Chicago Dermatological Society

May 2012
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, May 16, 2012
Rush University

Conference Host:
Department of Dermatology
Rush University Medical Center
Chicago, Illinois

Program

Committees & Registration

8:00 a.m. - 9:00 a.m.	CDS Plans & Policies Committee

Program Activities

8:30 a.m.	Registration, Continental Breakfast & Exhibitor Time Searle Conference Center
9:00 a.m. - 10:00 a.m.	RESIDENT LECTURE "Benefits and Challenges of Academic Dermatology: An Open Discussion" Elliot J. Androphy, MD *Room 542 Brainard*
9:30 a.m. - 10:45 a.m.	Clinical Rounds – Patient Viewing *Room 264 Professional Building (Elevator III)* Slide Viewing *Room 538 (Fenger)*
11:00 a.m. - 12:00 p.m.	General Session *Room 542 (Brainard)*
11:00 a.m.	FREDERICK MALKINSON LECTURE "Human Papillomavirus: From the Bench to the Patient" Elliot J. Androphy, MD
12:00 p.m. - 12:45 p.m.	Box Lunches & Visit with Exhibitors *Main Dining Area - Room 500*
12:45 p.m. - 1:00 p.m.	CDS Business Meeting *Room 542 (Brainard)*
1:00 p.m. - 2:30 p.m.	Case Discussions *Room 542 (Brainard)*
2:30 p.m.	Meeting adjourns

Mark the Date!

Next CDS monthly meeting – Wednesday, June 13, 2012
Loyola University Medical Center; Maywood
Watch for details on the CDS website: www.ChicagoDerm.org

Guest Speaker

Frederick Malkinson Lecture

Elliot J. Androphy, MD

Kampen-Norins Professor and Chair of Dermatology
Indiana University School of Medicine,
Indianapolis, IN

Degrees – AB, Brandeis University; MD, University of Rochester; Residency, University of Pittsburgh Health Sciences Center; Dermatology; Fellowship, National Cancer Institute , NIH; Medical and Senior Staff Fellow; Dermatology Branch and Laboratory of Cellular Oncology (with Douglas Lowy, MD)

Certification – American Board of Dermatology

Research Program Membership – IU Melvin and Bren Simon Cancer Center; Microbiology & Immunology Program

Research Interests – Mechanism of human papillomavirus induced malignancies. Development of novel antiviral drugs. Mechanism of p53 tumor suppression. Gene expression, DNA replication, DNA splicing. Pathogenesis of spinal muscular atrophy and development of therapy for SMA

Continuing Education Credit

Chicago Dermatological Society

"Chicago Dermatological Society Monthly Conference"

May 16, 2012 *Chicago, IL*

Participants must attend entire session to receive all types of credit. CFMC hosts an online evaluation system, certificate and outcomes measurement process. Following the conference, you must link to CFMC's online site (link below) to complete an evaluation form, in order to receive your continuing education statement of hours (certificate). Once the evaluation form is complete, you will automatically be sent a copy of your certificate via email.

Continuing Education evaluation and request for certificates will be accepted up to 60 days post activity date. The Colorado Foundation of Medical Care (CFMC) will keep a record of attendance on file for 6 years. CFMC contact information: 303-695-3300, ext. 3139.

Link address to evaluation form:

www.yourcesource.com/eval?act=664!05162012

JOINT SPONSOR STATEMENT

This Continuing Educational activity is Joint-sponsored by the **Colorado Foundation for Medical Care, Office of Continuing Education** and the **Chicago Dermatological Society**. **CFMC is accredited by the ACCME to provide continuing medical education for physicians.**

GOAL/PURPOSE

To broaden the clinical knowledge of dermatologists with respect to diagnostic and treatment options.

SESSION OBJECTIVES

Upon completion of sessions, participants will be able to apply new knowledge and skills in the area of physician learning.

1. Discuss the evaluation and treatment options for patients with HPV.
2. Describe the indications for HPV vaccine in a clinical setting.

.CREDIT STATEMENTS

CME CREDIT

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 joint sponsorship of the Colorado Foundation for Medical Care, Office of Continuing Education (CFMC OCE) and Chicago Dermatological Society. CFMC is accredited by the ACCME to provide continuing medical education for physicians.

The Colorado Foundation for Medical Care designates this Live Activity for a maximum of 4.5 *AMA PRA Category 1 Credit(s) ™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

OTHER HEALTH CARE PROFESSIONALS

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 STATEMENTS

All other members of the faculty and planning team have nothing to disclose nor do they have any vested interests or affiliations. **It is the policy of the Chicago Dermatological Society and Colorado Foundation for Medical Care (CFMC) that the faculty discloses real or apparent conflicts of interest relating to the topics of the educational activity.**

Case Presentations

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #1**

Presented by Hina Ahmad, MD, and Arthur Rhodes, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 12-year-old, healthy Black male presented to our Dermatology clinic with a 6-year history of an isolated lesion on the right volar wrist. The patient recalled having a "non-healing scar" in the same location from a fall when he was younger and stated that the lesion has otherwise been stable over time. He denied any symptoms of pain or pruritus. The family denied any history of exposure to ionizing radiation, well water, or insecticides. Family history was negative for skin cancer. A biopsy was performed at the patient's initial visit; however, he was subsequently lost to follow-up. One year later, the patient returned to our clinic with the lesion unchanged. Further confirmatory biopsies were performed.

PAST MEDICAL HISTORY

Asthma

FAMILY HISTORY

Negative for skin cancer

PHYSICAL EXAM

On the right volar wrist there was a 2.0 cm by 2.0 cm, well-demarcated, very dark brown, hyperkeratotic plaque, which was raised about 1-2 mm.

HISTOPATHOLOGY

An initial incisional biopsy of the lesion was performed and revealed squamous cell carcinoma in-situ. One year later, three additional incisional biopsies were performed from different areas of the lesion and also revealed squamous cell carcinoma in-situ.

HPV immunohistochemistry for types 6, 11, 16, 18, 31, 33, 42, 51, 52, and 58 was negative; however, further testing with in-situ hybridization revealed weak positivity for high-risk HPV types.

DIAGNOSIS

Squamous cell carcinoma in-situ in an African American pediatric patient.

TREATMENT AND COURSE

The patient was started on topical 5-fluorouracil therapy twice daily under occlusion for 2 weeks. The patient occluded the lesion for only one hour at a time and two weeks into therapy had a minimal response with mild erosive changes at the center of the lesion. An additional six weeks of therapy with 24-hour occlusion under duct tape resulted in increased erosive change, with no clinical evidence of residual SCC.

DISCUSSION

Squamous cell carcinoma (SCC) is the second most common skin cancer in White adults and the most common skin cancer in darkly pigmented adults. Squamous cell cancer is exceedingly rare in the pediatric age group in which melanoma surpasses both primary squamous and basal cell carcinomas of the skin. The incidence of SCC becomes greater if the child is immunocompromised, has a predisposing condition such as xeroderma pigmentosum or basal cell nevus syndrome, or if there is chronic trauma or inflammation as in lichen sclerosus et atrophicus and epidermolysis bullosa. There are also a few case reports of squamous cell

carcinoma arising within congenital lesions like nevus sebaceous and epidermal nevus and in patients who have undergone treatment with voriconazole. For isolated squamous cell carcinomas and those arising on mucosal sites, high-risk human papillomavirus must also be excluded. Without predisposing factors, however, squamous cell carcinoma remains rare in pediatric patients, and only a handful of cases have been reported.

Treatment options for squamous cell carcinoma in-situ are numerous, offering the patient surgical as well as non-surgical approaches. Surgical treatment options include Mohs micrographic surgery, simple excision, electrodessication and curettage, and cryotherapy. Cure rates for each of these procedures is difficult to establish as many of the larger studies lack long term follow up. Recurrence rates that have been reported in the literature for SCC in-situ range from 4.6% to 19.4% for simple excision, and 6.3-8.3% for Mohs micrographic surgery. These rates are even more variable for electrodessication and curettage, with recurrences reported anywhere from 1.9% to 18.8% of the time. The recurrence rates continue to increase and encompass an even broader range with cryotherapy, where the thaw time affects outcomes. For anatomical areas where surgical intervention may impair functional outcome, topical and laser therapies are appealing alternatives.

Topical therapies include 5-fluorouracil and imiquimod. Successful clearance has been achieved with monotherapy as well as combination therapy. Larger prospective studies are lacking, and no one regimen is uniformly accepted. Treatment regimens with 5-fluorouracil can range from twice daily applications to less aggressive once weekly applications. Total treatment times also vary anywhere from 3 weeks to 4 months, with the average treatment duration being 4 weeks. Clearance rates are higher in those patients with a more aggressive and longer treatment regimen, and with occlusion of the treatment area. Recurrence rates as high as 33% have been reported with topical therapy. Imiquimod may also be used as monotherapy, and treatment regimens include once daily application for 9-16 weeks. Clearance rates range from 73-93%, with one study reporting no recurrences. However, these studies are limited by their small sample size as well as lack of long-term follow up. Rarely, imiquimod therapy may cause flu-like symptoms or eruptive keratoacanthomas in the treatment field. In patients who fail monotherapy, combination therapy with 5-fluoruracil and imiquimod has led to successful clearance of squamous cell carcinoma in-situ.

Photodynamic therapy is yet another alternative treatment regimen that may be employed for large or numerous lesions. A total of four treatments have resulted in clearance rates ranging from 84-96%, with recurrence rates ranging from 10-31%. Additional treatment regimens that have been described in case reports include ablative carbon dioxide laser, radiation therapy, intralesional interferon, intralesional bleomycin, oral isotretinoin, oral acitretin, and topical tazorac with topical diclofenac. Treatment selection should be tailored to each individual patient, taking in to consideration predisposing factors, extent of lesions, and comorbidities.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #2**

Presented by Jill C. Anderson, MD, Hina Ahmad, MD, and Michael D. Tharp, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 31-year-old African American female presented to our dermatology clinic with lesions on the right distal thumb and index finger, which had been present for 3 years. Despite treatment with over-the-counter wart removers and freeze therapy, the lesions continued to grow and fissure, causing the patient pain. Of note, the patient additionally had a long-standing history of recurrent squamous cell carcinoma in situ of the vulva, labia, clitoris, and perianal skin. She had undergone numerous excisions, laser ablation, topical 5-fluorouracil, and topical imiquimod therapy, all with eventual recurrence of the lesions. She denied any history of other recurrent infections, and otherwise felt well, with no fevers, chills, night sweats, or unintentional weight loss.

PAST MEDICAL HISTORY

Asthma
Anemia
Recurrent squamous cell carcinoma in situ of the vulva, labia, clitoris, and perianal skin

MEDICATIONS

None

ALLERGIES

No known drug allergies

FAMILY HISTORY

Patient denies family history of skin cancer or recurrent infections.

SOCIAL HISTORY

Patient denies alcohol, tobacco, or illicit drug use.

PHYSICAL EXAM

On the right medial distal thumb and the right lateral distal index finger, there were well-demarcated, erythematous, and hyperkeratotic plaques with deep fissures and a peripheral rim of dark brown pigmentation.

Vulva, labia majora, clitoral hood, clitoris, and perianal skin with too numerous to count, hyperpigmented verruciform papules, some coalescing into plaques.

HISTOPATHOLOGY

Right distal thumb, shave biopsy (2/7/12) and right distal index finger, shave biopsy (3/30/12): consistent with verrucous carcinoma. Human papillomavirus (HPV) immunohistochemistry and fluorescence in situ hybridization were negative for high- and low-risk HPV types.

Vulva, labia majora, clitoris, perianal biopsies performed by gynecology in December 2009, July 2010, and July 2011: revealed squamous cell carcinoma in situ. In December 2009, a P16 immunostain was performed and was positive, indicating the presence of high risk HPV types.

LABORATORY RESULTS

The following were positive or abnormal:
Quantitative Immunoglobulin A: ..... 371 (normal 59 – 292)

Quantitative Immunoglobulin G: ..... 1770 (normal 596 – 1584)

The following were negative or normal:
Complete Blood Count, Comprehensive Metabolic Panel, Human Immunodeficiency Virus Antibody, Quantitative Immunoglobulin M, Thyroid Stimulating Hormone, INR, PTT, and Hemoglobin A1c

RADIOLOGY
CT of the abdomen and pelvis was within normal limits.

DIAGNOSIS
Verrucous carcinoma of the right distal thumb and right index finger in a patient with recalcitrant vulvar and perianal squamous cell carcinoma in situ

TREATMENT AND COURSE
The patient is scheduled for Mohs surgery for the verrucous carcinoma on the right distal thumb and right index finger. She will also be consulting with a hand surgeon for repair of the final defects.

Additionally, after an extensive discussion with the patient and her partner, the decision to proceed with skinning vulvectomy and partial clitorectomy was made by her gynecologic oncologist. She is scheduled for surgery in the near future.

DISCUSSION
Verrucous carcinoma is an uncommon low-grade squamous cell carcinoma. It presents clinically as a slowly enlarging, exophytic vegetative papule or plaque. It is most common in older white males. Verrucous carcinoma can be locally invasive, but rarely metastasizes. Verrucous carcinomas are often categorized by their anatomic subtype: (1) anogenital (giant condyloma of Buschke and Löwenstein); (2) palmoplantar or periungual (epithelioma cuniculatum); (3) oropharyngeal (oral florid papillomatosis); and (4) verrucous carcinoma of other cutaneous sites. Multiple verrucous carcinomas have been rarely reported.

The pathogenesis of verrucous carcinoma is unknown; however, human papillomavirus (HPV), chronic inflammation, trauma, tobacco use, and poor dental hygiene have been implicated. In particular, HPV types 6, 11, 16, 18, and 33 are frequently identified in these lesions; however, HPV is not always identified, as in our case.

On histology, verrucous carcinoma is characterized by papillomatosis, acanthosis, and hyperkeratosis. There is an exophytic and endophytic proliferation of well-differentiated squamous cells. Tumor cells bluntly invade the dermis by “bulldozing,” rather than by a “stabbing infiltration.” The basement membrane is intact with minimal basal layer keratinocyte atypia. A variable mixed dermal infiltrate may be seen.
When evaluating patients with verrucous carcinoma, an underlying acquired or inherited immunodeficiency may be considered. Our patient has multiple cutaneous lesions, which are histologically consistent with verrucous carcinoma. In addition, she has a history of recurrent squamous cell carcinoma in situ of the vulva, labia, clitoris, and perianal skin, which was positive for high risk HPV.

Verrucous carcinoma has been reported in patients with various causes of acquired and inherited immunodeficiency. In particular, human immunodeficiency virus (HIV) infection testing should be considered in these patients. In 1999, Massad *et al*. reported a case of vulvar verrucous carcinoma in a 32-year-old female infected with HIV. Moreover, the risk of vulvar and cervical intraepithelial neoplasia is increased fivefold in patients with HIV. Additionally, verrucous carcinomas in HIV-infected patients may be more aggressive. This is highlighted by a case of a rapidly progressive anal verrucous carcinoma that metastasized in an HIV-infected

patient (Handisurya *et al.*, 2009). Iatrogenic causes of immunodeficiency should also be considered, as verrucous carcinoma has been reported in organ transplant patients who are on immunosuppressive agents.

Inherited causes of immunodeficiency may also be considered in patients with verrucous carcinoma. Some of the diagnoses to consider include: epidermodysplasia verruciformis, WHIM syndrome (warts, hypogammaglobulinemia, infections, and myelokathexis), WILD syndrome (warts, immunodeficiency, lymphedema, and dysplasia), and combined immunodeficiency associated with DOCK8 mutations (a recently described disorder that has features similar to Job's syndrome, as well as widespread, recalcitrant viral infections).

Our patient's work-up for an immunodeficiency syndrome is negative to date. An underlying immunodeficiency should be considered in patients with multiple verrucous carcinomas and HPV-induced squamous cell carcinomas.

Surgical treatment with either excision or Mohs is the preferred treatment for verrucous carcinoma. Radiation is generally contraindicated, due to the risk of recurrence and possible transformation into a more aggressive subtype. Other therapies, such as systemic chemotherapy, topical imiquimod, topical 5-fluorouracil, electrodessication and curettage, cryotherapy, intralesional interferon alfa, carbon-dioxide laser, and photodynamic therapy, have also been tried. Overall, there is a good prognosis. The 5-year survival rate is greater than 75%.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #3**

Presented by Andrea Kassim, MD, Arthur Rhodes, MD and Lady Dy, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 16-year-old African American girl presented with a lesion on the root of the helical rim of the left ear extending to the superior postauricular area. An asymptomatic lesion in this site had been present since birth and had been growing in proportion to growth of the head. Six months prior to presentation, however, the patient developed a pink to red, friable, bleeding nodule at posterior aspect of the lesion. A full review of systems was within normal limits. No treatment had been instituted for the lesion.

PAST MEDICAL HISTORY

Normal growth and development

MEDICATIONS

None

ALLERGIES

No Known Drug Allergies

FAMILY HISTORY

No family history of skin cancer

SOCIAL HISTORY

Lives with parents and sibling

PHYSICAL EXAM

Physical examination of the superior helical rim of the left ear was notable for a 15 mm x 4 mm peach-colored to hyperpigmented linear plaque with a mammillated surface, approximately 2 mm in height. Contiguous with this lesion at the posterolateral margin and hidden by the superior helix was an 8 mm x 7 mm pink to red, friable mass that was 4 mm in height with hemorrhagic crusting. There was no cervical, post-auricular, submandibular or supraclavicular lymphadenopathy.

HISTOPATHOLOGY

Histopathology was significant for a syringocystadenoma papilliferum with focal reactive keratinocytic atypia, in association with a nevus sebaceous.

LABORATORY RESULTS

In-situ hybridization for HPV types 6, 11, 16, 18, 31, 33, 35, 42, 43, 44, 45, 51, 52, 56, 58, 59, 68 and 70 was performed. The patient's focal reactive keratinocytic atypia was positive for both high- and low-risk HPV types.

RADIOLOGY

None

DIAGNOSIS

Syringocystadenoma papilliferum with focal reactive keratinocytic atypia arising within a nevus sebaceous.

TREATMENT AND COURSE

The patient was referred to our dermatologic surgeon for Mohs micrographic surgery of the focal reactive keratinocytic atypia and syringocystadenoma papilliferum, with complete clearance achieved after one stage. A staged excision of the nevus sebaceous is planned. At the patient's one month follow-up, there was no clinical evidence of recurrence of either the focal reactive keratinocytic atypia and syringocystadenoma papilliferum.

DISCUSSION

Nevus Sebaceous of Jadassohn (NSJ), first described in 1895, is a congenital, organoid hamartoma. The lesion consists of ectoderm- and mesoderm-derived structures including sebaceous, apocrine and eccrine glands. With a prevalence of 0.3% among a cohort of over four thousand newborns, most NSJs occur on the head, in particular the scalp with equal prevalence in males and females. Although relatively inconspicuous during childhood, most NSJs grow into the more characteristic thick, waxy, peach-colored mammillated plaques during puberty, presumably as a result of androgenic stimulation.

Considered by some to be merely a cosmetic concern, a minority of NSJs may develop both secondary benign and malignant tumors. Trichoblastoma and syringocystadenoma papilliferum are the most common benign tumors known to arise within a NSJ followed by trichilemmoma, sebaceous adenoma, sebaceous epithelioma, leiomyoma, nodular hidradenoma, syringoma, chondroid syringoma, trichoadenoma, trichilemmal cyst, apocrine adenoma and poroma formation. While basal cell carcinoma is the most common malignant tumor complicating a NSJ, other neoplasias may occur such as sebaceous carcinoma, apocrine carcinoma, squamous cell carcinoma, melanoma, porocarcinoma, adenocarcinoma, leiomyosarcoma and syringocystadenocarcinoma papilliferum. Keratoacanthomas have also been known to occur. Malignancies occurring in conjunction with a NSJ are relatively rare. While the overall incidence of malignant change has been reported to be approximately 0.8 to 8%, the exact incidence is unknown given that there have been no long term prospective studies. In addition, many trichoblastomas may have been misdiagnosed as basal cell carcinomas in prior epidemiological studies, which may have led to an overestimation of the incidence of secondary malignancies in association with NSJs.

The presence of focal reactive keratinocytic atypia in our patient’s biopsy specimen is likely attributable to an antecedent human papilloma virus (HPV) infection as evidenced by the positive *in-situ* hybridization testing of the patient's tumor for both low- and high-risk HPV types. Interestingly, previous studies have demonstrated that maternal HPV-positivity may play a role in nevus sebaceous development. The keratinocyte atypia in the patient’s tumor may have significance. Progression to frank squamous cell carcinoma arising within a NSJ is an extraordinarily rare event, with only 12 cases previously described, most in middle-aged to elderly white adults, with two cases reported in the pediatric age group. The overall frequency of an SCC occurring within an NSJ is thought to be 1 per 2043 NSJs, according to a recent retrospective case series/meta-analysis of over 2000 cases of NSJ. An aggressive course with fatal metastatic disease within months of SCC diagnosis has been reported.

Biopsy of our patient’s new-onset mass revealed the presence of a syringocystadenoma papilliferum, which rarely may degenerate into a syringocystadenocarcinoma papilliferum. In addition, mutations in the PTCH gene have been reported in both trichoadenomas and lesions of syringocystadenoma papilliferum as well as basal cell carcinoma. Specifically, one study demonstrated that allelic loss of the PTCH gene at 9q22 was consistent with the clinical observation of transition of syringocystadenoma papilliferum to basal cell carcinoma. For this reason, a conservative approach with Mohs micrographic surgery of the keratinocyte atypia and syringocystadenoma papilliferum was performed followed by staged excision of the remaining nevus sebaceous components.

In summary, the rapid appearance of a mass within or contiguous to an NSJ should raise the clinical index of suspicion of a secondary benign or malignant tumor formation. Further management is dictated by biopsy results, although excision of any nevus sebaceous regardless of secondary tumor formation should be considered in any patient at or slightly puberty due to its potential for malignant degeneration. A secondary malignancy, if it develops, is most likely to occur in adulthood, with a median age in the sixth- to seventh decade of life. However, malignant transformation may occur before puberty. Patients must therefore be followed periodically until excision.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #4**

Presented by Jessica Hsu, MD, and Katherine K. Brown, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 59-year-old Hispanic female with past medical history significant for end stage renal disease status post renal transplant in 2005 presented to clinic with a 1 year history of a new lesion on the left anterior thigh. The lesion had been gradually enlarging but was otherwise asymptomatic and not painful. It had never bled, and the patient denied any history of trauma to the site. She denied any recent fevers, chills, night sweats, unintentional weight loss, or fatigue. Of note, she also reported a lesion on the right wrist present for about a year and a half which was not changing in size and asymptomatic.

PAST MEDICAL HISTORY

Diabetes mellitus type 2 complicated by nephropathy
End stage renal disease status post renal transplant in 2005
Hypertension
Hypercholesterolemia
Ureteral stricture status post stent placement in 2008 and 2010
Headache
Depression
Glaucoma

MEDICATIONS

Enalapril	Mirtazapine	Ferrous Sulfate
Gabapentin	Docusate	Tramadol
Alendronate	Calcitriol	Tacrolimus
Fluoxetine	Lansoprazole	Simvastatin
Insulin aspart	Aspirin	Prednisone
Insulin glargine	Sirolimus	Clonidine

ALLERGIES

There were no known drug allergies.

FAMILY HISTORY

There was no history of skin cancers or melanoma or other malignancies.

SOCIAL HISTORY

Patient denied illicit drug use. Patient smoked 1 cigarette a day for less than 1 year and quit in 1981. Patient reported occasional alcohol consumption at family gatherings on a weekly basis.

PHYSICAL EXAM

On the left anterior thigh, there was a 1.8 cm by 1.6 cm dome-shaped, shiny, red, firm nodule with peripheral telangiectasias. Lymph node exam did not reveal any inguinal lymphadenopathy. Her right wrist had a 7 mm well-circumscribed, non-tender, mobile, bluish cystic appearing mass.

HISTOPATHOLOGY

A 4 mm punch biopsy from the left thigh demonstrated a dermal infiltrate of atypical blue cells with minimal cytoplasm arranged in a trabecular pattern. CK20 and CAM 5.2 immunoprotein stains highlighted the atypical basaloid cells in the dermis. An S-100 stain was negative. These

immunostains supported the diagnosis of Merkel cell carcinoma. Subsequent resection of the left thigh lesion with 1.5cm margins demonstrated Merkel cell carcinoma measuring 2.1cm in greatest diameter and extending to a depth of 1.3 cm.

LABORATORY RESULTS

Complete metabolic panel was normal, except for a BUN of 32 and Cre of 2.95, which were stable from prior. Complete blood count with differential was normal.
LDH level was elevated at 275.

RADIOLOGY

CT scans of the chest, abdomen, and pelvis were negative.
PET whole body scan was negative for any metastasis.

DIAGNOSIS

Metastatic merkel cell carcinoma

TREATMENT AND COURSE

After initial biopsy of the left thigh lesion demonstrated Merkel cell carcinoma, the malignant nature of this carcinoma was discussed with the patient in depth, and she was referred to surgical oncology for additional work up. Staging work up including a CT of the chest, abdomen, and pelvis in addition to a total body PET scan were negative for any evidence of metastatic disease. The patient underwent wide local excision of the left thigh tumor with 1.5 cm margins and sentinel lymph node biopsy of the left groin which demonstrated one node positive for microscopic foci of metastic Merkel cell carcinoma. Immunohistochemical stains for cytokeratin AE1/AE3 and cytokeratin 20 were positive and supported the diagnosis.
The surgical oncologist also excised the right wrist lesion, which demonstrated a Merkel cell carcinoma. The neoplastic cells were positive for chromogranin and synaptophysin. Stains for cytokeratin AE1/ AE3 and cytokeratin 20 showed characteristic perinuclear dot-like positivity in the lesional cells, which supported the diagnosis. The small size and circumscribed nature of the dermal nodule was most suggestive of a metastasis. The case was extensively discussed with the patient with input from dermatology, oncology, and surgical oncology. The current plan is to pursue systemic chemotherapy, possibly with imatinib.

DISCUSSION

Merkel cell carcinoma (MCC) is a rare neuroendocrine carcinoma of the skin with incidence rates in the United States estimated at 0.44 cases per 100,000 persons in 2001 and increasing by 8% annually. It typically occurs in older individuals and is associated with a poor prognosis due to the high rate of local recurrence and metastases. MCC presents mostly in Caucasians (94% of cases), with a higher incidence noted in males and the elderly, reaching 4.28 cases per 100,000 in the 85+ age group. The pathogenesis of MCC is still being clarified, but known risk factors for development of the disease include ultraviolet exposure and immunosuppression. More recently, a viral etiology has been elucidated, with a novel polyomavirus known as the Merkel cell polyomavirus (MCPyV), being detected in 80% of MCCs compared to only 8% of control tissues from various body sites of patients with MCC and in 16% of control skin tissues. Since that initial study, MCPyV has been detected in 24-77% of MCC samples.

MCC typically present as solitary, firm, asymptomatic, flesh-colored to red, dome-shaped nodules with a smooth shiny surface, and occasional telangiectasias. They characteristically occur on chronic sun-damaged skin and develop quickly over the span of months. Lesions on sun-protected sites such as the mucous membranes are rare and associated with a particularly poor prognosis. Presentation and diagnosis are often delayed given the lesion’s rather benign

appearance, and the lesion can resemble basal or squamous cell carcinoma, cyst, adnexal tumor, pyogenic granuloma, amelanotic melanoma, or lymphoma cutis.

The tumor is typically a dermal nodule composed of small blue cells with basophilic nuclei and minimal cytoplasm that extends into the subcutaneous fat. Mitoses are frequently seen, associated with a high apoptosis index, but the papillary dermis and adnexa are usually spared. Three histologic subtypes- intermediate, small cell, and trabecular, are recognized based on the arrangement of tumor cells, but a single lesion can exhibit a mixture of subtypes. Pathological prognostic features have yet to be validated, but recent evidence suggests that tumor thickness, the presence of a nodular growth pattern, low tumor depth, and absence of lymphovascular invasion are significantly associated with better survival. Immunohistochemical stains can also be performed to help differentiate MCC from other tumors. MCC cells are positive for both epithelial and neuroendocrine markers, but negative for lymphoid and melanoma markers. Specifically, cytokeratin 20 (CK20) is a highly sensitive marker for MCC, and thyroid transcription factor (TTF)-1 is commonly seen in small-cell lung carcinoma but consistently absent in MCC. Neurofilament protein (NFP) is another useful marker which is usually positive in MCC and consistently negative in small-cell lung carcinoma. In comparison to malignant melanoma, MCC is negative for HMB-45 and S-100.

Despite surgical excision of the primary lesion, 45-91% of patients will develop regional node involvement, with distant metastases seen in 18-52% of patients, within 2 years of the initial diagnosis. Distant metastatic disease occurs at a mean of 18 months and is associated with poor prognosis and mean survival of <6 months. Recently, a new international consensus MCC prognostic/staging was developed. (Table 1)

In terms of management, for local disease, wide local excision to muscle fascia or pericranium with clear pathological margins is the treatment of choice. For small lesions < 2 cm in diameter, margins of 1 cm appear to be sufficient, but for lesions >2cm, a 2cm margin is standard. Mohs micrographic surgery may be preferable over conventional surgery in certain cases. Sentinel lymph node biopsy should be performed prior to wide local excision or Mohs surgery since up to 40% of patients with clinically negative lymph nodes have microscopic nodal metastases. The issue of elective lymph node dissection is controversial due to its potential morbidity and unproven survival benefit, but it may be warranted in the head and neck region, where sentinel node biopsy are less reliable. For regional nodal disease, management includes excision of the primary site, regional lymph node dissection, and radiotherapy to the primary tumor and regional nodal site. If only microscopic nodal disease is found, radiotherapy can be omitted after axillary or groin node dissection. Finally, for distant metastatic disease, management is individualized, but radiotherapy, surgery, and chemotherapy should be considered as monotherapy or in combination. All MCC patients should be followed closely with complete skin and lymph node examinations every 1-3 months for the first year, every 3-6months in the second year, and annually thereafter.

TABLE 1:

Stage I: Local disease, tumour diameter ≤ 2 cm
Ia: Nodes negative by pathological examination
Ib: Nodes not clinically detectable (no pathological evaluation done)
Stage II: Local disease, tumour size > 2 cm
IIa: Nodes negative by pathological examination
IIb: Nodes not clinically detectable (no pathological evaluation done)
IIc: Primary tumour invades bone, muscle, fascia or cartilage
Stage III: Regional node disease
IIIa: Micrometastasis
IIIb: Macrometastasis (clinically detectable)
Stage IV: Distant metastatic disease

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #5**

Presented by Jessica Hsu, MD, Hina Ahmad, MD, Sheetal Mehta, MD and Arthur Rhodes, MD
Department of Dermatology, RUSH University Medical Center

Case A:

HISTORY OF PRESENT ILLNESS
A 50-year-old Chinese female presented with a 5-year history of a darkly pigmented lesion on the left thumb, which had become a non-healing ulcer in the last 5 months. The patient noted a "dark black mark" under the thumbnail that she attributed to a "cuttle fish spine" getting stuck in her thumb while preparing seafood. The lesion had been gradually enlarging over the past 5 years until 5 months prior to presentation, when the patient used a nail clipper to remove the dark area of the nail plate, hoping that normal nail would grow out to replace it. However, the area she clipped never healed and the dark area spread onto the distal tip of the thumb, past the end of the nail plate. The lesion was asymptomatic, but she noted some mild serosanguinous drainage from the thumb when she pressed on it. For the month prior to presentation she had been using a Chinese antibacterial liquid to the thumb without any improvement. There was no personal or family history of skin cancer or melanoma. She never had any nevi removed in the past. She otherwise felt well, denying any fevers, chills, night sweats, unintentional weight loss, or fatigue.

PAST MEDICAL HISTORY
Breast cancer, status post mastectomy and tamoxifen treatment
Type 2 diabetes mellitus
Hypertension

MEDICATIONS

Glipizide	Gemfibrozil
Metformin	Aspirin
Valsartan	Tamoxifen

ALLERGIES
There were no known drug allergies.

FAMILY HISTORY
There was no history of skin cancer or melanoma.

SOCIAL HISTORY
Patient denied alcohol, tobacco, or illicit drug use.

PHYSICAL EXAM
On the left thumb the lateral two-thirds of the nail plate was destroyed by a large, pink, friable, exophytic tumor with dark brown to grey pigmentation noted at both the proximal nail fold and distal fingertip. There was minimal serous drainage. On dermoscopy, blue-grey appearing pigment was located on the ridges of the fingertip with a blue-white veil.

HISTOPATHOLOGY
An initial 3 mm punch biopsy was performed from the darkly pigmented aspect of the distal fingertip and demonstrated an acral type atypical junctional melanocytic nevus with architectural disorder and moderate cytologic atypia.

Excisional biopsy of the left thumb nail plate demonstrated malignant melanoma.
Excisional biopsy of the left thumb nail matrix demonstrated malignant melanoma, at least Clark's level 4 with Breslow thickness 4.3mm, transected at the base and lateral edges. Ulceration was present, with 5 mitotic figures/mm^2. No changes of regression were identified. Immunohistochemical stains for S100 protein, HMB45 and Melan A were positive.

LABORATORY RESULTS

Aerobic culture from excisional biopsy tissue grew heavy amounts of group B beta-hemolytic streptococcus, light amounts of staphylococcus aureus, and minimal amount of enterococcus species from the broth only.
Acid-fast bacilli culture from excisional biopsy tissue was negative.
Fungal culture from excisional biopsy tissue was negative.

Complete blood count with differential was normal.
Complete metabolic panel was normal.
LDH level was normal.

RADIOLOGY

CT of the chest, abdomen and pelvis showed no evidence of metastatic disease.

MRI of the brain was normal.

MRI of the left thumb demonstrated masklike edema and enhancement within the dorsal soft tissues and underlying marrow of the distal phalanx.

DIAGNOSIS

Subungual malignant melanoma.

TREATMENT AND COURSE

The patient was treated with cephalexin 500 mg by mouth twice daily for a month after excisional biopsy of the lesion and referred to oncology. Screening labs, CT scans of the chest, abdomen, and pelvis along with MRI of the brain revealed no metastases, therefore the decision was made to proceed with left thumb amputation and sentinel node biopsy with input from oncology, surgical oncology, and hand surgery.

Left thumb amputation revealed residual melanoma, 5mm in thickness. The surgical margins, including bone, soft tissue and skin were free of involvement. Perineural invasion and scar tissue were additionally present. Stains for S-100 protein, HMB-45 and Melan-A were positive and supported the diagnosis. Left axillary sentinel lymph node excision demonstrated one node positive for metastatic malignant melanoma. There were multiple microscopic foci of metastatic melanoma but no extracapsular extension. Epitrochleal lymph node excision demonstrated three nodes positive for metastatic malignant melanoma. Metastatic melanoma was also present within the lumina of blood vessels in the adipose tissue surrounding one of the nodes. The patient was presented at tumor board, where the consensus decision was to proceed with complete dissection of the axilla followed by adjuvant systemic chemotherapy and careful follow up.

Left axillary lymph node dissection demonstrated 8 lymph nodes negative for metastasis. Fibroadipose tissue with focal fat necrosis and chronic inflammation was seen but negative for melanoma and melan-A stains were negative. Given the negative axillary dissection, adjuvant systemic interferon alpha therapy was begun. She is healing without problems and thus far tolerating interferon therapy well with some mild fatigue noted after 3 weeks of treatment.

Case B
A 34-year-old East Indian female, with no family history of melanoma, presented to our clinic with a new, 2 mm dark brown to black longitudinal streak on the left hand ring fingernail, which was noted during her first trimester of pregnancy 9 months prior. Biopsy confirmed a melanoma in-situ of the nail matrix. An amputation of the finger between the proximal and distal interphalangeal joints was performed. She is doing well and being followed closely every 4 months.

Case C
A 31-year-old Puerto Rican female, with family history negative for melanoma, presented to our clinic with a darkly pigmented band of the left middle fingernail. Biopsy revealed melanoma in-situ, and the patient had an excision of the nail matrix. Four months subsequently, the patient developed a very light brown macule over the proximal nail fold in the same digit. Biopsy revealed recurrence and the patient underwent amputation of the left third digit proximal to the distal interphalangeal joint. The patient has since been doing well and is being monitored closely.

Case D
A 16-year-old Hispanic female, with no family history of melanoma, presented to our clinic with a 7 year history of nail plate darkening of the middle finger on the left hand. She reported trauma to the same finger 7 years before, with subsequent darkening of the nail plate. Over time the nail failed to return to its normal color. Biopsy revealed melanoma in-situ and the patient had a matrix excision performed with skin graft placement over the distal phalynx. Three years later, she is doing well and being examined every 6 months.

Case E
A 2-year-old Black female, with no family history of melanoma, presented to our clinic with a darkly pigmented band on the index fingernail of the right hand which had been present since 1 week of age. The lesion has remained stable over time. She recently underwent an excisional nail matrix biopsy with a Pediatric hand surgeon. Biopsy was consistent with melanoma in-situ, and the treatment options are further being discussed with the family.

DISCUSSION

A rare variant of acral lentiginous melanoma, subungual melanoma accounts for 0.7-3.5% of all cutaneous melanomas. The disease usually arises from the distal or intermediate nail matrix, but may involve additional components of the nail unit, including the proximal nail fold, nail bed, and hyponychium. Subungual melanoma accounts for approximately 20% of all melanomas in dark-skinned and Asian populations, compared with 1–2% of cutaneous melanomas in whites, though the incidence appears to be equal among different racial groups. The majority of cases are diagnosed in the sixth to seventh decades of life, but presentation may occur at any age. Pathogenetic risk factors that predispose to development of subungual melanoma are still unknown. Genetic traits or family history of melanoma are not related to development of the condition, nor is UV light exposure. A history of trauma preceding development of subungual melanoma has been reported in 25-55% of cases, but a causal relationship is controversial. Traditionally, subungual melanoma has been thought to carry a worse prognosis than other types of melanoma, with a 5-year survival rate ranging from 18-58%, but the metastatic behavior of subungual melanoma is actually comparable to other melanoma subtypes at equivalent Breslow thickness. The more aggressive behavior that is often clinically observed is mainly due to delayed diagnosis.

Early on, subungual melanoma typically presents as longitudinal pigmentation of the nail plate, also known as melanonychia striata. At this stage, the disease is usually minimally invasive or in-situ. The most common location is the big toe (24-43% of cases), followed by the thumb (18-

31%). Discoloration of the nail and periungual pigmentation is often followed by a recalcitrant wound, a tumor, nail plate destruction, or bleeding. Often, cases exhibit features typical of late-stage lesions since many patients wait several months to years before consulting a physician. Hutchinson's sign, defined as the spreading of pigmentation to the proximal and/or lateral nail folds and/or the hyponychium, represents radial extension of intraepidermal melanocytes and warrants further histopathologic evaluation. However, this sign has limited utility in the evaluation of amelanotic lesions and can be observed in certain benign settings, such as congenital nevi of the nail matrix. Other features suspicious for subungual melanoma include adult-onset, involvement of a single digit, polychromia, history of rapid enlargement, and absence of other feasible causes of nail pigmentation. Any band wider than 3mm and/or triangular in shape should be considered suspicious for subungual melanoma.

Diagnosis of subungual melanoma can be challenging since some cases may present as amelanotic tumors, often corresponding to a late phase of development of an initially pigmented lesion. Additionally, the disease can be confused with post-traumatic subungual hemorrhage, onychomycosis, or even pigmented Bowen's disease of the nail unit. Furthermore, melanonychia striata can be seen in a variety of other nonmalignant conditions including nail matrix nevi, lentigo, drug-induced nail pigmentation, and certain metabolic abnormalities. Dermoscopy provides limited utility in the evaluation of melanonychia striata, and surgical biopsy of the nail matrix remains the gold standard for accurate diagnosis.

The mainstay of treatment for subungual melanoma is surgical excision with margin control. If histopathologic features are consistent with melanoma in-situ, excision with negative margins may be adequate. A tissue sparing approach that avoids digit amputation involves en bloc excision of the whole nail unit, including the proximal nail fold, both lateral nail folds, the supramatrical skin, and the distal pulp of the involved finger or toe. An extra margin ranging from 5-10 mm beyond is also obtained, with deep margins that are typically no greater than 1-2 mm because of underlying bone, which may be the reason for recurrence after modest excision of the tumor. Once margins are confirmed to be negative, a full thickness skin graft or flap is placed. This tissue sparing approach has good success rates with melanoma in-situ, but as mentioned, recurrences are not uncommon, and digit amputation may become the only surgical option.

For tumors with a depth greater than 1 mm but clinically negative regional lymph nodes, the question of pursuing a sentinel lymph node biopsy arises. Sentinel lymph node biopsy has been a variably useful method in assessing prognosis, but studies examining its effect on decreasing mortality have not shown significant benefit. It is, however, used commonly as a staging procedure for melanoma. In 2009, the TNM staging system of the American Joint Committee on Cancer (AJCC) was revised to include mitotic rate of the tumor in addition to tumor thickness, the presence of ulceration, the number of positive lymph nodes, lactate dehydrogenase level, regional metastasis, and distant metastasis.

If nodal metastasis is confirmed (stage III disease), adjuvant therapy with interferon alpha is considered. Interferon alpha is also considered in those patients with cutaneous melanoma whose risk of recurrence is thought to be high, i.e. stage IIB and IIC disease. Multiple trials examining different doses and schedules of interferon alpha have been performed, but an optimal approach has yet to be established. Other systemic therapies are constantly being studied, with recent advances in those available for stage IV metastatic disease. Options for metastatic, stage IV melanoma include surgical debulking of metastatic disease, radiation therapy, chemotherapy, immunotherapy, and the more recent molecularly targeted therapies. Approaches that have demonstrated clinically significant benefit include high dose IL-2, immunotherapy with ipilimumab (a monoclonal antibody targeting CTLA-4), and vemurafenib (inhibits the MAP kinase pathway). The choice of systemic therapy is based on factors such as the overall health of the patient, tumor burden, and specific tumor characteristics. No guidelines

with exact therapeutic regimens exist, and the majority of patients undergoing treatment with these therapies do so as part of clinical trials.

As most clinicians are aware, the diagnosis of subungual melanoma can be a difficult one to make. Clinical history, thorough physical examination, and the use of dermoscopy can all aid in clinical decision making; however, nail matrix biopsy is the only way to make a definitive diagnosis. If the diagnosis is made early, amputation of the digit may be avoided and local excision with skin grafting or flap recruitment may be performed, with good cosmetic outcomes. For the unfortunate patients who have metastatic disease, the options are vast; however, most offer minimal, if any, survival benefit. The best treatment remains early detection.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #6**

Presented by Sherri Korman, MD, Sheetal Mehta MD and Arthur Rhodes, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 53-year-old white male presented to our clinic 10/3/11 for surgical consultation regarding biopsies done on 9/12/11 at an outside hospital, demonstrating multiple melanomas. The results showed invasive melanoma at the left ear (0.55 mm thickness) and right forearm (0.35 mm thickness), as well as melanoma in-situ at right temple and an intraepidermal proliferation of atypical melanocytes at the left posterior calf. These slides were submitted to our dermatopathologist for review prior to surgical excision. The results are as noted in the histopathology section. In the interim, the patient was referred for melanoma surveillance using baseline imaging comparison.

The patient had last been seen in 2006 and had baseline photographs taken for surveillance. He had a photo surveillance examination on 10/13/11, at which time, a change was detected in a preexisting nevus on the patient's right upper back. The patient returned to clinic on 12/15/11 for an excisional biopsy of the unstable lesion.

PAST MEDICAL HISTORY

Melanoma in-situ, right scapula, 8 years ago s/p primary excision at outside hospital with subsequent re-excision
Numerous nevi removed in the past, with mild to moderate atypia
Diabetes, Hypertension, Coronary Artery Disease

MEDICATIONS

Metoprolol succinate, Atorvastatin, Clopidogrel bisulfate, Aspirin, Multivitamin, Magnesium

ALLERGIES

Vancomycin

FAMILY HISTORY

Sister with melanoma. Mother with breast cancer.

SOCIAL HISTORY

Nonsmoker

PHYSICAL EXAM

Eyes: Blue with yellow variegation
Freckling density: torso/extremities/face: dense and confluent
Findings included an abnormal nevus pattern: nevi ≥ 2 mm diameter = 238, nevi ≥ 5 mm diameter and atypical > 24
Negative for nevi in the following sites: scalp/acral/nails/mouth/conjunctivae/anus
+ nevus at left side of penile shaft at base, circumsized
Lymph nodes: none was enlarged in the neck (anterior + posterior), submental, preauricular, supraclavicular, axillary, or inguinal sites.
Liver and spleen: not enlarged
Melanoma site at right scapula: 80 mm scar. No evidence of recurrence.
Right upper back, 10 mm from midline: 5x5 mm dark brown, thin, flat-topped plaque intersecting with 4x5 mm medium brown-pink, thin, flat-topped plaque located superiorly to it. 10x polarized: heterogenous reticular pattern

HISTOPATHOLOGY
Left ear: Melanoma, invasive, 0.55 mm Breslow depth, no ulceration, no regression.
Right temple: Melanoma in-situ
Right forearm: Melanoma, invasive, arising in association with a compound dysplastic nevus, 0.35 mm Breslow depth, no ulceration, no regression
Left posterior calf: Atypical junctional melanocytic nevus with architectural disorder and severe cytologic atypia. (Dysplastic melanocytic nevus).
Right medial scapula: Atypical compound melanocytic nevus with architectural disorder and moderate cytologic atypia with congenital features.

LABORATORY RESULTS
None

RADIOLOGY
None

DIAGNOSIS
Multiple cutaneous melanomas and dysplastic nevi in the setting of a family history of cutaneous melanoma in a sister.

TREATMENT AND COURSE
Left ear: Wedge excision of melanoma with 1 cm margins - 11/29/11
Right temple: Staged excision with en face examination - 12/5/11.
Right forearm: Excision with 1 cm margins - 11/1/11.
Left posterior calf: Excision with 1 cm margins - 11/8/11.
Right medial scapula: No further intervention was necessary.
Melanoma surveillance exams every 3 months.

DISCUSSION
Patients with a history of cutaneous melanoma (CM) have an estimated relative risk of 8.5 for developing a second primary CM. Retrospective studies have estimated the frequency of a second primary CM to range from 1% to 8.6% dependent on duration of follow-up and patient composition. In a retrospective study by Stam-Posthuma *et al*, of 56 patients with multiple CM, most patients developed 2 (55.4%) or 3 (30.4%) tumors, with a mean of 2.8 primary CM per patient. Three patients (5%) developed 4 CM, 2 patients (4%) had 5, one (1.8%) had 6, one (1.8) had 7, and one (1.8%) had 9 CM. In a group of 60 patients with multiple primary CM, Johnson et al, reported that 46 patients (72%) had 2 primary CM, 9 patients (15%) had 3, 4 patients (7%) had 4 and 1 (2%) had 7. In a prospective study conducted at New York Memorial Sloan Kettering Cancer Center, of 385 multiple CM patients, 78% had 2 primary tumors, 15% had 3 primary tumors, 5% had 4 and 2% had 5 or more. In this latter study, the incidence of death without developing a second tumor was higher than the incidence of developing a second primary tumor, which may account for a lower than expected prevalence of multiple CM. In addition, this group demonstrated that after a second melanoma, the incidence of a third CM nearly tripled. The 1- and 5-year incidences of a third CM from the date of the second primary CM were 16.5% and 30.9%, respectively.

Known risk factors for developing multiple primary CM include a personal history of dysplastic nevi, family history of dysplastic nevi, and family history of CM. Among patients with multiple CM, 38% to 46% are reported to have a history of dysplastic nevi, and 18% to 38% are reported to have a family history of CM. In a retrospective analysis by Timothy *et a*l, the majority of patients had skin types I, II, or III. The most common eye color was blue (51%), and the most common hair color was brown (61%). A male preponderance of multiple primary CM has been

reported by several authors. Tucker *et al* reported a higher risk of second primary CM when the first had developed before the age of 40. Giles *et al* similarly observed that patients diagnosed with CM before the age of 45 had roughly twice the risk of a second primary CM compared with the older age group.

CM surveillance using baseline comparison is a valuable tool in detecting early CM in high risk patients. In patients who have large numbers of melanocytic nevi, new or changing lesions are often undetectable without baseline photographic images for comparison. Multiple studies have shown significant numbers of new or changing lesions in these patients, as well as higher incidence rates of CM than would be expected in the general population. In most surveillance studies, the second CM identified was thinner than the first, highlighting the utility serial examinations in discovering melanoma at an early stage. In patients with multiple CM, subsequent CM often occur in different anatomic locations and several years after diagnosis of the original lesion, making it imperative that these patients undergo complete mucocutaneous examinations.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #7**

Presented by Mark Romanelli, MD, and Michael D. Tharp, MD
Department of Dermatology, RUSH University Medical Center

UNKNOWN

CHICAGO DERMATOLOGICAL SOCIETY **CASE #8**

Presented by Andrea Kassim, MD, Jessie Cheung, MD and Lady Dy, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 46-year-old white man with past medical history significant for Common Variable Immunodeficiency (CVID) presented with a five-month history of asymptomatic, fixed lesions on his face, trunk and upper and lower extremities.

PAST MEDICAL HISTORY

Common Variable Immunodeficiency
Non-Hodgkin Lymphoma
Kaposi's sarcoma
Basal cell carcinoma
Chronic lymphadenopathy
Chronic hepatitis
Recurrent infections (*Gardia, Campylobacter*, *Cryptosporidium*, CMV, molluscum contagiosum, verruca vulgaris)
Herpes zoster
Post-herpetic neuralgia
Alopecia areata
Depression

MEDICATIONS

Intravenous Immunoglobulin
Valacyclovir
Famciclovir
Metronidazole by mouth
Azelaic Acid
Capsacin gel
Ursodiol
Ciprofloxacin
Bupropion
Intramuscular Testosterone
Vitamin B12
Dyphenoxylate/Atropine

ALLERGIES

Sulfa drugs

FAMILY HISTORY

Hypertension, prostate cancer, dyslipidemia, asthma

SOCIAL HISTORY

Lawyer

PHYSICAL EXAM

Physical examination was significant for well demarcated, smooth, infiltrated, erythematous to violaceous papules and plaques on his face, trunk and bilateral proximal upper extremities.

HISTOPATHOLOGY

Punch biopsy of a facial and upper extremity lesion confirmed a histological diagnosis of non-caseating granulomatous dermatitis in the setting of papillary dermal vascular ectasia with special stains negative for fungi and acid fast bacilli. Similarly, lymph node, liver, spleen and terminal ileum biopsies demonstrated non-infectious, non-caseating granulomas.

LABORATORY RESULTS
Quantiferon gold testing was negative.

RADIOLOGY
None

DIAGNOSIS
Granulomatous dermatitis associated with Common Variable Immunodeficiency

TREATMENT AND COURSE
After medical therapy with metronidazole gel, 0.75%, metronidazole by mouth, dapsone by mouth, doxycycline by mouth, tacrolimus ointment, 0.1%, azelaic acid gel, 15% and intralesional triamcinolone injections with minimal response, the patient underwent six intense pulsed light (IPL) treatments employing the 560 nm vascular wavelength filter at two- to six-week intervals. The following settings were used: fluence of 12-23 J/cm2, pulse width of 10-20 ms and a cooling temperature of 20-25^{o} C. After two IPL treatments, the patient showed marked improvement in the color intensity, size and thickness of his lesions, which continued to improve over subsequent treatments. At follow-up, the patient noted gradual recurrence of his facial, but not truncal lesions, for which the patient received monthly triamcinolone injections from an outside dermatologist.

DISCUSSION
CVID is a rare immunodeficiency characterized by diminished B- or B- and T-lymphocyte functioning, hypogammaglobulinemia and recurrent infections, as well as a predisposition for skin cancer, in particular squamous cell carcinoma, autoimmune disease, lymphoproliferative malignancy and non-infectious, non-caseating granulomas of various organ systems including the skin. Although the mainstay of treatment for the immunologic abnormalities of CVID is intravenous immune globulin along with antimicrobial therapy for the increased susceptibility to infection, most treatment modalities for the persistent, non-caseating granulomas associated with CVID have proven to be ineffective. One exception may be a few isolated case reports on the successful treatment of CVID-associated non-caseating granulomatous dermatitis with TNF-alpha blocking agents, for which the patient was not a candidate.

This is the first report of IPL or any other light-based energy source such as lasers for the treatment of CVID-associated non-caseating granulomatous dermatitis in the medical literature. The proposed mechanism of action of IPL is reduction in the vascularity of the lesions, thereby resulting in decreased dermal inflammation and granuloma formation. It is hypothesized that IPL may have an additional benefit over other vascular light-based sources such as the pulsed dye laser because the IPL 560 nm filter allows for the synergistic penetration of longer wavelengths beyond 560 nm that are preferentially absorbed by some of the more violaceous CVID-associated granulomas. Although further research is necessary to establish the exact mechanism of action, long term efficacy, frequency and total duration of treatments, IPL may prove to be a well tolerated, minimally invasive, safe and effective alternative for the treatment of CVID- associated non-caseating granulomatous dermatitis.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #9**

Presented by Sherri Korman, MD, Jessie Cheung, MD and Michael D. Tharp, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

The patient is a 41-year-old female who presented with numerous asymptomatic white papules on her face since childhood. The lesions first began to appear when she was 6 years old and slowly progressed over time. She noted a significant increase in number approximately 5 to 10 years ago. She has been seen by dermatologists in the past and had two biopsies, which reportedly showed fibrous tissue and sebaceous gland hyperplasia. In the last year, she underwent an extensive dermabrasion treatment, but the lesions rapidly recurred. Her mother has similar lesions, but has never been biopsied. She denied chest pain, shortness of breath or history of pulmonary infections. She was diagnosed as having a pulmonary embolism in 2002.

PAST MEDICAL HISTORY

Pulmonary Embolism in 2002, Obesity, Depression, Hypothyroidism (no longer on medication)

MEDICATIONS

Lorazepam prn anxiety

ALLERGIES

NKDA

FAMILY HISTORY

Mother with similar papules on face

SOCIAL HISTORY

No history of tobacco use

PHYSICAL EXAM

Face, ears and neck with numerous firm, white papules on a background of erythema. Papules range in size from 1-3 mm. Mild scaling of glabella and eyebrows.

HISTOPATHOLOGY

A 2-mm punch biopsy from the right cheek demonstrated trichodiscoma. A CD34 immunohistochemical stain exhibited a stronger staining pattern compared to a lighter staining uptake of dermal fibroblasts seen with a Factor XIIIa immunohistochemical stain, supporting the above diagnosis. A colloidal iron stain showed increased dermal mucin deposit.

LABORATORY RESULTS

CBC and CMP normal.

RADIOLOGY

CT Chest, Abdomen and Pelvis with IV Contrast:
1. Multiple bilateral lung cysts. The cyst within the right upper lung is 11.2x7.8 cm. These findings are associated with Birt-Hogg-Dubé syndrome.
2. Multiple bilateral renal cysts. There are a few tiny renal lesions which are too small to characterize, but are potentially small cysts as well. Continued surveillance is recommended, in this high risk patient, No definite solid renal tumor mass is visualized.

DIAGNOSIS
Birt-Hogg-Dubé syndrome

TREATMENT AND COURSE
The patient was referred to an internist to establish care, and a pulmonologist and nephrologist for evaluation given her numerous cysts and risk of renal cell carcinoma and pneumothorax. Her pulmonologist has recommended obtaining a chest CT every 2 years as long as the patient remains asymptomatic. She has been instructed to avoid scuba diving and exposure to inhaled dust or fumes. A small test area using the erbium laser to fully ablate the lesions, with additional fractional ablation at the bases, has been performed to assess the cosmetic response.

DISCUSSION
Birt-Hogg-Dubé syndrome is an autosomal dominant disorder caused by mutations in the FLCN gene, which encodes a tumor suppressor protein, folliculin. Clinically, it is characterized by triad of skin fibrofolliculomas, trichodiscomas and acrochordons, as well as increased susceptibility to pulmonary cysts, spontaneous pneumothoraces and renal cell cancer.

The skin lesions in Birt-Hogg-Dubé syndrome usually appear after the age of 20, as multiple whitish dome-shaped or flat-topped papules on the face and neck. The current opinion is that the classic 3 lesions, fibrofolliculomas, trichodiscomas and acrochordons may all represent various morphologies of a fibrofolliculoma. Traditionally, fibrofolliculomas are derived from both hair follicle epithelium and mesenchyme whereas trichodiscomas are derived from pilosebasceous mesenchyme.

Approximately 90% of adult patients with Birt-Hogg-Dubé syndrome will have lung cysts on CT and roughly 25% will experience pneumothorax, usually occurring during the 3rd to 6th decade of life.

Patients with Birt-Hogg-Dubé syndrome have a 20-30% lifetime risk of developing one or more renal tumors. The most common tumors seen are hybrid chromophobe-oncocytic (50%) and chromophobe renal cancer (33%). Less commonly observed tumors are oncocytoma (5%), clear cell carcinomas (9%) and papillary carcinomas. Renal tumors are multifocal or bilateral in more than half of the cases. There have also been several reports of Birt-Hogg-Dubé patients with multiple renal cysts, as seen in this patient, and it has been hypothesized that this finding may represent a manifestation of the syndrome.

Management recommendations are as listed in the table below. Disfigurement by the benign facial tumors remains difficult to treat and lesion recurrence from most treatments is common. Treatment options include excision, electrocautery, dermabrasion and laser skin resurfacing. Jacob and Dover have reported successful treatment with carbon dioxide and Er:YAG laser skin resurfacing. This technique has been reportedly used for syringomas, trichoepitheliomas and sebaceous hyperplasia with good results. Fractional resurfacing relies on the production of microscopic arrays of thermal damage of controlled size and density. The small size of the treatment zones allows intervening areas to be spared the thermal effects of the laser, which in turn leads to less inflammation, minimal adverse effects, and more rapid healing. Deeper ablation and coagulation may prevent the lesions from recurring as rapidly.

Management considerations in patients with Birt-Hogg- Dubé syndrome

Site	Recommendation
Skin	Annual dermatologic skin exam.
Kidney	Surveillance beginning at age 20. Interval and technique (computed tomography, ultrasound, or magnetic resonance imaging) to be individualized.
Liver	For asymptomatic patients, an individual baseline high resolution chest computed tomography with follow-up study every 3 to 5 years. For patients with symptoms follow-up should be individualized. In patients undergoing surgery of any kind, the anesthesiologist should be aware of the potential for pneumothoraces.

Adapted from Reese et al. Cancer Syndromes [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2009-.2009 Sep 01 [updated 2009 Oct 05].

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Presented by Mark Romanelli, MD, and Arthur Rhodes, MD, MPH
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS
A 62 year old male presented for lesions on the right lower extremity for the prior six months. Lesions first appeared on the right dorsal foot with subsequent progression to the right lateral leg, posterior thigh, and buttock. Intermittent pruritus was treated with aloe vera cream without change. He denied obvious contactants or new medications in the months preceding the appearance of lesions.

PAST MEDICAL HISTORY
Prostate cancer s/p prostatectomy

MEDICATIONS
Excedrin (acetaminophen, salicylic acid, and caffeine) as needed (about every other week) for headaches

ALLERGIES
Tamsulosin

FAMILY HISTORY
Negative for skin cancer, including melanoma

SOCIAL HISTORY
Occupation: Jeweler

PHYSICAL EXAM
On the right dorsal foot, right posterior leg and thigh, and right buttock were red flat topped papules with minimal to no scale, coalescing into plaques with islands of sparing. There were no vesicles or pustules, and no mucosal or nail lesions. Total mucocutaneous examination was otherwise unremarkable.

HISTOPATHOLOGY
4 mm punch biopsy, right posterior thigh: superficial and mid dermis lymphocytic infiltrate consistent with lichen striatus

LABORATORY RESULTS
None

RADIOLOGY
None

DIAGNOSIS
Lichen Striatus

TREATMENT AND COURSE
The patient used pramoxine lotion as well as triamcinolone 0.1% ointment twice daily for two weeks without resolution. After initial evaluation and biopsy, the patient spent time on an equatorial cruise with frequent natural sunlight exposure to the affected areas. During this

period, his skin lesions rapidly began to improve, flattening in substance and decreasing pruritus. At follow up three weeks after returning from his sunny vacation, significant flattening and slight skin pigment variegation were noted in areas of previous lesions.

DISCUSSION

Lichen Striatus is an acquired, self-limited dermatosis of undetermined etiology that develops along Blaschko lines. Lesions are usually unilateral, papular, and asymptomatic, but also can be bilateral, vesicular, and pruritic. Lesions commonly occur on upper limbs more than lower limbs or trunk, and rarely head and neck. The disorder primarily affects children with a median onset of age two to three years. Adult cases are significantly less frequent. There is a slight female predominance and an association with atopic diathesis. Typically, resolution occurs after about a year, and the most common sequela is hypopigmentation. Nail involvement usually involves a single digit and may be the only manifestation of the condition.

Numerous theories about causation have been proposed, including environmental exposures, infection, and genetic predisposition. The current leading hypothesis involves a cytotoxic autoimmune response to a mutated clone of keratinocytes. This process may be triggered by viral infection. There are reports of lichen striatus occurring during pregnancy, after trauma, and after BCG and HBV vaccinations.

Histologic findings in lichen striatus are variable and depend on timing of biopsy. Most lesions demonstrate a discontinuous lymphocytic superficial and deep perivascular and periadnexal infiltrate with CD8+ lymphocyte exocytosis. Spongiosis, hyperkeratosis, parakeratosis, necrotic keratinocytes, and perineural infiltration also can be seen. Langerhans cell numbers can be increased, decreased, or unchanged.

Of late, reports of ‘Adult Blaschkitis’ have been described as separate from lichen striatus. However, most authorities believe that adult cases are a variant of lichen striatus, existing within a larger group of acquired blaschkolinear dermatoses that includes variants of psoriasis, lichen planus, fixed drug eruption, lupus erythematous, atopic dermatitis, and chronic graft versus host disease.

Treatment of lichen striatus is optional given its self-limited nature and has included topical steroids, topical calcineurin inhibitors, and short courses of systemic glucocorticoids. Recently, one case report describes lichen striatus in a child successfully treated with methylaminolevulinic acid photodynamic therapy. There are no reported cases treated with ultraviolet radiation (UVR). UVR may be of potential benefit as suggested by the improvement of lesions with intense equatorial sunlight exposure in our patient.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #11**

Presented by Andrea Kassim, MD, Brian Bonish, MD, PhD and Mark Hoffman, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

The patient is a 67-year-old African American woman who presented with an eight-month history of clustered superficial pustules coalescing into lakes of pus and scattered erosions within an edematous, slightly indurated, erythematous plaque on her right lower leg. In addition, the patient had three non-fluctuant pustular plaques on her right palm, left dorsal wrist and lower back. The lesions were both pruritic and tender with some lesions occurring as a result of trauma.

Prior treatments included IV antibiotics, PO metronidazole, colchicine, clobetasol ointment, silvadene ointment, mupirocin ointment and bleach baths with minimal response. The patient's lesions responded to courses of prednisone, but promptly recurred after cessation of therapy.

PAST MEDICAL HISTORY

End Stage Renal Disease
Diabetes Mellitus
Hypertension
Non-Hodgkin Lymphoma
Breast cancer
Secondary hyperparathyroidism
Dyslipidemia
Anemia

MEDICATIONS

Pravastatin
Amlodipine
Furosemide
Metoprolol
Paricalcitol
Glipizide
Ferrous sulfate
Aspirin
Clonidine
Erythropoietin alfa
Metolazone
Sevelame

PHYSICAL EXAM

Right medial lower leg: clustered, superficial 1-2 mm pustules coalescing into lakes of pus with few scattered erosions within an edematous, slightly indurated, erythematous plaque.
Right palm, left dorsal wrist and lower back: three non-fluctuant pustular plaques.

HISTOPATHOLOGY

Biopsy of a right palm lesion revealed a superficial and deep perivascular, perieccrine and interstitial dermatitis with numerous eosinophils admixed with occasional histiocytes and flame figures. Direct immunofluorescence was negative for IgG, IgA, IgM, C3, C1Q, Kappa and Lambda.

LABORATORY RESULTS

Wound cultures obtained prior to presentation were significant for enterococcus species and *Pseudomonas aeruginosa*. Bacterial wound culture during an admission for a flare of the patient's skin lesions showed rare growth of *Serratia marcescens,* which likely represented a contaminent, with subsequent bacterial, fungal and acid fast bacillus tissue cultures being negative. HIV-1 p24 antigen and HIV-1/HIV-2 antibody testing was also negative. A complete

blood count was notable for leukocytosis with a total white cell count of 12,850 cells/cubic millimeter and peripheral eosinophilia up to 26%.

Complete blood count:

White blood cell count 12.85 cells/cubic ml	(nl 4-10)
Hemoglobin 11.9 gram/deciliter	(nl 12.0-16.0)
Hematocrit 36.3%	(nl 37-47)
Platelet count 281,000 cells/cubic ml	(nl 150-399)
Mean corpuscular volume 85 femtoliters	(nl 82-103)
Mean corpuscular hemoglobin 27.8 picograms	(nl 26-34)
Mean corpuscular hemoglobin conc. 32.8%	(nl 30-37)
Red cell distribution width 15.2%	(nl 11.5-14.5)

White blood cell differential:

Neutrophils 82.6 %	(nl 46-78)
Immature granulocytes 0.2 %	(nl 0-1)
Lymphocytes 5.5 %	(nl 18-52)
Monocytes 4.8 %	(nl 3-10)
Eosinophils 6.7% to 26**%**	(nl 0-6)
Basophils 0.2 %	(0-3)

Iron studies:

Serum Iron 28 µg/dL	(nl 25-170)
Total iron-binding capacity 167 µg/dL	(nl 196-364)
Percent iron saturation 17%	(nl 25-66)
Ferritin 328 µg/L	(nl 12-260

RADIOLOGY

Right lower extremity venous duplex ultrasound was within normal limits

DIAGNOSIS

Eosinophilic pustulosis

TREATMENT AND COURSE

After completing a one-month prednisone taper with a starting dose of 1 mg/kg/day, the patient was transitioned to indomethacin 25 mg by mouth three times daily with complete resolution of her skin lesions. At the patient’s one-year follow-up, she remained lesion-free while maintained on 25 to 75 mg of indomethacin daily as sole therapy.

DISCUSSION

Among the thousand(s) of dermatologic conditions described in the medical literature, only a handful are classified as eosinophil-predominant dermatoses based on histopathology. Of the eosinophilic dermatoses recognized so far, the patient's biopsy findings are best described as an overlap between Well's syndrome and Ofuji's disease. Well's syndrome, also known as eosinophilic cellulitis, was first described in 1971 and is characterized by recurrent tender or pruritic, erythematous, edematous plaques resembling infectious cellulitis that often presents in an annular or arcuate configuation. The lesions of Well's syndrome typically occur on the extremities followed by the trunk. Although the exact pathogenesis is unknown, the lesions of Well’s syndrome are thought to represent a local hypersensitivity reaction to arthropod bites. Histologically, the prototypic findings in Well's syndrome include a dense (deep) dermal infiltrate consisting of numerous eosinophils admixed with lymphocytes, histiocytes and occasional flame figures. Papillary dermal edema and epidermal spongiosis may lead to secondary supepidermal bulla and intraepidermal vesicle formation, respectively.

Classic eosinophilic pustular folliculitis (EPF), first described in 1970 and widely known by its eponym, Ofuji's disease, is of uncertain etiology and is characterized by recurrent, pruritic, annular, circinate or serpiginous, infiltrated plaques with superimposed follicular, erythematous papules and papulopustules. Ofuji's disease most commonly presents in young Asian men and favors a seborrheic distribution with prominent facial involvement. Since its original description, two additional variants have been described, namely immunosuppression-associated EPF, most

commonly seen in the setting of HIV, and infancy-associated EPF. Appropriately coined, eosinophilic pustular folliculitis tends to be a folliculocentric process with the hallmark finding being infundibular eosinophilic pustules with eosinophilic spongiosis. However, lesions on acral surfaces devoid of hair follicles have been reported.

Both Well's syndrome and Ofuji's disease are characterized by peripheral blood eosinophilia with corticosteroids and indomethacin being first-line therapeutic agents for each disease, respectively. Interestingly, our patient demonstrated excellent and expeditious response to indomethacin, resulting in prompt resolution of her skin lesions with continued remission at her one-year follow-up. Indomethacin is a potent cyclooxygenase inhibitor that decreases the production of arachidonic acid-derived eosinophil chemotactic factors such as prostaglandin D2 (PGD2). Indomethacin has also been shown to attenuate the expression of PGD2's chemoattractant receptor of T12 (CRTH2) receptor on eosinophils. The regulation of PGD2 production and CRTH2 expression has been postulated to play a key role in the pathogenesis of Ofuji's disease as well as in our patient's skin lesions and peripheral eosinophilia.

Although from a histological perspective, our patient appeared to have elements of a Well's syndrome-Ofuji's disease hybrid, one may argue that such an overlap diagnosis does not adequately describe our patient's skin lesions clinically. Although a few cases of bullous Well's syndrome have been described, no purely pustular variant has been reported. Similarly, erythematous, annular, circinate or serpiginous plaques studded with papules and papulopustules are a hallmark finding in Ofuji's disease, yet, no cases of agminated, minute, superficial pustules coalesing into pustular lakes on a background of erythema have been reported. As there is no unifying histological and clinical diagnosis that encompasses our patient's striking clinical and histopathological findings, we propose a new term to describe this diagnostic entity: eosinophilic pustulosis.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #12**

Presented by Sherri Korman, MD, and Katherine Brown, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS
The patient is a 31-year-old male with significant past medical history of vitiligo, who presented with several blue bumps on his back, buttocks, left wrist and left foot since birth. These lesions were occasionally painful, particularly with pressure or rubbing on his belt. He had one biopsied in the past but the results were unavailable. He denied any history of oral or gastrointestinal bleeding and anemia. His father and brother have similar lesions.

PAST MEDICAL HISTORY
Vitiligo, Tonsillectomy, Wisdom tooth extraction, Inner ear tubes

MEDICATIONS
None

ALLERGIES
NKDA

FAMILY HISTORY
Father and brother with similar lesions. He has one daughter who is unaffected.

SOCIAL HISTORY
Nonsmoker. Married. Works as a teacher.

PHYSICAL EXAM
Right low back with a cluster of approximately 50 soft, compressible blue papules, ranging from 2 mm to 7 mm. Two papules located at superior and superiolateral edge of affected area are tender. Largest measures 11x4 mm. Blue compressible papules on right volar and dorsal wrist, two of which are tender to palpation. Left sole with blue compressible papule. Depigmented patches over MCPs on bilateral hands and few dorsal fingertips. No lesions on lips or oral mucosa.

HISTOPATHOLOGY
12/6/11 Right low back x 2: Within the reticular dermis there are several irregularly-dilated, thin-walled blood vessels that are lined with monotonous cells with large, round dark nuclei and little cytoplasm, consistent with glomuvenous malformations.

LABORATORY RESULTS
None

RADIOLOGY
None

DIAGNOSIS
Glomuvenous Malformations (Familial Glomangiomas)

TREATMENT AND COURSE

The larger lesion on the back was surgically excised. The smaller lesion on the back did not require treatment beyond biopsy. Two 3 mm lesions on right dorsal wrist were test treated with one session 1064 Nd:YAG laser, 3 mm spot size, 40-millisecond intervals and 240 J/cm^2 fluence. At one month follow-up, the patient noted resolution of pain in the treated lesions and gradually improving hyperpigmentation.

DISCUSSION

Glomus cells are neuromyoarterial cells that surround arteriovenous anastamoses acting as thermoregulatory units called glomus bodies. There are two major types of benign tumors characterized by presence of these cells, glomus tumors and glomuvenous malformations, formerly referred to as glomangiomas. Glomus tumors usually present in young adults as solitary, painful, red-blue papules or nodules on the extremities with a predilection for subungual sites. In contrast, glomuvenous malformations are often multiple and generally elicit pain only with palpation. They are rare, representing approximately 5% of all venous anomalies. Typically, they present in infancy or childhood as widely distributed or confluent red-to-blue nodules that may become more intensely blue with time. Histologically, these lesions resemble venous malformations with dilated blood vessels rimmed by a few rounded glomus cells. Hence, glomuvenous malformation (GVM) has recently become the preferred term for these lesions.

Glomuvenous malformations can occur sporadically or in an autosomal dominant pattern with variable penetrance and expression. An estimated 63% of GVMs are hereditary. They are caused by several loss-of-function mutations in the glomulin gene, which has been mapped to chromosome 1p21 in familial linkage studies. The lesions can be subdivided into localized, disseminated and congenital plaque-type forms. Localized and disseminated forms tend to favor the extremities over the trunk, and rarely involve the face. Congenital GVMs usually enlarge over time and coalesce and thicken into plaques with a cobblestone-like appearance. Some patients with familial GVMs have reported the appearance of new lesions in previously unaffected areas following localized trauma.

Treatment options that have been described for glomuvenous malformations include surgical excision, sclerotherapy and laser surgery employing carbon dioxide, argon, pulsed dye laser and Nd:YAG. Surgical resection is acceptable for treatment of small focal lesions, but impractical to treat multiple GVMs and gradual recurrence is common. Possible complications of sclerotherapy include necrosis, ulceration, hyperpigmentation and telangiectatic matting. Ablative therapies with erbium and carbon dioxide lasers often result in unacceptable scarring. Laser treatment with the 1064 Nd:YAG appears to be more effective than treatment with pulsed dye laser, likely due to the deeper penetration of the Nd:YAG laser into the upper or mid dermis, where GVMs are usually located. The 1064 Nd:YAG appears to be a safe and effective treatment for multiple GVMs, with adverse effects limited to dyschromia and slight atrophic scarring at larger treatment sites.

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Presented by Jill C. Anderson, MD, and Katherine K. Brown, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 1-day-old full term female was noted to have two nodules over her right forearm at delivery. The patient was born to a 26-year-old female (G1P1) via spontaneous vaginal delivery. The delivery was unremarkable. Maternal history was significant for human papillomavirus infection, anemia, and a shortened cervix. Of note, there was no maternal history of preeclampsia.

PAST MEDICAL HISTORY

None

MEDICATIONS

None

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Mother denies tobacco, alcohol or substance use during pregnancy.

PHYSICAL EXAM

On physical examination, the patient was a well-appearing African American infant. Over the right forearm, a 1.0 cm x 0.8 cm (height 0.7 cm) dome-shaped grey-blue firm nodule and a 0.6 cm x 0.6 cm (height 0.3 cm) firm grey-blue papule with irregular surface were noted.

HISTOPATHOLOGY

Excision, right forearm, proximal: consistent with Masson's tumor (intravascular papillary endothelial hyperplasia). There is a prominent vessel present with thrombus. There is intravascular proliferation of endothelial cells, some forming slit-like spaces and papillary projections. There are extravasated red blood cells, serum nuclear dust and debris, and granulomatous infiltrates and calcification. Hemosiderin is also present.

Excision, right forearm, distal: consistent with infantile hemangioma with Masson's features. Immunohistochemical stains were performed, and the endothelial cells were highlighted by GLUT-1 and Wilms tumor 1, confirming the diagnosis of an infantile hemangioma. GLUT-1 is characteristically positive in infantile hemangiomas. Wilms tumor 1 immunostaining is used to distinguish vascular neoplasms from vascular malformations.

LABORATORY RESULTS

The following were negative or within normal limits:
Prenatal screening tests

RADIOLOGY

Ultrasound of the right forearm: Two solid appearing ovoid hypoechoic structures superficially within the soft tissues of the right forearm. The proximal lesion has a non-shadowing hyperechoic center, which may relate to ischemia or hemorrhage, rather than calcification. No discrete calcifications identified. These two lesions are of uncertain etiology, but may relate to

vascular malformations, such as hemangiomas. Other etiologies, such as a neurofibroma, cannot be excluded.

Abdominal ultrasound: Borderline small kidneys for age. No abdominal mass identified. No hepatic abnormalities.

DIAGNOSIS

Congenital Masson's tumor (intravascular papillary endothelial hyperplasia) and infantile hemangioma with Masson's features

TREATMENT AND COURSE

The patient and the lesions were followed clinically by pediatrician until 4 months of age, when both lesions were excised by plastic surgery. The mother reports that the lesions were stable in appearance prior to the excision.

DISCUSSION

When approaching subcutaneous and cutaneous nodules in infants, a broad differential diagnosis, including both benign and malignant diseases, is necessary. In this case, the following etiologies were considered: atypical-appearing hemangiomas, mixed vascular malformations, rhabdomyosarcoma, neuroblastoma, and congenital dermatofibrosarcoma protuberans. Other diagnoses to consider for nodules in infancy could include: infantile myofibromatosis, congenital leukemia, congenital Ewing sarcoma, dermoid cysts, teratomas, hamartomas, extramedullary hematopoiesis, and many others. Due to the broad differential, which included malignant diagnoses, an excisional biopsy during the neonatal period was suggested. However, the decision was made to monitor the lesions clinically until the patient was older. Fortunately for our patient, her lesions remained stable, and benign histopathologic diagnoses of Masson's tumor and infantile hemangioma were made.

Masson's tumor was first described in 1923 by Pierre Masson, and was originally named "hémangio-endothéliome végétant intravasculaire." Masson's tumor represents approximately 2% of benign and malignant vascular tumors of the skin and subcutaneous tissues. The majority of Masson's tumors present during adulthood, commonly between the third and fourth decade, but they may present at any age. There is a slight female predominance. These tumors are frequently located in the skin and subcutis of the fingers and head and neck region, but there are cases of Masson's tumor arising in other areas, including oral soft tissues, lateral neck, mandible, thyroid, tongue, orbit, brain, maxillary sinus, superior vena cava, popliteal artery, ulnar artery, calf, lung, parotid, renal vein, adrenal gland, kidney, gastrointestinal tract, cervix, and liver.

Masson's tumor is thought not to be a specific disease, but instead a distinct histopathologic pattern that may be mistaken for angiosarcoma. The exact pathogenesis of this lesion is unknown, but it is thought to represent a reactive hyperplastic process of endothelial cells, which develops in response to a thrombus.

Three types of Masson's tumors have been described: 1) a "pure," primary type, which arises de novo in dilated vessels; 2) a secondary, "mixed" form, which occurs focally within preexisting vascular anomalies that are prone to thrombosis, including hemangiomas, venous malformations, pyogenic granulomas, lymphangiomas, and arteriovenous malformations; 3) an extravascular type, which occurs in hematomas and is quite rare. Primary mucocutaneous lesions often present as solitary firm masses with red or blue discoloration. In the secondary type, the presentation is the usually same as the underlying vascular anomaly. Rare reports of intraabdominal Masson's tumors have presented with hematuria and hematochezia. Cases of intracranial lesions presented with neurologic symptoms (i.e., seizures, hemiparesis, diplopia). Intramuscular lesions produce a subcutaneous mass.

Congenital and infantile primary Masson's tumors are rare. A review of the literature yielded very few reports of Masson's tumors occurring during infancy. Shogo *et al.* (2002) from Japan report a case of a congenital intravascular papillary endothelial hyperplasia of the dorsal hand of a male neonate. In this case, the lesion grew significantly prior to removal at 57 days of life. A congenital intracranial Masson's tumor was reported in 2012 by Shih *et al.* Sickler and Lanford (1990) report a case of intracranial Masson's tumor in a 12-day-old twin. A fatal case of intracranial Masson's tumor in an infant was reported by Chen and Kuo in 1984. Juan *et al*. in 2008 reported a Masson's tumor arising in the calf of a 1-year-old infant. While reports of Masson's tumors in infancy are rare, it is known that Masson's tumors may arise in precursor vascular lesions, such as hemangiomas, and features of Masson's tumors (i.e., thrombosis) are often found in hemangiomas and may invite comparisons to Masson's tumors. In a study characterizing histopathologic features of different type of vascular tumors, North *et al.* noted that one of the six congenital nonprogressive hemangiomas in their study had Masson's tumor-like features with a "large central area of intravascular pseudopapillary capillary proliferation without true fibrinous or fibrous papillary cores."

Masson's tumor is a histologic diagnosis. Clinically, the lesions have a non-specific appearance. Surgical excision is often curative; however, in the setting of underlying vascular anomalies, local recurrences may occur.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #14**

Presented by Jessica Hsu, MD, and Katherine K. Brown, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

A 24-year-old G2P1 Hispanic female at 31 weeks gestation presented with a 1 month history of pruritic lesions developing over the trunk and proximal extremities. The initial lesions started on the abdomen and eventually spread to the back, arms, upper thighs, and lower face. Pruritus was exacerbated by hot showers and somewhat alleviated by over the counter hydrocortisone 1% cream and diphenhydramine she had been taking a few days prior to presentation. Patient denied any blisters or vesicle formation. There was no involvement of the oral or genital mucosa. Patient denied any fevers, chills, or night sweats. There were no new medications prior to onset. Her current pregnancy was complicated by gestational diabetes. She did not have a history of skin problems during her first pregnancy.

PAST MEDICAL HISTORY

Gestational Diabetes

MEDICATIONS

Diphenhydramine
Hydrocortisone 1% cream
Prenatal vitamins

ALLERGIES

There were no known drug allergies.

FAMILY HISTORY

There was no history of autoimmune disorders or bullous diseases.

SOCIAL HISTORY

Patient denied alcohol, tobacco, or illicit drug use.

PHYSICAL EXAM

Diffusely over the entire trunk, there were numerous discrete erythematous papules and polycyclic erythematous to hyperpigmented plaques, most with slight central scale and brightly erythematous borders. Few plaques were slightly urticarial in appearance. Lesions were accentuated and confluent over the abdomen and breasts, with involvement of the umbilicus. There was no striae accentuation, periumbilical sparing, vesicles, bullae, or dermatographism. There was mild involvement of the left lower face. Oral and genital mucosa as well as palms and soles were spared.

HISTOPATHOLOGY

4 mm punch biopsy from the right upper flank: Spongiotic dermatitis with superficial perivascular infiltrate with abundant eosinophils, suggestive of pemphigoid gestationis.

Direct Immunofluorescence: Minimal to mild linear IgG and moderate C3 deposition at the dermal-epidermal junction, consistent with pemphigoid gestationis.

LABORATORY RESULTS

Liver function tests obtained by the patient's obstetrician were within normal limits.

RADIOLOGY
None

DIAGNOSIS
Pemphigoid gestationis

TREATMENT AND COURSE
The patient was treated with oral antihistamines and topical triamcinolone 0.1% ointment twice daily to all affected areas for 3 weeks with significant clinical improvement of her lesions. After three weeks of treatment she developed a small flare, so was switched to fluocinonide 0.05% ointment twice daily for 2 weeks with improvement until she delivered a healthy, full term child via planned cesarean section. The baby was unaffected. One day postpartum, she began to develop new lesions on the breasts and abdomen. The patient was extensively counseled regarding her prognosis and postpartum treatment options, but the decision to continue with topical corticosteroids was made with input from the obstetrician, due to concern over the effect of systemic corticosteroids on impaired wound healing following a cesarean section. She was switched from oral diphenhydramine to cetirizine and advised to use clobetasol 0.05% ointment twice daily to all new lesions, avoiding the face, along with comfort measures such as sitz baths. Counseling regarding avoidance of oral contraceptive pills and recommendations regarding placement of a copper intra-uterine device were also discussed with the patient.

DISCUSSION
Pemphigoid gestationis, also known as herpes gestationis, is a rare, self-limited autoimmune bullous disorder with incidence ranging from 1:2,000 to 1:50-60,000 pregnancies depending on the prevalence of the HLA-haplotypes DR3 and DR4. Although typically presenting in late pregnancy or the immediate postpartum period, it can occur during any of the three trimesters. During subsequent pregnancies, pemphigoid gestationis tends to recur with earlier onset and increasing severity. “Skip pregnancies,” when the disease fails to manifest during a subsequent pregnancy, are extremely rare, seen in only about 5% of cases. Beyond pregnancy, pemphigoid gestationis can also be seen in association with trophoblastic tumors (choriocarcinoma, hydatidiform mole) and other autoimmune diseases, particularly Grave’s disease.

Pathogenically, abnormal MHC II expression in the amniochorionic stromal cells and trophoblasts results in circulating complement fixing IgG antibodies of the subclass IgG1 being able to bind to the NC16a domain of a 180-kDA protein known as BP-180 (Bullous pemphigoid antigen 2) located in the hemidesmosomes of the dermo-epidermal junction (DEJ), leading to blister formation and tissue damage. Of note, the primary site of autoimmunity is the placenta, not the skin, since antibodies bind to both chorionic and amniotic epithelia of ectodermal origin, not just to the basement membrane zone of the epidermis. Recently, both IgA and IgE antibodies to either BP-180 or BP-230 have also been detected in pemphigoid gestationis.

Clinically, the disease often presents with intense pruritus preceding the onset of skin lesions. Erythematous urticarial papules and plaques develop over the abdomen, with involvement of the umbilicus being a characteristic feature. Lesions may then spread to the entire skin surface, with sparing of the facial and mucous membranes. During this pre-bullous stage, the disease closely resembles polymorphic eruption of pregnancy, both clinically and histopathologically, but progression to tense bullae often aids in clarifying the diagnosis.

Histopathology from lesional skin will vary depending on the stage and severity of disease. The pre-bullous stage often demonstrates upper and mid-dermal edema with a perivascular inflammatory infiltrate composed of lymphocytes, histiocytes, and variable number of eosinophils while the bullous stage is characterized by subepidermal blistering at the level of the lamina lucida. The gold standard in the diagnosis of pemphigoid gestationis remains direct immunofluorescence of perilesional skin. Linear C3 deposition along the DEJ is seen in 100% of

cases, and additional IgG deposition occurs in 25-30%. With indirect immunofluorescence, serum IgG antibodies may be detected binding to the roof of the cleft on salt-split skin in 30-100% of cases. ELISA and immunoblot techniques can also be utilized to monitor antibody levels that correlate with disease activity.

The natural course of the disease is marked by exacerbations and remissions during pregnancy, frequently with improvement in late pregnancy followed by immediate post-delivery flare in 75% of patients. The lesions gradually resolve without scarring weeks to months after delivery, though recurrences have been reported with menstruation and hormonal contraception. Severe courses with persistent skin lesions over several years are rarely seen. While fetal prognosis is generally good, disease severity does correlate with increased risk of prematurity, intrauterine growth retardation, and small-for-date babies. Additionally, about 10% of newborns may develop mild skin lesions due to the passive transfer of maternal antibodies to the fetus, but the lesions typically resolved spontaneously within days to weeks.

The goal of therapy is to control pruritus and prevent blister formation, so treatment will depend on the stage and severity of disease. In mild cases of pre-bullous pemphigoid, topical corticosteroids with or without oral antihistamines may be sufficient. In all other cases, systemic corticosteroids (prednisolone, usually started at a dose of 0.5-1 mg/kg/day) are generally required and considered safe to administer during pregnancy. The dose can be reduced during pregnancy if the disease improves, but should be increased in time prior to delivery to prevent the common flare. Immunoapheresis may be considered in recalcitrant cases when disease is unresponsive to systemic steroids. Post-delivery, the full range of immunosuppressive treatments may be utilized as necessary. Successful postpartum treatments with tetracyclines, nicotinamide, cyclophosphamide, cyclosporine, goserelin, azathioprine, dapsone, rituximab, plasmapharesis, or intravenous immunoglobulin have all been reported.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #15**

Presented by Mark Romanelli, MD, Michael Tharp, MD, Marianne O'Donoghue MD, and Jessie Cheung, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS
A fourteen year old female presented with a lesion on the left infraorbital cheek for approximately one year. She stated that she tripped and fell into a classmate who was holding an uncapped felt tip fluorescent pink highlighter. The immediate injury resulted in bleeding and mild pain. The lesion healed over several weeks, leaving behind a pigmented lesion similar in color to the highlighter that traumatized the area. The lesion persisted and did not change despite several attempts at removal with soap, shampoo, acetone, and alcohol. The patient was somewhat bothered by the lesion and desired treatment.

PAST MEDICAL HISTORY
None

MEDICATIONS
None

ALLERGIES
None

FAMILY HISTORY
Not contributory

SOCIAL HISTORY
Student. Lives with mother.

PHYSICAL EXAM
On the left infraorbital cheek, there were two linear pink macules approximately 4mm x 1mm. Fluorescence noted under ultraviolet light. No surface change or palpable masses were noted at the site. A wart was noted at the left vertex scalp. An examination of the upper body otherwise was unremarkable

HISTOPATHOLOGY
2 mm punch biopsy of left infraorbital cheek inferior lesion: Dermal fibrosis and vascular proliferation consistent with healing trauma site. No evidence of foreign material observed.

LABORATORY RESULTS
Not performed

RADIOLOGY
Not performed.

DIAGNOSIS
Traumatic tattoo due to fluorescent highlighter.

TREATMENT AND COURSE

The patient and mother desired removal of the lesion. After the punch biopsy healed for 1 month, the lesion was treated with an ablative fractionated laser (Erbium, 2940 nm) at a density of 22% and depth of 250 micrometers for 3 passes. At follow up, the lesion had improved slightly without post treatment dyschromia. A second treatment 1 month later at a depth of 300 micrometers yielded mild improvement. Patient has not had further treatment due to her school schedule. She will consider further treatment during the summer.

DISCUSSION

Tattoos are the result of pigment material deposited in the dermis, either intentionally or accidentally, that the body is unable to remove. Typical accidental tattoos are the result of trauma from abrasions or explosions. The most common materials include amalgam, dirt, sand, glass, wood, soot, suture, and surgical pen. Most traumatic tattoos are black or blue in color due to the carbon content of the penetrating material delivered deep into the dermis.

As with intentional tattoos, treatment options for removal include excision, salabrasion, cryotherapy, and lasers. While many of the former risk scarring and permanent pigment alteration, newer laser therapies have been developed that more precisely target the implanted material, therefore improving the cosmetic outcome compared to previous treatment options.

The theory of laser tattoo removal is based on selective photothermolysis, wherein optimal pigment absorption spectra can be targeted with specific wavelengths of light. It is believed that this targeted therapy of energy delivery creates a thermal gradient and a resultant acoustic shock wave fragments larger particles into smaller particles. These fragments subsequently can be removed by the body's phagocytic system. Standard lasers used for this procedure include Q-switched Ruby (595 nm), Alexandrite (755 nm), and Nd:YAG (1064 nm) lasers. Usually, multiple treatments are needed and the risk of adverse outcomes increases with each subsequent treatment.

If the nature of the chromophore is unknown, or laser treatment may have an increased likelihood of creating paradoxical darkening (via oxidation of compounds used in tattoos containing some white or yellow pigment), alternative laser modalities can be used. In these cases, treatment has been successful using carbon dioxide or fractionated resurfacing laser treatments. This approach is based on reports of successful fractional resurfacing treatment of dermal melanocytosis that is resistant to Q-switched laser therapy. Similar thermal shock waves fragment the exogenous material as with other laser types. In addition, ablative destruction and transepidermal elimination of pigment and pigment laden macrophages are proposed secondary mechanisms by which fractional resurfacing lasers exert their tattoo lightening effect. Combined approaches of Q-switched laser treatment immediately followed by fractional photothermolysis can increase the clearance of tattoo, possibly by an increased inflammatory and phagocytic response to more completely remove Q-switched laser treated pigment.

Highlighter markers contain hydrophilic coloring agents combined with a hydrophilic fluorescent compound, typically pyranine (trisodium 8-hydroxypyrene-1,3,6-trisulfonate). The removal of these aqueous soluble particles by the ethanol and/or xylene used in tissue fixation for routine histology likely explains the absence of exogenous material on the patient's biopsy. Specific compositions of coloring agents are proprietary information that can vary between manufacturers. Therefore, chromophores cannot be determined with certainty.

There are no reports in the literature of a traumatic tattoo due to a highlighter marker. Elemental analysis of pink tattoo pigment composition includes titanium, aluminum, copper, and oxygen. Because of the risk of laser induced pigment darkening due to oxidation of an unknown chromophore, the existence of a small scar from the previous biopsy, and the potential for transepidermal elimination of pigment treatment with a fractionated ablative laser was deemed most appropriate in this case. Similarly, without specific knowledge of the nature of the

deposited material, a cautious treatment with conservative laser settings over multiple visits is the most suitable approach in order to facilitate pigment clearance while minimizing the potential adverse effects of more aggressive treatment.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE #16**

Presented by Jill C. Anderson, MD, and Lady C. Dy, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

Patient is a 14-year-old female with past medical history significant for leiomyosarcoma of her right scapula diagnosed in July 2011. She was treated initially with chemotherapy and radiation. She then underwent definitive surgical resection in October 2011, followed by additional chemotherapy. The patient was admitted in December 2011 for neutropenic fevers following chemotherapy with doxorubicin, ifosfamide, and mesna. Her hospital stay was complicated by sepsis of unknown source. She was treated with broad spectrum antibiotics, including fluconazole, acyclovir, trimethoprim/sulfamethoxazole, and amoxicillin/clavulanate. Dermatology was consulted on the seventh day of admission for evaluation of new right axilla lesions. The lesions were thought to be present for at least four days. The patient noted mild tenderness, but denied drainage. Prior to dermatology consultation, local wound care was performed utilizing Duoderm, Polymem, and barrier cream with no improvement.

PAST MEDICAL HISTORY

Leiomyosarcoma of right scapula (diagnosed July 2011)
Peripheral neuropathy secondary to chemotherapy
Right scapulectomy
Renal tubular acidosis (type 2)

MEDICATIONS

acyclovir
acetaminophen
amoxicillin-clavulanate
calcitriol
desmopressin
fluconazole
lorazepam
ondansetron
pantoprazole
spironolactone
trimethoprim/sulfamethoxazole

ALLERGIES

Adhesive

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

Denies alcohol, tobacco, or illicit drug use.

PHYSICAL EXAM

Right axilla: Patchy hyperpigmentation with four punctate pink erosions with central eschar, which are minimally tender to palpation. No fluctuance was noted.

HISTOPATHOLOGY

Punch biopsy, right axilla (12/13/2011): Granulomatous deep dermal infiltrate with abscess formation and focal necrosis. Fungal hyphae consistent with *Aspergillus* species noted with PAS staining.

LABORATORY RESULTS

The following were positive or abnormal:

White blood count:	12.34	(normal 4.0 – 10.0)
Neutrophil %:	79.3	(normal 46.0 – 78.0)
Immature Granules %:.....	4.9	(normal 0.0 – 1.5)
Lymphocyte %:.	4.4	(normal 18.0 – 52.0)
Monocyte %:……..	15.7	(normal 3.0 – 10.0)
Hemoglobin:.....	10.1	(normal 13.5 – 17.5)
Platelets:	18	(normal 150 – 399)
Sodium:……..	148	(normal 137 – 147)
Potassium:……..	3.3	(normal 3.4 – 5.3)
Chloride:……..	127	(normal 99 – 108)
Bicarbonate:……	12	(normal 20 – 28)
Phosphorus:……...	2.0	(normal 4.5 – 6.5)
INR:……..	1.29	(normal 0.83 – 1.20)
PTT:……	41.8	(normal 23.0 – 33.0)
TSH:……	0.020	(normal 0.35 – 4.94)
Tissue culture, right axilla:……	Growth of *Aspergillus flavus*	

The following were negative or within normal limits:

Basophil %, Eosinophil %, BUN, Creatinine, Glucose, Calcium, Magnesium, Albumin, Total Protein, AST, ALT, Alkaline Phosphatase, Total Bilirubin, Free Thyroxine, Total T3, Blood Cultures, Urine Culture, Throat Culture, MRSA Culture.

RADIOLOGY

Ultrasound of right axilla (12/13/2011): Normal sonographic appearance of the right axilla with no focal abnormalities identified.

MRI of right shoulder (12/15/2011): There is a rim enhancing fluid collection in the operative bed of the right axilla along the right chest wall. This most likely represents a postoperative seroma, although a complicated postoperative seroma/abscess cannot be excluded. There is no surrounding inflammatory change. There is no nodular enhancement to suggest tumor recurrence.

CT Chest with IV Contrast (12/31/2011): There is a somewhat well-demarcated area of ground glass opacity in the posterior peripheral portion of the upper half of the right lung consistent with post-radiation change. There are stable post-surgical changes in the right posterior chest and right axilla from right scapula resection and posterior thoracic mass resection. There are no new discrete/drainable fluid collections identified.

DIAGNOSIS

Cutaneous aspergillosis

TREATMENT AND COURSE

Our patient was started on voriconazole 200 mg twice daily with good clinical response and resolution of lesions. No evidence of systemic infection was found. Follow-up imaging revealed resolution of the fluid collection in the right axilla. Voriconazole was discontinued after three months of therapy.

DISCUSSION

Aspergillus species are located worldwide and are ubiquitous in the environment, commonly found in soil, water, and decaying vegetation. *Aspergillus* infections are uncommon in immunocompetent individuals and are most commonly seen in immunocompromised patients.

High risk groups include those with malignancy (especially hematologic), solid organ transplant, bone marrow transplant, inherited immunodeficiency (i.e., chronic granulomatous disease), prolonged neutropenia, chronic glucocorticosteroid use, HIV/AIDS, and primary lung pathology (i.e., COPD).

The most common presentation of *Aspergillus* infection is pulmonary disease, representing 80 to 90% of cases. Pulmonary disease may be due to allergy (known as allergic bronchopulmonary aspergillosis) or infection. Other less common presentations include rhinosinusitis, cutaneous disease, or disseminated infection.

Cutaneous disease may present as either primary or secondary skin lesions. Primary cutaneous aspergillosis is due to direct cutaneous inoculation of the organism. Cutaneous inoculation has been described at peripheral and central venous sites, surgical sites, burn sites, and other traumatic sites. In some cases, infection may be due to contamination of occlusive dressings or bandages. In secondary cutaneous aspergillosis, skin lesions may develop either by direct extension (often on the chest wall in pulmonary aspergillosis) or by hematogenous spread.

Cutaneous aspergillosis usually presents as violaceous papules, nodules, or plaques, which rapidly ulcerate to form a black eschar. Hemorrhagic bullae and pustular lesions have also been described. Lesions may mimic ecthyma gangrenosum. Diagnosis of aspergillosis requires positive tissue culture and histopathological documentation of infection. On histology, *Aspergillus* organisms appear as septate hyphae which branch at 45° angles. Once cutaneous aspergillosis is diagnosed, investigations should be conducted to determine if the infection is primary or secondary.

Treatment of choice for cutaneous aspergillosis is voriconazole. Alternative therapies include: liposomal amphotericin B, posaconazole, itraconazole, caspofungin, or micafungin. Surgical resection may be considered in some situations. Finally, recovery from neutropenia and reduction in glucocorticosteroid dosage may play a critical role in recovery.

Clinicians should have a high level of suspicion for cutaneous aspergillosis in immunocompromised patients with skin lesions, especially those with a central eschar. Early detection of aspergillosis and initiation of antifungal treatment is critical for favorable patient outcomes.

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