to PTH.

Physical findings in patients with AHO include short stature, stocky build, round facies, developmental delay, dental hypoplasia, brachymetacarpals or brachymetatarsals resulting in short digits (usually 4th or 5th digits), cataracts, and soft tissue ossification.

Treatment aims to correct vitamin D and calcium levels. Excision of osteoma cutis is not necessary, unless concern exists for functional or cosmetic impairment.

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Key location: Diffusely across body CASE 6

Presented by Vidya Shivakumar, MD, Kavita Menon, MD, and Warren Piette, MD

History of Present Illness

A premature infant was born via vaginal delivery at 35 weeks gestational age with diffuse plate-like scale covering his skin. Apgar scores were 6 and 7, and intubation was briefly required at 2 minutes of life due to cyanosis; shortly thereafter, the baby was transferred to the neonatal intensive care unit with adequate respirations and oxygen saturation on room air. Hand, foot, and ear deformities were noted at birth; mild ectropion was visible by day two.

Past Medical History

Mother is G4P1112, current pregnancy complicated by preterm premature rupture of membranes.
The patient's newborn screen was unremarkable.

Medications/Allergies

None/NKDA

Family History

There is no consanguinity of parents. Brother A is unaffected. Brother B was similarly affected at birth and later developed a phenotype resembling non-bullous congenital ichthyosiform erythroderma with two *ABCA12* mutations detected.

Physical Exam

Vitals unremarkable

Skin	Diffuse yellow/white hyperkeratotic polygonal plates of scale, confluent on the head, and fissured on the trunk and extremities which exposed erythrodermic skin Bilateral mild upper lid ectropion Mild eclabium Ears encased in scale Edematous hands and feet with hypoplastic digits/nails and toes with claw-like deformity; band-like constriction around fingers and toes; no signs of infarction
Respiratory	No respiratory distress, symmetric chest expansion
Musculoskeletal	Spontaneously moves extremities, opens eyes and mouth, good suck reflex

Laboratory Data

The following labs were negative/within normal limits:
Sodium, potassium, chloride, bicarbonate, blood urea nitrogen, creatinine.

Diagnosis

Harlequin Ichthyosis

Treatment and Course

Multiple services were involved in the patient's care including Dermatology, Orthopedic Surgery, Ophthalmology, Genetics, Physical Therapy, and Occupational Therapy. Key elements in the treatment plan included adequate hydration, temperature regulation, sepsis prevention, ectropion management, and monitoring for digital infarction.

The infant remained in isolation and was placed on contact precautions; he was swathed in a polyethylene occlusive wrap and placed in a heated isolette with high humidity settings. Humidity settings initially ranged between 90-95% but were slowly titrated down until he was eventually placed in an open crib on day of life 35. Skin care consisted of emollient application every 2-3 hours and gentle cleansing daily. Electrolytes were carefully monitored and repleted as needed. A high caloric diet was implemented, given both orally and by nasogastric tube. Lubricating eye drops every 2 hours and erythromycin eye drops daily prevented potential complications of ectropion, including keratitis and infection. Prophylactic IV gentamycin and ampicillin were started on day one of life and discontinued on day 13. By the time of discharge at day 40, the infant's scale had desquamated, exposing scaly, erythrodermic skin. Improvement of ectropion, hand, foot, and ear deformities were noted. He required no supplemental oxygen, had stable electrolytes, and maintained adequate urine and stool output.

The patient and his two-year old brother currently receive their dermatology care at Lurie Children's Hospital.

Discussion

Harlequin ichthyosis (HI) is the most rare and most severe form of congenital ichthyosis. It is inherited in an autosomal recessive manner. Patients desquamate a keratotic cuirass during the first months of life, exposing skin that is similar to non-bullous congenital ichthyosiform erythroderma. Known as the only molecular cause of HI, adenosine triphosphate-binding cassette, subfamily A, member 12 (*ABCA12*) heterozygous missense mutations may also lead to lamellar Ichthyosis and nonbullous congenital ichthyosiform erythroderma. The clinical severity of HI is dependent upon the residual protein function of the ATP transporter; typically, mutations that result in a truncated protein cause a HI phenotype. At the molecular level, there is disruption of lipid transport by lamellar granules in the upper epidermal keratinocytes, leading to malformation of the intercellular lipid layers in the stratum corneum. This results in epidermal hyperkeratinization and defective desquamation.

Given the high mortality rate and wide array of complications, infants with HI should be monitored in the NICU under multidisciplinary care. Major complications include respiratory impairment from restricted movement of the thoracic cavity, a common cause of mortality, as well as hypernatremic dehydration, thermoregulatory dysfunction, and infection, which are caused by increased transepidermal water loss and compromised epidermal barrier. To avoid these complications, multiple preventative steps must be undertaken: there should be a low-threshold for intubation; fluid and electrolyte status must be monitored with attention to greater-than-normal fluid and caloric needs, often six times and 25% more than a healthy newborn respectively; high-humidity incubators with strict temperature regulation must be utilized; and insensible water-loss should be prevented by meticulous skin care consisting of daily gentle cleansing and liberal emollient use. Manual debridement, except for detaching constrictive bands that impede circulation, and the use of keratolytics, which can be percutaneously absorbed, should be avoided. While antibiotic prophylaxis is controversial, monitoring for signs of infection is crucial. Limb contractures and severe ectropion may require surgical intervention.

The utility of initiating early oral retinoid therapy remains controversial. Retinoid therapy reduces hyperkeratinization; however, the armour sheds spontaneously within the first few months of life. There are no reports to date of a harlequin phenotype extending beyond the neonatal period. Retinoid use may be warranted in situations were accelerated shedding is needed (i.e., impending digital necrosis, functional impairment of a limb, severe ectropion, or pulmonary compromise).

While biopsy is not necessary for diagnosis, genetic analysis of the child and parents is helpful. DNA-based prenatal testing and radiologic imaging can also aid in perinatal diagnosis of HI. Since the discovery of ABCA12 gene mutation as the cause of HI, DNA-based testing of chorionic villus or amniotic fluid sampling in the earlier stages of pregnancy is now possible. Three-dimensional ultrasound can detect facial disfigurement, such as ectropion, eclabium, and arthrogryphosis, suggestive of a diagnosis of HI. Undoubtedly, these children will face numerous medical and psychosocial obstacles. Families should be educated, counseled, and connected with support groups.

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Key locations: Abdomen, upper and lower extremities CASE 7

Presented by Steven Nwe, DO, Donna Sadowski, MD, Julia Kasprzak, MD, and Warren Piette, MD

Unknown #2

Fast Break #2

Key locations: Skin, eyes CASE 8

Presented by Mona Gandhi, MD, Joerg Albrecht, MD, and Warren Piette, MD

History of Present Illness

A 21 year-old Hispanic female presented with atopic dermatitis (AD) that started in childhood. She had been treated with multiple short courses of prednisone and topical corticosteroids by different providers over the years. For the last 3 years, she only used emollients. The patient had been referred from the Ophthalmology clinic where she was recently diagnosed with advanced chronic angle closure glaucoma of the right eye, thought to be secondary to anterior uveitis, as well as cataracts in both eyes. She first noted a change in vision 2 years earlier, which had progressed to complete loss of vision in the right eye and markedly decreased vision in the left eye.

Past Medical History

Atopic dermatitis

Medications

Pred forte drops, brinzolamide drops

Allergies

Strawberries, chocolate, peanuts

Review of Systems

The patient denied eye pain, swelling, tearing, infection, or trauma.

Physical Exam

Skin	Perioral, periorbital: Ill-defined lichenified thin plaques
	Extremities, torso: Erythematous scaling papules and plaques; reticular scaling on lower legs
	Right eye: Covered completely by hair forelock
	Hyperlinear palms
Eyes	OU: Blepharitis
	OD: Corneal scar, mature cataract, pupil block
	OS: Anterior capsular cataract

Laboratory Data

The following labs were remarkable/abnormal:

Absolute eosinophils	1.1 k/ uL	[0 – 0.4 k/μL]
Eosinophil percentage	11.9 %	[0.4 - 5.8 %]

Diagnosis

Advanced Chronic Angle Closure Glaucoma and Anterior Subcapsular Cataracts associated with Atopic Dermatitis

Treatment and Course

The patient was seen by the Ophthalmology service and noted to have severe scarring and inflammation from chronic uveitis in both eyes. She had bilateral anterior subcapsular cataracts and chronic angle closure glaucoma of her right eye. An urgent laser iridectomy of the right eye

was performed to reduce ocular pressure and relieve pupil block. She was started on oral prednisone, cyclosporine, and brinzolamide ophthalmic drops to treat inflammation prior to undergoing surgical management of the cataracts. Topical and systemic corticosteroids were used for management of her atopic dermatitis after discussion with Ophthalmology.

Discussion

Ocular complications occur in approximately 20-43% of atopic dermatitis patients. Atopic keratoconjunctivitis (AKC), a chronic, noninfectious inflammatory disease, is a severe complication that can occur at any time point and is not affected by the severity of cutaneous symptoms. AKC can lead to cataracts, keratoconus, infectious keratitis, blepharitis, tear dysfunction, and glaucoma in its most extreme form.

The pathophysiology is unclear, but inflammatory cytokines, including interleukin-33, which promotes eosinophil infiltration, has been shown to be elevated in AKC conjunctival tissue. Activated eosinophils release gelatinase B, major basic protein, and eosinophil cationic protein, which contribute to corneal disease. Over time, chronic inflammation leads to corneal erosion, ulceration, and mucous plaques. Corneal scarring and neovascularization can lead to permanent vision loss.

AKC tends to present in late teens and early adulthood but can persist into the fourth and fifth decades of life. Peak incidence occurs between ages 30 and 50. Most patients report itching, tearing, and burning of the eyes, as well as pain, redness, and blurred vision. Treatment options include ophthalmic drops and systemic medications, including mast cell stabilizers, antihistamines, corticosteroids, and calcineurin inhibitors.

AD and AKC are both risk factors for development of cataracts. Both anterior and posterior subcapsular cataracts have been described. Anterior subcapsular cataracts (ASC) are more specific to AD, but posterior subcapsular cataracts (PSC) are more common. The mechanism of cataract development is not entirely clear. Older literature links AD severity (i.e., repetitive rubbing of the eye) to cataract formation, but this has largely been disproven. Oxidative stress has also been implicated in the pathogenesis. A study by Niwa et al, showed that patients with AD and cataracts had decreased inducibility of superoxide dismutase (an enzyme that inhibits free radical formation) compared to atopic patients without cataracts. Interestingly, these findings were not seen in patients with other inflammatory skin conditions (i.e., psoriasis) who were exposed to chronic topical corticosteroid use. There also have been studies of patients with bilateral and posterior subcapsular cataract formation secondary to systemic corticosteroids, described in those receiving prednisone 10-15 mg daily for at least one year. However, cataract formation in AD was recognized before the advent of corticosteroids in dermatology. In addition, Niwa et al, showed that there was no difference in incidence percentage between three groups of atopic patients: those treated with topical corticosteroids, those treated with both topical and systemic corticosteroids, and corticosteroid naïve patients.

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Key location: Diffuse across body CASE 9

Presented by Sumul Gandhi, MD, Christina Kranc, MD, Jerry Feldman, MD, and Warren Piette, MD

History of Present Illness
An 81 year-old Hispanic male presented to the Dermatology clinic with a two-week history of a diffuse pruritic papular and nodular eruption. Initially, he had just two discrete nodules on the right shoulder and left arm, but the condition later generalized with the development of smaller pruritic red papules and nodules on the scalp, trunk, and extremities.

Past Medical History
Early dementia

Medications/Allergies
None/NKDA

Social History
No current tobacco use (quit smoking 20 years ago). No history of drug or alcohol use.

Review of Systems
Reports fatigue and weakness for several months and unintentional weight loss of 30 pounds over 3 months. Denies fevers, chills, nausea, vomiting, chest pain, shortness of breath, urinary changes, joint pain, night sweats.

Physical Exam

General	Alert and oriented but appears confused at times
Skin	Occipital scalp, neck, chest, back (upper>lower), abdomen, arms (shoulders/upper arms>forearms), lower extremities: Multiple confluent and discrete red to violaceous edematous papules and plaques; several scattered large, firm, mildly tender, deep red to violaceous nodules on shoulders and trunk
Lymph nodes	Non-tender lymphadenopathy of right submandibular lymph nodes

Laboratory Data
The following labs were remarkable/abnormal:

Hemoglobin	11.2 g/dL	[12.9 – 16.8 g/dL]
Hematocrit	35.6%	[38.1 - 49%]
WBC	2.7 k/μL	[4.4 – 10.6 k/μL]
Absolute neutrophil count	1.2 k/μL	[2.2 – 6.9 k/μL]

Histopathology

RIGHT CHEST AND RIGHT SHOULDER, PUNCH BIOPSIES:
Blastic plasmacytoid dendritic cell neoplasm. Sections of skin demonstrate periadnexal as well as dense and deep dermal infiltrate of atypical hyperchromatic hematopoietic cells of intermediate to large size and angulated irregular nuclear contour with prominent nuclei. There is no epidermotropism or angio-invasion.

Immunohistochemical stains demonstrate the neoplastic cells are positive for LCA, CD4, CD43, focal weak CD56, and co-express TCL1 and CD123.

All additional immunostains performed (CD20, CD79A, CD3, CD5, CD1-A, CD8, CD7, CD10,CD34, CD117, CD138, CD30, MUM1, BCL6, TdT, MPO, MART-1, AE1/EA3, S100, ISH KAPPA, ISH LAMBDA, ISH EBER) are negative. Few cells in the dermis are positive for CD68 with very rare CD163 positivity; the neoplastic proliferation is interpreted as negative for those markers.

Bone Marrow Studies

LEFT POSTERIOR ILIAC CREST:
The bone marrow biopsy shows cellularity of 90%. Trilineage hematopoiesis with maturation is present. An infiltrate of large, atypical immature cells that stain positively with CD4 and CD56, but not CD3 and CD20, are present.

Flow cytometry studies performed on bone marrow identify an abnormal population that is positive for CD56 but is negative for other T/NK markers.

Cytogenic studies performed on bone marrow show the following karyotype:
46,XY,del(13)(q12q22)[4]/46,XY[16].

Radiology

Chest radiograph (10/13/13): Interstitial changes at the bases of the lungs. Compression fractures of the thoracic spine. No identifiable masses.

CT neck (10/13/13): Necrotic right submandibular lymph nodes. Enlarged right supraclavicular lymph node. Six mm nodule in right upper lobe of lung.

CT neck (12/27/13): Interval improvement of cervical lymphadenopathy with borderline right submandibular lymph nodes remaining.

CT chest (12/27/13): Pulmonary micronodules. Questionable metastasis to T10 vertebral body.

CT abdomen/pelvis (12/27/13): Borderline mesenteric lymphadenopathy. Lytic lesions in left anterior aspect of T10 vertebral body, concerning for metastatic disease.

Diagnosis

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)

Treatment and Course

Prior to being seen in Dermatology clinic, the patient was started on a seven-day course of prednisone 40 mg daily and diphenhydramine. He noted improvement of both pruritus and

cutaneous lesions. After skin biopsy established the diagnosis of BPDCN, the patient was referred to the Hematology service. Bone marrow biopsy showed infiltration of large, immature cells positive for CD4 and CD56, consistent with the diagnosis seen on skin histopathology. Imaging suggested metastatic disease. The patient was started on CHOP chemotherapy, with continued improvement in symptoms and skin lesions. Hematopoietic stem cell transplantation as a therapeutic option in the event of remission was not possible due to the patient's age.

Discussion

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare hematologic malignancy that arises from the precursors of plasmacytoid dendritic cells. These cells are part of the innate immune defense and are capable of producing large amounts of type I interferons (interferons alpha and beta) in response to viruses or virally-derived nucleic acids. While it is possible that viral exposure may play a role in disease pathogenesis, no direct association has been reported to date, and the true pathogenesis of the condition is not well understood.

The true incidence of BPDCN is unknown, but fewer than 50 cases are reported in the United States each year. BPDCN most commonly affects older adults, with a median age at diagnosis between 65 and 67 years. The male to female incidence ratio is 2.5:1.

Most patients present with cutaneous lesions, but many may also exhibit bone marrow involvement (80%) and/or leukemic dissemination. Classic skin lesions consist of brown to violaceous nodules (73%), but can also include bruise-like patches (12%) and disseminated and mixed lesions (14%). Some patients may exhibit a more solitary pattern. Cytopenias (most commonly thrombocytopenia), lymphadenopathy, and splenomegaly are present in a majority of patients, with less frequent involvement of the tonsils, lungs, eyes, central nervous system, and paravertebrae. A minority of cases, however, can present with purely leukemic involvement.

A biopsy of lesional skin demonstrates an infiltrate of medium-sized cells that spares the epidermis but can extend to the subcutaneous fat. The tumor cells are monomorphic, poorly differentiated blasts with fine chromatin and two to three nucleoli. Mitotic activity is usually infrequent. Tumor cells classically express CD4 and CD56, but the expression of one of the markers CD123, BCDA-2/CD303 (blood dendritic cell antigen 2), TCL1, or SPIB is required for a definitive diagnosis.

There is minimal data to guide treatment regimens. While the optimal treatment of BPDCN is unknown, small studies suggest that the clinical course and response to therapy differs between children and adults. Patients under 18 years of age appear to benefit from a treatment regimen similar to that of high-risk acute lymphoblastic leukemia, in which allogeneic hematopoietic stem cell transplantation (HSCT) is reserved for patients who relapse and achieve a second remission after induction chemotherapy. Generally speaking, the disease is much more aggressive in adults, and induction chemotherapy is supplemented by allogeneic HSCT during the first remission.

While the absence of large prospective trials makes it difficult to comment on factors predictive of prognosis, a better prognosis is generally seen in younger patients, those with only cutaneous involvement, and cases in which tumor cells do not express BDCA-2. It is imperative to evaluate the extent of disease and systemic involvement; however, even localized disease may portend a poor outcome.

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Fast Break #3

Not Your Usual Suspects

Cases A-H