Chicago Dermatological Society

October 2015
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, October 14, 2015
Gleacher Center - Chicago

David Fretzin Lecture

Conference Host:
Department of Dermatology
University of Illinois at Chicago
Chicago, Illinois

Program

Host: University of Illinois at Chicago

Conference Location

Gleacher Conference Center
450 N. Cityfront Plaza Dr., Chicago

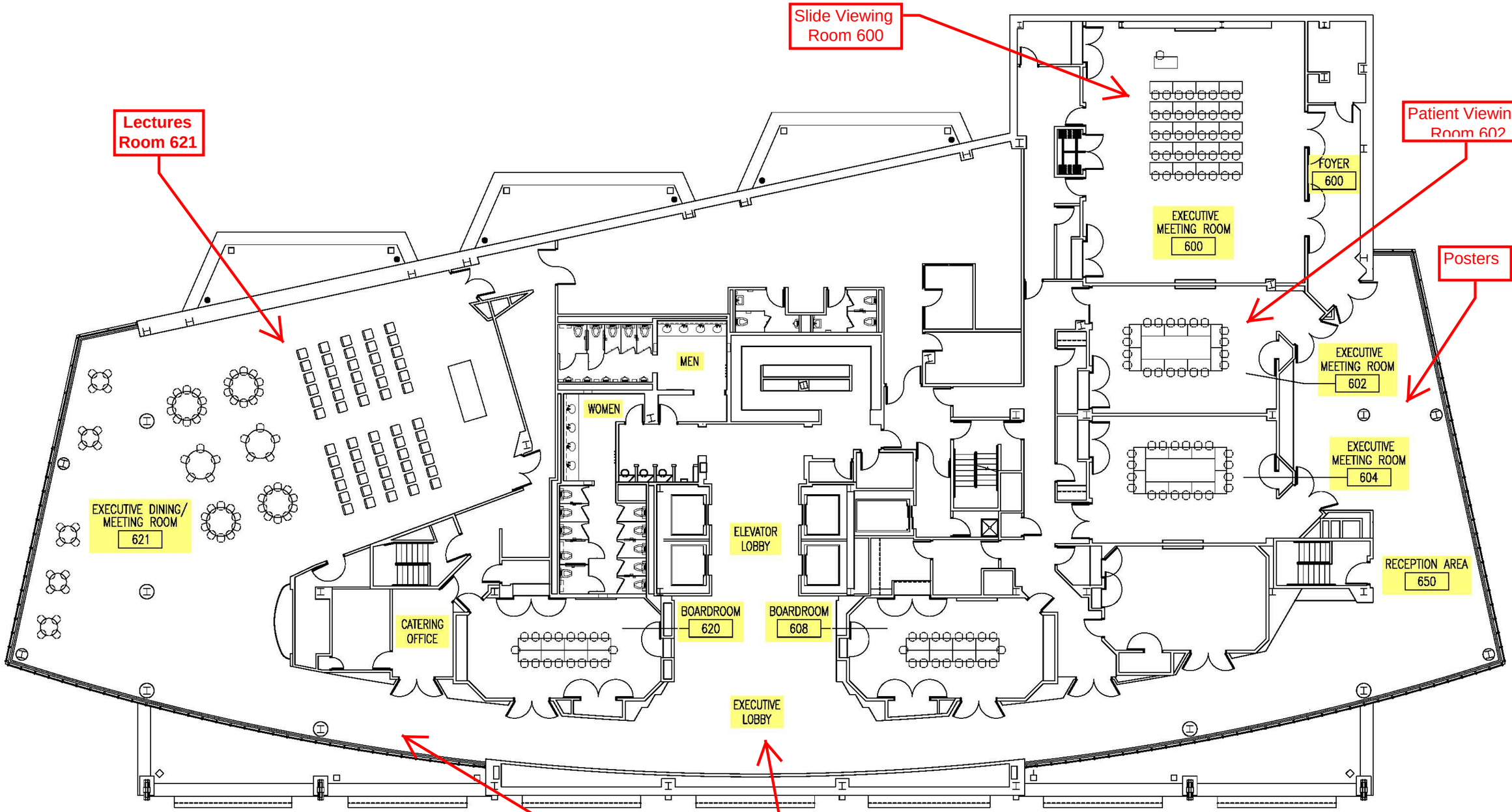
All meeting activities take place on the 6th Floor of the Gleacher Center.

8:00 a.m.	**Registration & Continental Breakfast with Exhibitors** *6th Floor Lobby and Foyer*
8:30 a.m. - 10:00 a.m.	**Clinical Rounds** Patient Viewing – *Rooms 602* Posters – *North Foyer (available throughout the morning)* Slide viewing – *Room 600 (available throughout the morning)*
9:00 a.m. - 10:00 a.m.	**Resident/Basic Science Lecture** – *Room 621* "Flaps and Grafts" *Timothy M. Johnson, MD*
10:00 a.m. - 10:30 a.m.	**Break and Visit with Exhibitors**
10:30 a.m. - 12:00 p.m.	**Resident Case Presentations & Discussion** *Room 621*
12:00 p.m. - 12:15 p.m.	**MOC Self-Assessment Questions** *Room 621*
12:15 p.m. - 12:45 p.m.	**Box Lunches & visit with exhibitors** *Foyer Area*
12:45 p.m. - 1:00 p.m.	**CDS Business Meeting** *Room 621*
1:00 p.m. - 2:00 p.m.	**General Session** – *FRETZIN LECTURE*: Melanoma Sentinel Node Biopsy: Past, Present, and Future in the New Era of Systemic Therapies *Timothy M. Johnson, MD*
2:00 p.m.	**Meeting adjourns**

Mark the Date!

Next CDS monthly meeting – Wednesday, November 4, 2015 at the Gleacher Center
Hosted by Northwestern University; Guest speaker: Youn Kim, MD, Stanford University

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



Gleacher Center - 6th Floor

CHICAGO BOOTH

The University of Chicago Booth School of Business

Guest Speaker

TIMOTHY M. JOHNSON, MD

Lewis and Lillian Becker
Professor of Dermatology
University of Michigan Health System
Ann Arbor, M

Delivering the David Fretzin Lecture

Dr. Tim Johnson received his medical degree and dermatology residency training at the University of Texas at Houston. After completing additional fellowship training in cutaneous surgery and oncology at the University of Michigan and the University of Oregon, he joined the University of Michigan faculty in 1990 with appointments in the departments of Dermatology, Otolaryngology and Surgery (Division of Plastic Surgery). Dr. Johnson has served as clinical director of the Cutaneous Oncology and Multidisciplinary Melanoma Programs since 1990.

Dr. Johnson has received many clinical, teaching, and research honors; delivered numerous national and international keynote and named lectureships over the last two decades; and is a benchmark for clinical care. He served on the board of directors and executive committees of several national and international organizations that impact dermatology, melanoma and non-melanoma skin cancer. Dr. Johnson is an investigator on grants, clinical trials, and numerous research activities, and his publication portfolio includes more than 200 original peer-reviewed publications and 25 chapters published in mainstream dermatology, surgery, and oncology journals.

CONTINUING MEDICAL EDUCATION CREDITS

Chicago Dermatological Society

Presents

"Chicago Dermatological Society Monthly Meeting Series"

October 14, 2015 *Chicago, IL*

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

JOINT SPONSOR STATEMENT

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

GOAL / PURPOSE

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

EDUCATIONAL OBJECTIVES

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

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

Continued next page

CREDIT STATEMENTS

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

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The faculty, planner and/or content managers have no conflicts of interest to disclose nor do they have any vested interests or affiliations.

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

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Case Presented by Kimberly Jerdan, MD,
Claudia Hernandez, MD, and Milena Lyon, MD

History of Present Illness:
This 44 year old female presented with a 10 year history of a slow growing plaque in her groin. She was sent by her primary care physician for intralesional steroid injection of what he believed was a keloid from a surgical procedure eight years prior. Due to the irregular appearance of the mass, a biopsy was recommended prior to any injections. The pathology was consistent with a diagnosis of dermatofibrosarcoma protuberans (DFSP). Review of her medical records revealed she had been previously diagnosed with a DFSP in the same location in 2007. This DFSP had been excised; however, the patient insisted she had a keloid removed eight years prior. She was informed this was a recurrent DFSP and referred to oncology.

Past Medical and Surgical History:
Dermatofibrosarcoma protuberans excision 2007 and cesarean section 1999

Medications:
Vitamin D IU, and calcium

Allergies:
No known drug allergies

Family History:
No history of skin cancer, skin conditions, or autoimmune conditions. The patient reported a history of keloids in her brother.

Review of systems:
The patient denied any fevers, chills, night sweats, weight loss, vision changes, dyspnea, or joint pains.

Physical Examination:
The patient has a 9 cm x 4 cm flesh-colored to violaceous irregularly shaped tumor in the right inguinal fold, along with two 1 cm smooth papules in the left subrapubic area, approximately 10 cm from the above noted tumor.

Diagnostic Procedures and Tests:
06/15 Computed tomography, Chest/Abdomen/Pelvis: Right lung with four nodular opacities measuring 0.2 to 0.3 cm, and an additional nodule in the left lung measuring 0.2 cm. Small nonspecific liver lesions also could represent metastases. Cutaneous and subcutaneous tumor lesions in the right groin and possible smaller additional lesions to the left of the midline near the cesarean scar.

Histopathology:
Right inguinal, skin: Spindled and stellate fibroblasts are present in the dermis and expand into the subcutaneous tissue forming anastamosing and palisading bundles. Lesional cells are positive for CD34 and negative for S100 and Factor XIIIa. Fluorescent in-situ hybridization testing is positive for the fusion of collagen type I, alpha 1 (COL1A1) (17q21) and platelet-derived growth factor-beta (PDGFB) (22q13) loci.

Left suprapubic, skin: Spindle cells with a fascicular growth pattern are present in the dermis with foci of keloidal-like collagen. The findings are compatible with keloid, tissue edges are involved. The spindle cells are negative for CD34, Factor-XIIIa and S100.

Diagnosis:
Dermatofibrosarcoma protuberans

Treatment and Course:
Given the recurrent nature of this DFSP, the patient was referred to oncology for further work-up. CT scan of the chest, abdomen and pelvis was significant for nodular opacities in the lungs as well as the liver. These lesions were concerning for possible metastatic disease but were deemed too small to biopsy. Therapy with imatinib mesylate was initiated at 600mg per day with a plan to repeat the CT scan after three months and to re-evaluate the cutaneous tumor's size after one month for possible surgery. After approximately one month of therapy the imatinib mesylate was decreased to 200mg daily, as patient was unable to tolerate the higher dose due to a "rash." Despite a multidisplinary team discussion where the use of Mohs micrographic surgery (MMS) was discussed, the oncology team sent the patient to surgical oncology who recommended wide excision of the lesion with 3 cm margins and a flap closure by plastic surgery.

Discussion:
DFSP is a dermal sarcoma that can be locally aggressive and has a tendency to recur, although it rarely metastasizes. These tumors have slow progression, are localized mainly on the trunk, and are typically asymptomatic papules or patches that grow into more irregular nodules or plaques. Greater than 90% DFSPs have the chromosomal translocation involving 17q22;22q13, with fusion of the genes encoding collagen type 1, alpha 1 and platelet-derived growth factor beta (COL1A1-PDGFB). The tumor's growth can be attributed to the constitutively expressed PDGF receptor that acts as an autocrine factor stimulating the growth of DFSP cells. There are several variants of DFSP. Included in these variants is a pigmented DFSP (Bednar tumor) with melanin-containing dendritic cells and a fibrosarcomatous DFSP, the variant most at risk for metastasis and recurrence. Rapid change in a lesion is suggestive of a fibrosarcomatous transformation due to TP53 missense and silent mutations, as well as high microsatellite instability.

Current treatment for DFSP is mainly surgical. Complete removal must involve the deep and lateral extensions of this tumor until clear margins are achieved. Margins of 1-1.3cm for MMS seem sufficient while 3cm margins are advisable with wide local excisions. Recurrence rates depend on the type of surgery performed including: conservative surgical resection (26-60%), wide local excision (0-30%), and MMS (0-8%). Chemotherapeutic agents may be used to treat inoperable tumors, metastatic disease, high-risk DFSP, or lesions greater than 5cm in an attempt to reduce the size of the tumor prior to excision. Possible treatments include gemcitabine, docetaxel, sorafenib or imatinib mesylate. Imatinib mesylate, which was used in this case, is a multi-targeted tyrosine-kinase inhibitor of breakpoint cluster region-Abelson (BCR-ABL), cellular KIT gene (c-KIT), and PDGFR. It acts by inhibiting the enzyme activity of these proteins, thus decreasing cell proliferation. Imatinib mesylate has been shown to be effective at a dose of 400 to 600 mg daily in 50% of DFSPs that require preoperative reduction or in those that are unresectable.

Our case demonstrates the potential for DFSPs to recur years after the initial diagnosis, and for metastases to occur despite its low-grade classification. Recommended follow-up for DFSP

patients includes clinical examination every six months for five years, then every year for 10 years.

Essential Lessons:

- DFSP should be included in the differential diagnosis of patients with persistent or unusual keloids.
- The chromosomal translocation found in 90% of cases is 17q22;22q13 with fusion of the genes COL1A1 and PGFB.
- Treatment is mainly surgical. Regardless of the surgical procedure used, assessing the deep fascia for infiltrating tumor cells is very important.
- Consider imatinib mesylate therapy for large tumors with the above positive translocation to aid in debulking prior to surgical removal.

References:

1. Glaser ES, et al. Current approaches to cutaneous sarcomas: Dermatofibrosarcoma protuberans and cutaneous leiomyosarcomas. *Curr Probl Cancer*. 2015; 39(4):248-57.
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Case Presented by Rosemara Hughart, MD
and Maria Tsoukas, MD, PhD

History of Present Illness:
A 65 year old Mexican-American female, status-post renal transplant five months prior, presented with a three month history of the insidious onset of a painless nodule on her right distal forearm. The lesion appeared at first as a papule following external pressure on her wrist. It was subsequently drained as a presumed hematoma and the patient completed a short course of cephalexin. She then travelled to Colima, Mexico. During the trip she denied any outdoor exposures or trauma although she did admit to draining the lesion at home using insulin needles. Upon returning to the United States the lesion was drained again by a physician as a presumed hematoma and she completed a course of clindamycin without improvement.

Past Medical and Surgical History:
Diabetes mellitus type two, hypertension, end-stage renal disease, and cadaveric renal transplant

Medications:
Tacrolimus, mycophenolic acid, ergocalciferol, insulin lispro, levothyroxine, nifedipine, valgancyclovir, and sulfamethoxazole-trimethoprim

Allergies:
No known drug allergies

Review of Systems:
The patient denied any fevers, chills, night sweats, weight loss, cough, shortness of breath, headaches, dizziness, chest pain, nausea, vomiting, diarrhea, or dysuria.

Physical Examination:
The patient has a 5 cm x 5 cm symmetric dome-shaped exophytic nodule located on her right forearm with diffuse overlying hemorrhagic eschar and underlying pink friable tissue. No lymphadenopathy is appreciated.

Laboratory Data:
The following were positive or abnormal:
Absolute lymphocyte count 0.6 thousand per µl (1.3-4.2), glucose 397 mg/dl (65-110), (1,3) beta-D-glucan >500 pg/ml (≥80 is positive)

The following were negative or within normal limits:
Urinalysis, complete metabolic panel, and complete blood count with differential with the exceptions noted above

Diagnostic Procedures and Tests:
01/15 **Radiograph, right forearm/wrist:** Soft tissue swelling on the lateral aspect of the wrist, no radiopaque foreign body, no findings of osteomyelitis
01/15 **Tissue culture, right forearm:**
Bacterial, aerobic: Rare *Klebsiella pneumoniae*, few *Enterococcus* species, rare *Candida tropicalis*
Fungal: Many *Biatriospora mackinnonii* (dematiaceous mold)

Anaerobic bacterial, viral, acid-fast bacilli: No organisms isolated

02/15 **Magnetic resonance imaging, right forearm/wrist, with and without contrast:** Large fungating mass at dorsal radial wrist without extension below the skin, no involvement of tendon or bone.

03/15 **Radiograph, chest:** Hyperexpansion consistent with chronic obstructive pulmonary disease, no focal airspace consolidation.

Histopathology:

Right forearm, skin: H&E shows dermal involvement by fungal hyphal elements, marked pseudoepitheliomatous hyperplasia of the epidermis, and moderate to severe acute and chronic dermal inflammation with micro abscesses. There is an absence of granules and no sclerotic bodies are noted. PAS and GMS stains reveal dermal fungal elements and Fontana-Masson staining confirms this finding.

Diagnosis:

Cutaneous phaeohyphomycosis caused by *Biatriospora mackinnonii*

Treatment and Course:

Following the biopsy, the patient was started on itraconazole with a known interaction with tacrolimus requiring close monitoring and a decrease in tacrolimus dosing. After two weeks of pre-treatment with itraconazole 200 milligrams twice daily the lesion was excised and a split thickness skin graft was used to close the surgical site without complication. The patient was continued on itraconazole to complete a six month course. The patient has been followed closely and no evidence of recurrence has been noted up to six months postoperatively.

Discussion:

The term “phaeohyphomycosis” was first introduced by Ajello et al. in 1974 to describe infections caused by dark walled, also known as dematiaceous or melanised, fungi that are clinically, pathologically, and mycologically distinct from classic chromoblastomycosis. In 1983 phaeohyphomycosis was further sub-classified by McGinnis into four clinical presentations: superficial, cutaneous and corneal, subcutaneous and systemic. Recent advances in molecular techniques have led to the ability to rapidly and accurately speciate non-sporulating melanized molds. This is very important as different species may have tropism for different organs and varying susceptibilities to antifungals. Gene sequencing of the internal transcribed spacer region remains one of the most widely accepted molecular methods. Using gene sequencing we identified *Biatriospora mackinnonii* as the causative species in this case. To our knowledge, this species has only been implicated in one case of phaeohyphomycosis to date. Until recently many reported cases of phaeohyphomycosis did not include the causative species or did so based on descriptions of the macroscopic and microscopic morphology, identifying features such as septations in hyphae or the appearance of conidia. Thus, the true prevalence of this and other species implicated in phaeohyphomycosis may be understated due to lack of and unreliability of non-molecular strain identification methods. Ajello defined phaeohyphomycosis as a subcutaneous or systemic infection caused by fungi with a mycelial tissue form. Thereby, the histological criterion for diagnosis of phaeohyphomycosis is based solely on the finding of dematiaceous mycelia.

There are no standardized treatment protocols for the treatment of phaeohyphomycosis but voriconazole, posaconazole, and itraconazole have demonstrated the most consistent in vitro activity against this group of fungi. Oral itraconazole is considered the empiric drug of choice for phaeohyphomycosis given the most clinical experience with this drug in the literature, however,

molecular identification of the organism may assist in timely more potent antifungal selection. For cutaneous nodules in particular, surgery alone has been effective in many cases but oral antifungals are often used as co-adjunctive therapies especially in immunosuppressed patients to prevent dissemination.

Biatriospora is a genus that is widely distributed in soil, on wood and other plant debris and as plant pathogens. Phaeohyphomycosis is often preceded by a history of trauma but the role of injury in this case is unclear. Of note, dematiaceous fungi contain melanin and carotenoids within their cell walls and these pigmented molecules are thought to play an important role in the virulence of these fungi. Melanin pigment is thought to aid in the organism's ability to evade host immune responses by scavenging of free radicals released during the oxidative burst amongst other mechanisms.

Essential Lesson:

- Although cutaneous phaeohyphomycosis is a rare entity there should be a high index of suspicion in renal transplant recipients to allow for timely diagnosis and management.
- Renal transplant recipients are often taking calcineurin inhibitors such as tacrolimus, it is important to be aware of the potentially dangerous interaction of this class of medications with the main class used to treat phaeohyphomycosis, the azoles.

References:

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Case Presented by Monica Boen, MD,
Amy Flischel, MD, and Jane Scribner, MD

UNKNOWN

This 78 year old male presented with scaly, hyperkeratotic plaques and ulcerations on the scalp.

Case Presented by Drew Taylor, MD,
Iris K. Aronson, MD, and Carolyn I. Jacob, MD

History of Present Illness:
A 25 year old female presented with a two year history of pruritic lesions in the bilateral axillae. The pruritus was exacerbated by exercise and stress. She had been using a sensitive skin deodorant and could not recall any changes in her shaving cream or razor brands. There had been no changes to her axillary sweating patterns or volume. The patient denied any history of axillary hair removal procedures or family history of similar lesions.

Past Medical History:
None

Medications:
None

Allergies:
No known drug allergies

Review of systems:
The patient reported pruritus and irritation to the involved areas.

Physical Examination:
There are multiple, monomorphic, skin colored to slightly yellow, conical papules in the bilateral axillary vaults with extension to the axillary folds.

Laboratory Data/Diagnostic Procedures and Tests:
None

Diagnosis:
Fox-Fordyce disease

Treatment and Course:
The patient was clinically diagnosed with Fox-Fordyce disease. Initially, she was started on tretinoin 0.1% cream to the affected areas daily, but returned after three months without any improvement in appearance or symptoms. At that time, MiraDry® (Miramar Labs, Incorporated, Santa Clara, California) microwave technology, given its capability to target hair follicles, apocrine, apoeccrine, and eccrine sweat glands, was recommended to the patient. We utilized an energy level of three for the first treatment session followed by a maximum energy level of five for the second treatment nine months later. The patient had marginal improvement of the symptomatic lesions following the first treatment but significant clearance following the second procedure. The pruritus resolved following the second treatment session with a dramatic impact on her quality of life. Additionally, there was a marked decrease in the axillary hair density following the two treatment sessions.

Discussion:
Fox-Fordyce disease (FFD) was first described by George Henry Fox and John Addison Fordyce in the early twentieth century. It is believed that the primary pathophysiologic process involves a hyperkeratotic plug causing infundibular obstruction with resultant dilation of the

apocrine duct. This may lead to formation of a retention cyst, ductal rupture and subsequent inflammatory response to the spewed material. The lymphohistiocytic infiltrate may be the cause of the intense pruritus. The precise pathogenesis of FFD remains unknown but hormonal factors, genetics, and stress are all thought to be contributors. There are also rare case reports that suggest exogenous factors, for example laser hair removal, may contribute to the development of FFD.

Currently, there has yet to be a consistently effective treatment for FFD. However, many different therapeutic modalities have shown variable efficacy in small subsets of patients. These include topical clindamycin, oral contraceptive pills, topical and oral retinoids, topical pimecrolimus, topical and intralesional corticosteroids, excision-liposuction with curettage, and fractional carbon dioxide laser.

Since the pathophysiology of FFD is now believed to be a follicular process in which keratinous plugs in the infundibula lead to apocrine outflow obstruction and subsequent rupture and phagocytosis of the spewed contents, we hypothesized that the thermolysis of hair follicles and sweat glands may potentially alter this pathogenic pathway. Therefore, we looked to a new non-invasive technology device that utilizes microwave energy to preferentially target the dermal-hypodermal junction. This microwave device, currently marketed as MiraDry®, emits a 5800 Megahertz microwave frequency to cause dielectric heating at the dermal-hypodermal junction resulting in destruction of the sweat glands and hair follicles. Application of concurrent hydro-ceramic contact cooling to the epidermis and upper dermis restricts the zone of thermolysis to the dermal-subcutaneous interface, between the cooled upper layers and the inert subcutaneous tissue.

To the authors' knowledge, this is the first reported case of successfully treating FFD utilizing non-invasive microwave technology. We observed a decrease in the number of papules, hair density, and sweating of the treated areas with complete resolution of the associated pruritus. Further follow-up showed no signs of recurrence and the patient continues to be extremely satisfied with the therapeutic outcome. The average gravimetric sweat reduction for patients treated with Miradry is reported to be 82% at 12 months and may explain why we were unable to achieve complete clearance of the lesions with two treatment sessions. The residual folliculo-sebaceous-apocrine units may not have reached the temperature threshold necessary to achieve thermal ablation, and thus are still susceptible to the above pathogenic pathway. A third treatment session at the maximum energy level will be performed. This procedure is generally not covered by insurance and may cost $1000-2000 per treatment. Larger scale studies and long-term follow up are warranted to determine this treatment's efficacy.

Essential Lesson:

- A dysfunctional folliculo-sebaceous-apocrine unit drives the pathogenic pathway in Fox-Fordyce disease.
- Miradry utilizes microwave energy to cause dielectric heating at the dermal-hypodermal junction, resulting in destruction of sweat glands and hair follicles.

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Case Presented by Leigh Stone, MD,
Claudia Hernandez, MD, Milena Lyon, MD, and Sophie Worobec, MD

Fast Break: The Spectrum of Darier Disease

Case 6

Case Presented by Eden Pappo, MD,
and Maria Tsoukas, MD, PhD

UNKNOWN CASE

This 16 year old male presented with a lesion on the right eyelid.

Case Presented by Michael Sotiriou, MD
and Carlotta Hill, MD

History of Present Illness:
A 25 year old male originally from Guerrero, Mexico, presented to the clinic as a referral from an infectious disease physician in Minnesota. The patient had originally presented to the emergency room in Minnesota with complaints of itching of the hands, feet, and right ear. At that time, he was noted to have thinning of the lateral eyebrows and loss of the right eye lashes. He was referred to dermatology and underwent two skin biopsies which demonstrated numerous acid-fast bacilli. He was started on treatment for Hansen's disease with rifampin 600mg monthly, minocycline 100mg daily, and dapsone 50mg daily. He initially improved, but several months later developed new painful skin lesions. The new flare was attributed to erythema nodosum leprosum. He was then started on prednisone 40mg daily, but failed to improve and was eventually increased to prednisone 80mg daily and started on pentoxifylline 800mg TID. He was referred to UIC for further evaluation and treatment.

Past Medical History:
Leprosy diagnosed in 2007
Syphilis based on positive RPR and borderline fluorescent anti-treponemal antibody absorption test, treated with intramuscular benzathione penicillin

Medications:
Rifampin, minocycline, dapsone, prednisone, and pentoxifylline

Allergies:
No known drug allergies

Family History:
No previous known exposures to Hansen's disease

Social History:
The patient is from the state of Guerrero, Mexico, and has a total of six siblings: two sisters and four brothers. Two of his brothers still live in Mexico. The patient lives with his sister and her five children in Minnesota. Prior to moving to Minnesota, the patient lived with his mother and three siblings. While living in Mexico, the patient and sister had frequent contact with armadillos which he would catch and bring home to eat.

Review of Systems:
The patient confirmed fevers, chills, swelling of the fingers and hands, and weakness.
The patient denied nausea, vomiting, shortness of breath, chest pain, numbness, tingling, pain, depression, oral pain, or difficulty swallowing.

Physical Examination:
The patient has madarosis, non-pitting edema of the ears, hands, and feet, bilateral loss of eyelashes, and ill-defined, dusky, hyperpigmented patches scattered symmetrically and bilaterally on the extremities sparing the neck and trunk. No neurologic deficits are appreciated.

Laboratory Data:
The following were positive or abnormal:
White blood cell count: 14.4 k/uL (3.9-12.0)
Differential: Neutrophils 11.0 k/ul (1.3-7.5)
Hemoglobin: 12.2 g/dl (13.2-18.0)
Protein: 5.8 g/dl (6.0-8.0)
Albumin: 3.0 g/dl (3.4-5.0)
Antinuclear Antibody: 1:320 with speckled pattern (negative)

The following were negative or within normal limits:
Basic metabolic panel and liver function test are negative.

Diagnostic Procedures and Tests:
None

Histopathology:
Left anterior thigh, skin: There are chronic inflammatory infiltrates composed of organized aggregates of lymphocytes and histiocytes appearing in perivascular and perineural locations. Fite stain reveals moderate to large numbers of bacilli within these infiltrates.

Diagnosis:
Hansen's disease – lepromatous LL-BL, erythema nodosum leprosum (active)

Treatment and Course:
The patient was started on clofazamine 100mg daily, continued dapsone, prednisone 80mg tapered by 20mg every two weeks, continued rifampin, and was instructed to stop pentoxifylline and minocycline. Shortly after his visit, he was noted to have worsening symptoms of hand and foot pain, as well as fevers and additional skin lesions. His prednisone was increased to 100mg daily, which he continued until his next clinic visit, with minimal improvement. Due to the need to decrease systemic corticosteroids, he was started on thalidomide 100mg daily and instructed to taper his prednisone dose. Over the following year his clofazamine was stopped due to depressed mood with suicidal ideation, and the prednisone was decreased.

Five years after the patient's diagnosis, his older sister, with whom he lives in Minnesota, presented with violaceous patches bilaterally on her malar cheeks and multiple hypoesthetic erythematous violaceous plaques on the upper back, arms, left upper thigh, and distal legs. No neurologic deficits were noted at the time. Biopsy of the left thigh and right lower leg showed granulomatous inflammation and acid-fast bacilli suggestive of borderline lepromatous leprosy. She was started on rifampin, clarithromycin, and clofazamine. Polymerase chain reaction (PCR) demonstrated a match for the organism *Mycobacterium lepromatosis (M. lepromatosis)*. Later deep biopsy confirmed presence of acid-fast bacilli inside cutaneous nerves. In light of the new findings in the patient's sister, retrospective PCR analysis of the patient's original biopsy confirmed the presence of *M. lepromatosis* as well.

Six years after initial presentation to UIC, the patient is maintained with thalidomide 50mg daily and prednisone 1.5mg daily.

Discussion:
Leprosy, also known as Hansen's disease, is a chronic dermatologic infection that has affected humans for over 50,000 years. Until 2008, *Mycobacterium leprae* was the only organism known to cause leprosy, when the discovery of a new organism, *Mycobacterium lepromatosis,* was

identified in two patients from Mexico with diffuse lepromatous leprosy. Since then four cases have been identified in the United States.

Other than humans, armadillos are the only known animals to become infected with *M. leprae* by natural means. This finding is believed to be related to the low core body temperature of the armadillos.

Erythema nodosum leprosum (ENL) is a circulating immune complex-mediated disease characterized by widely-distributed erythematous, subcutaneous, and dermal nodules as well as nonspecific systemic symptoms including fever, chills, myalgias, arthralgias, and anorexia. Of note, the nodules of ENL do not occur at the sites of existing skin lesions. ENL can affect multiple organ systems, resulting in conjunctivitis, neuritis, keratitis, iritis, synovitis, nephritis, and hepatosplenomegally. These reactions can be severe and are an important cause of permanent nerve damage. ENL occurs in up to half of patients with borderline or lepromatous leprosy. Thalidomide is known to be effective against ENL. In addition to thalidomide, clofazamine and pentoxifylline are used as steroid-sparing agents in the treatment of ENL.

Essential Lesson:

- Madarosis in any patient should prompt consideration of lepromatous leprosy as a differential diagnosis
- Armadillos in the southeastern United States are known to harbor a natural infection with *M. leprae.*
- Erythema nodosum leprosum is a reactional state with multi-system involvement often seen following the initiation of multi-drug therapy in the treatment of Hansen's disease.

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Case Presented by Lisa Blackwood, MD
and Michelle Bain, MD

History of Present Illness:
This 3 day old term baby boy was born to a 36 year old G4P3 mother with no prenatal complications via uncomplicated spontaneous vaginal delivery. At birth he was found to have extensive congenital vascular and pigmentary cutaneous abnormalities involving the face (with V1, V2, and V3 trigeminal distribution), trunk, and extremities. Dermatology was consulted due to concern for a neurocutaneous syndrome, such as Sturge-Weber syndrome.

Past Medical History:
None

Medications:
None

Allergies:
No known drug allergies

Family History:
The patient's mother has a port wine stain on her right neck, present since birth and measuring 3.5 cm x 5 cm. His maternal aunt and maternal first cousin also have small port-wine stains with no other medical problems.

Physical Examination:
The patient has an extensive red vascular patch covering approximately 50% of the body, including the entire left side of the face (involving V1, V2, V3), part of the right face (involving V1), and extending to the neck, anterior and posterior trunk, buttocks, left upper leg, and left scrotum. Admixed with the vascular patch is a bluish-gray patch involving the mid to lower back extending to bilateral flanks and buttocks. The left cornea is hazy and the left iris is larger than the right (buphthalmos). There is minimal periorbital edema. The left palate has an erythematous vascular patch. There is no apparent limb asymmetry, no dysmorphic features, and no palpable thrill noted on any of the vascular patches.

Diagnostic Procedures and Tests:
07/15 Magnetic resonance imaging, brain, with and without contrast: Unremarkable, negative for signal abnormality to suggest Sturge-Weber syndrome.
07/15 Magnetic resonance angiogram and venography, brain: Hypoplastic left sigmoid and transverse sinus without thrombosis

Diagnosis:
Phakomatosis pigmentovascularis type IIb and Sturge-Weber overlap syndrome

Treatment and Course:
Due to the concern for a neurocutaneous syndrome, the patient was also evaluated by ophthalmology and neurology soon after birth. Examination by ophthalmology revealed elevated left intraocular pressure and left optic nerve cupping, suggestive of congenital glaucoma. The exam was also notable for a diffuse choroidal hemangioma in the left eye. The patient was

diagnosed with glaucoma and started on latanoprost drops to the left eye to reduce the elevated intraocular pressure.

The presence of a port-wine stain along with dermal melanocytosis (Mongolian spot) was consistent with the characteristic manifestations of phakomatosis pigmentovsacularis type II. The combination of V1 distribution of cutaneous capillary malformation along with glaucoma and the presence of a choroidal hemangioma confirmed the diagnosis of Sturge-Weber syndrome. Although magnetic resonance imaging of the brain was largely unremarkable, the patient will need to be followed closely by neurology as most patients with Sturge-Weber syndrome develop seizures within the first year of life.

Given the extensive distribution of skin abnormalities and the potential to dramatically impact the patient's quality of life, the patient was referred to a pediatric dermatology center to begin serial treatments with pulsed dye laser. The patient will continue to be monitored by a multi-specialty team.

Discussion:

Phakomatosis pigmentovascularis (PPV) is a rare congenital cutaneous malformation syndrome characterized by a combination of capillary abnormalities and dermal melanocytosis. It is thought that the syndrome may be the result of a twin spotting phenomenon. The syndrome is classified into four different types based on associated pigmentary changes. Nevus flammeus, or port wine stain (PWS), is a component of all four types of PPV. In addition, type I has an epidermal nevus, type II has dermal melanocytosis (Mongolion spot) with or without nevus anemicus, type III has nevus spilus with or without nevus anemicus, and type IV has dermal melanocytosis and nevus spilus with or without nevus anemicus. Each type is further subdivided into two subtypes based on the absence (type 'a') or presence (type 'b') of associated systemic manifestations. Approximately 50% of patient with PPV type II have associated systemic comorbidities. Ocular, neurologic, and skeletal abnormalities are the most common, and there have been several case reports of PPV associated with Sturge-Weber syndrome or Klippel-Trenaunay syndrome.

Sturge-Weber Syndrome (SWS) is a sporadic neuroectodermal disorder characterized by a capillary malformation (port-wine stain) in the first branch of the trigeminal nerve (V1) in association with leptomeningeal angiomatosis and glaucoma. Infants with a V1 PWS should have early neuroimaging to evaluate for central nervous system abnormalities. Leptomeningeal vascular malformations ipsilateral to the V1 PWS are most common; cerebral hemiatrophy and calcifications may develop over time during childhood. Seizures are the most common neurologic symptom, and epilepsy typically develops within the first year of life. Other neurologic findings include hemiparesis, developmental delays, behavioral and emotional problems, and migraine headaches. There is ocular involvement in approximately 60% of patients with SWS, with glaucoma being the most frequent manifestation. Choroidal vascular malformations may also be found in the affected eye.

There is no specific treatment for this overlap syndrome of PPV and SWS. Recognition of possible systemic manifestations is critical to dictate further management of the disorders. Therefore, it is extremely important for all patients with cutaneous findings consistent with PPV type II to be evaluated by other specialties, such as neurology and ophthalmology, so that appropriate diagnosis, treatment, and monitoring can take place, including control of seizures and management of congenital glaucoma. In addition, the cutaneous manifestions of PPV and SWS may have a significant impact on the patient's quality of life. Pulsed dye laser is the gold standard for treatment of PWS and should be initiated to minimize the cosmetic and

psychosocial consequences. There is also evidence that Q-switched neodymium-doped yttrium-aluminum-garnet laser may be effect in lightening dermal melanocytosis, which may or not fade spontaneously over time.

Essential Lesson:

- Patients with the characteristic cutaneous findings of PPV type II, especially those with a V1 port-wine stain, should be carefully evaluated for systemic associations, such as Sturge-Weber syndrome.

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Case Presented by Iona Chapman, MD
and Lawrence Chan, MD

UNKNOWN CASE

This 76 year old male presented with two lesions on the lower lip.

Case 10

Case Presented by Benjamin Garden, MD
and Iris K. Aronson, MD

History of Present Illness:
An 83 year old immunosuppressed male, with a history of a renal transplant, was referred by orthopedics for evaluation of red lesions located on the bilateral plantar surfaces. The patient stated that over the course of one year the lesions had progressed in size, but he denied any associated pain, pruritus, or bleeding. A biopsy of a lesion on the left plantar foot was performed.

Past Medical History:
Renal transplant (two years prior), coronary artery disease, diabetes mellitus, and hypertension

Medications:
Amlodipine, atorvastatin, carvedilol, clopidogrel, furosemide, insulin aspart, insulin glargine, lisinopril, mycophenolic acid, and tacrolimus

Allergies:
No known drug allergies

Family History:
No history of skin conditions or skin cancers

Social History:
The patient lives with his wife and he denies smoking, alcohol intake, or illicit drug use.

Review of systems:
The patient denied any fevers, chills, night sweats, gastrointestinal symptoms, or weight loss.

Physical Examination:
The patient has well-demarcated, blanchable, crimson to violaceous patches on the bilateral plantar feet. These changes extend to the lateral areas of both feet and to the heel on the left foot. A few small vesicles are present within the patches.

Laboratory Data:
The following were negative or within normal limits:
Complete blood count, tacrolimus level were within normal limits. HIV antibody screening was negative.

Diagnostic Procedures and Tests:
Polymerase chain reaction studies for BK virus, Epstein-Barr virus and cytomegalovirus were negative.
Arterial studies were without any evidence of occlusive disease.

Histopathology:
Left plantar foot, skin: There are ill-defined fascicles of spindle cells associated with irregularly shaped vessels that dissect through dermal collagen and native vessels. Extravasated red blood cells and hemosiderin deposits are present. There is a lymphangioma-like foci, consisting of interanastomosing, ectatic, irregularly shaped spaces lined by an attenuated layer of mildly

atypical endothelial cells. Immunohistochemical stains for anti-human herpesvirus-8 latent nuclear antigen-1, and anti-CD31 antibodies are positive in the atypical vascular cells.

Diagnosis:
Kaposi's sarcoma, lymphangioma-like variant

Treatment and Course:
Following the biopsy, the patient's immunosuppressant medications were transitioned from tacrolimus to sirolimus, with improvement noted. The patient is to follow-up with dermatology and oncology for further management.

Discussion:
Lymphangioma-like Kaposi's sarcoma (LLKS) is a rare histologic presentation of Kaposi's sarcoma (KS), first characterized histologically by Gange and Jones in 1979, with only 28 reported cases in the literature. LLKS has been described in acquired immunodeficiency syndrome-associated immunosuppression, endemic African-type and classic indolent KS. This case is unique as there have been no reported cases of LLKS in transplant-associated iatrogenic immunosuppression. The clinical appearance of LLKS is often typical with the development of violaceous patches, plaques or nodules; however, an increased number of LLKS present with vesicles and bullae (13 out of 28 cases). Additionally, the lower extremities are the predilected site of presentation (23 out of 28 cases).

Histologically, LLKS contains a prominent ectatic meshwork of lymphangioma-like spaces within an otherwise typical pathology of KS. These typical findings of KS include spindle cell proliferation around native vessels, irregular vessels with atypical endothelial cells dissecting reticular dermal collagen and dermal structures, extravasated red blood cells and hemosiderin deposits, and an associated lymphoplasmacytic infiltrate. Immunohistochemistry of the tissue would show expression of CD34, CD31 and human herpesvirus-8 (HHV-8) latent nuclear antigen-1 (LNA-1) in both the spindle cells and the cells lining the lymphangioma-like spaces, assisting in the diagnosis.

LLKS is reported to be a less aggressive form of KS, with slow progression of the lesions. In iatrogenic immunosuppression-associated KS, changing from a calcineurin inhibitor to an mTOR inhibitor (sirolimus or everolimus), which inhibits the HHV-8 lytic replication cycle and has antineoplastic and antiangiogenic as well as immunosuppressive effects, can result in improvement or disappearance of KS lesions, while avoiding organ rejection. In the study by Stallone G, et al, transition to sirolimus resulted in resolution of KS lesions in 15 renal transplant patients within three months, with no episodes of rejection or kidney dysfunction.

Essential Lessons:
- LLKS is a rare histologic presentation of KS, exhibiting lymphangioma-like areas of ectatic, irregularly shaped spaces lined by atypical endothelial cells.
- The spindle cells and the cells lining the lymphangioma-like spaces stain positive for CD34, CD31 and HHV-8 LNA-1.
- Switching from a calcineurin inhibitor to an mTOR inhibitor can result in resolution of KS in iatrogenic immunosuppressed transplant patients.

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