Chicago Dermatological Society

May 2013
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, May 15, 2013
Rush University Medical Center

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 "Genodermatoses: Tales of a Labless Investigator" Seth J. Orlow, MD PhD *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 "Isotretinoin Treatment: Facts and Fallacies" Seth J. Orlow, MD PhD
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 12, 2013
Loyola University Medical Center; Maywood
Watch for details on the CDS website: www.ChicagoDerm.org

Guest Speaker

Frederick Malkinson Lecture

Seth J. Orlow, MD PhD

Samuel Weinberg Professor of Pediatric Dermatology; Ronald O. Perelman Chair, Department of Dermatology; New York University Langone Medical Center; New York, NY

Education

MD - 1986; PhD (molecular pharmacology) - 1986, Albert Einstein College of Medicine, Bronx, NY; Internship (pediatrics) - 1986-1987, Mount Sinai Medical Center (Pediatrics), New York, NY; Dermatology Residency - 1987-1989, Yale - New Haven Medical Center, New Haven, CT; Clinical Fellowship (pediatric dermatology) - 1989-1990, Yale - New Haven Medical Center, New Haven, CT; Visiting scientist - 1986, INSERM Clinical Immunology Unit, Hopital Necker-Enfants Malades, Paris, France

Research Interests

Development of novel targeted therapies in melanoma and other cancers; molecular and cellular basis of pigmentation.

Continuing Education Credit

Chicago Dermatological Society

"Chicago Dermatological Society Monthly Conference"

May 15, 2013 *Chicago, IL*

Participants must attend entire session to receive full credit. Please sign-in at the CDS registration table before you leave the conference. A certificate will be sent to you following the meeting. Also, we ask that you complete the evaluation form and return to the CDS registration table. The information collected as part of this process represents an important part of the CME planning process.

The Colorado Foundation of Medical Care (CFMC) will retain a record of attendance on file for six years. CFMC contact information: 303-695-3300, ext. 3372

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 therapeutic options.

SESSION OBJECTIVES

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

1. Describe how to monitor patients undergoing isotretinoin therapy.Explain the spectrum of xanthogranulomatous disease of the skin.
2. Discuss current thinking on a variety of side effectis associated with isotretinoin use.

.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

Dr. Orlow has been a consultant for Hoffman LaRouche. **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.**

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

HISTORY OF PRESENT ILLNESS

The patient is a 9-year-old light-skinned Hispanic female who presented with an enlarging, asymptomatic blue-black papule at her left temporal hairline. The lesion was first noted approximately one year ago. Her mother reported that it was initially a very small dot that had grown radially and in thickness over several months before presentation to dermatology.

PAST MEDICAL HISTORY, MEDICATIONS & ALLERGIES

None relevant

FAMILY HISTORY

Father had a darkly pigmented papule removed from his nose one year before. Grandmother has a darkly pigmented lesion on her neck. No family history of melanoma or skin cancer.

SOCIAL HISTORY

Lives with parents

PHYSICAL EXAM

Left temporal scalp, near hairline: soft, dark blue-black papule measuring 3 mm in diameter and 2 mm height.

HISTOPATHOLOGY

Left temporal scalp, near hairline, shave biopsy: fairly symmetrical dome-shaped papule composed of heavily pigmented spindle and epithelioid melanocytes that stained positively for S100 protein, Melan-A and HMB-45. The base of the wound was black.

Left temporal scalp, near hairline, re-excision: heavily melanized nodule with similar histomorphology of atypical cells, with no evidence of necrosis or mitotic figures.

LABORATORY RESULTS & RADIOLOGY

None

DIAGNOSIS

Pigmented Epithelioid Melanocytoma

TREATMENT AND COURSE

The patient was referred to a surgical oncologist for wide local excision with 5 mm peripheral margins. The margins were clear. However, the tumor extended to within one mm of the deep margin, which extended to the galea. The family prefers to proceed with close observation, with continued surveillance in dermatology every 3 months, rather than having additional surgery that would require partial excision of the skull.

DISCUSSION

Pigmented epithelioid melanocytoma (PEM) is a term introduced by Zembowicz et al. in 2004, which encompasses lesions previously described as “animal-type melanoma” and epithelioid blue nevus. Animal-type melanoma and epithelioid blue nevus are virtually indistinguishable histopathologically. Both lesions are composed of a mixture of epithelioid and spindle-shaped melanocytes with heavy melanin pigmentation. Loss of expression of a Carney complex gene, PRKAR1A, is seen in the majority of PEMs. Animal-type melanoma is a rare melanocytic tumor

with uncertain behavior, deriving its name from its similarity to usually non-lethal melanomas observed in aging gray horses.

PEM seems to show a predilection for children and young adults. No ethnic predominance has been observed, and it has frequently been described in populations considered less susceptible to melanoma, including Hispanic, African-American, and Asian patients.

The original authors considered PEM “a borderline melanocytic tumor.” In their publication of 40 patients presenting with lesions consistent with PEM, 23 (59%) underwent sentinel lymph node (SLN) biopsy, and 11 (46%) of these patients had at least one positive node. Liver metastasis occurred in one case. Clinical follow-up of greater than one year was available in 27 (67%) cases, and no patients had died of the disease. In a long-term follow-up study of 26 patients with PEMs, 8 of 18 patients who underwent SLN biopsies had nodal metastases. Complete lymphadenectomies were performed in all cases with positive SLNs, and five patients received interferon. After a median follow-up of 67 months (range 39 to 216 months), all patients were alive and disease free.

Although the available information on PEM is still limited, the entity is considered to be a low-grade malignancy with limited metastatic potential. Long-term studies to date have shown a favorable prognosis in this patient population. The management of patients with PEM is not clearly defined. Most authors recommend wide local excision, and some advocate SLN biopsy. The predictive value of SLN biopsy for predicting melanoma-specific survival appears to be limited, regardless of tumor thickness.

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

HISTORY OF PRESENT ILLNESS

Patient is a five-year-old, otherwise healthy male, who presented with an eruption of blisters over the left shin and right cheek. Initially, a diagnosis of bullous impetigo was made, and the lesions improved with a ten-day course of cephalexin and mupirocin. Subsequently, the patient developed new blisters in the same locations, which repeatedly improved and recurred. No other blisters or oral lesions had been noted. The patient takes only a daily multivitamin and does not take any other over-the-counter or prescription medications.

PAST MEDICAL HISTORY

None

MEDICATIONS

Multivitamin

ALLERGIES

No known drug allergies

FAMILY HISTORY

Family history of psoriasis in mother
No family history of blistering diseases

SOCIAL HISTORY

Lives with family

PHYSICAL EXAM

Left shin: tense vesicles and bullae in an annular configuration
Right cheek: clustered and crusted papules

HISTOPATHOLOGY

Punch biopsy (H&E), left shin: subepidermal blister with neutrophilic infiltrate and rare eosinophils
Punch biopsy (direct immunofluorescence), left shin: specimen lost in processing by an outside lab

LABORATORY RESULTS

The following were positive or abnormal:
Serum basement membrane zone IgA antibodies

The following were negative or within normal limits:
BP 180 ELISA, BP 230 ELISA

DIAGNOSIS

Localized Linear IgA Bullous Dermatosis

TREATMENT AND COURSE

Treatment options were discussed with the patient's mother. Due to the localized nature of the patient's disease and the mother's preference to avoid systemic agents, topical triamcinolone ointment 0.1% twice daily was started for acute flares. Topical pimecrolimus 1% cream twice

daily was initiated recently to be used during quiescent phases. The patient continues to have localized disease only.

DISCUSSION

Linear IgA bullous dermatosis (LABD) is an autoimmune subepidermal vesiculobullous eruption that occurs in both children and adults. The childhood form is commonly called "chronic bullous disease of childhood." It is caused by the linear deposition of IgA along either the lamina lucida or sublamina densa of the basement membrane. The most likely antigens in LABD are thought to be degradation products of BP180, including a 97kD protein and a 120kD protein. Histology demonstrates subepidermal blistering, a neutrophilic inflammatory infiltrate in the superficial dermis, and papillary microabscesses. The resulting clinical manifestations are diverse, but the classic presentation includes erythema, vesicles, and bullae that occur in an annular distribution, referred to as the "string of pearls" or "crown of jewels." The lesions are usually widespread, with a predilection for the trunk and extremities, but they can also involve the buttocks, face, and oral mucosa. To our knowledge, nine cases of localized LABD have been reported in the literature. The anatomic locations, causes, associations, treatments, and outcomes for these cases are summarized in the table below.

Age / Gender	Locations	Causes & Associations	Treatments	Outcomes
34F	Palms, wrists	Idiopathic	Dapsone 50mg daily x 6 months	Resolved
46F	Right forearm	Monoclonal gammopathy of undetermined significance	Dapsone 100mg daily	Rapid improvement in 1 month and resolution in 11 months
67M	Right waist	Mixed wave-length ultraviolet light for herpes zoster	Niacinamide 1.5 g daily + tetracycline 1.5 g daily + dapsone 100 mg daily + clobetasol propionate cream BID	Complete resolution in 2 weeks and no recurrence
76M	Palms	Supratherapeutic vancomycin in the setting of renal failure	Discontinuation of vancomycin, hemodialysis, and clobetasol	Complete clearance with outpatient hemodialysis
22F	Neck	Resembling contact dermatitis	Clobetasol ointment daily x 1 week	Complete resolution
74M	Perianal, intergluteal fold	Ampicillin/sulbactam	Discontinuation of ampicillin/sulbactam + 0.3% pyoctanin solution	Complete resolution in 3 weeks
64F	Right breast	Idiopathic	Colchicine 0.6mg BID x 5 weeks	Complete resolution in 3 weeks
84F	Palms, wrists and buttocks	Idiopathic	High dose intravenous immunoglobulin 1g/kg over 2 days for 4-6 weeks + dapsone 50mg daily + methylprednisolone 10mg daily	Considerable improvement, but did not resolve
44F	Left upper arm	Quantitative and qualitative platelet abnormalities	Dapsone 300mg weekly	Recurs if dapsone is decreased below 300mg weekly

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Presented by Andrew Nesterovitch, MD, James Ertle, MD, and Michael D. Tharp, MD
Department of Dermatology, RUSH University Medical Center

HISTORY OF PRESENT ILLNESS

The patient is a 4-month-old Hispanic female, who presents with changing skin lesions. Her parents reported no skin lesions at the time of delivery; however they noted blisters on the legs, arms and trunk starting 3-4 weeks after birth. Patient was treated by her pediatrician with Vitamin A+D ointment for 2-3 days, mupirocin ointment BID for 1 month and mometasone cream 0.1% BID for 1-2 weeks without an effect. The blisters resolved at age 3 months, leaving swirled hyperpigmentation on the skin. A work-up by ophthalmology and neurology was unremarkable.

PAST MEDICAL HISTORY

Otherwise unremarkable

MEDICATIONS

None

ALLERGIES

None

FAMILY HISTORY

No known family history of skin disorders.

SOCIAL HISTORY

Lives with parents

PHYSICAL EXAM

Trunk, arms and legs: swirled grey brown pigmentation. No blisters
Right 4th interdigital space: 4 mm round hyperkeratotic papule
Coronal scalp: patchy areas of alopecia

DIAGNOSIS

Incontinentia Pigmenti

TREATMENT AND COURSE

We recommended close follow up with neurology, ophthalmology, dentistry, and dermatology.

DISCUSSION

Incontinentia Pigmenti (IP) is an X-linked dominant disorder caused by a mutation in the NEMO gene. This condition is almost always lethal in males. Rare males may have features of IP thought to be secondary to Klinefelter syndrome or genomic mosaicism. Skin involvement in mosaics is limited.

The presentation of IP consists of the following stages:

- Stage 1 (birth - 2 weeks): linear erythema and vesicles, most often on the extremities, scalp, trunk, and rarely on the face
- Stage 2 (2 - 6 weeks): verrucous linear plaques on the extremities
- Stage 3 (3 - 6 months): swirled hyperpigmentation
- Stage 4 (2^{nd} - 3^{rd} decade): swirled hypopigmentation with possible atrophy

Additional manifestations of incontinentia pigmenti include (from Bolognia et al.):

Surface ectodermal defects
- Missing and conical teeth (60–80% of patients)
- Linear absence of hair (swirled at the vertex in 30–40% of patients) and sweat glands
- Dystrophic nails (ridging, pitting > subungual keratoses; 10–30% of patients)
- Asymmetric breast development or supernumerary nipples

Eye anomalies (20–40% of patients)
- Retinal vascular abnormalities
- Strabismus
- Cataracts
- Microphthalmia
- Optic atrophy

Central nervous system abnormalities (20–30% of patients)
- Seizures
- Developmental delay
- Spastic hemi/di/tetraplegia

Consultation and close follow up with neurology, ophthalmology, and dentistry is recommended.

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CHICAGO DERMATOLOGICAL SOCIETY **CASE 4**

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

Case A

HISTORY OF PRESENT ILLNESS
The patient is a 4-year-old light-skinned Hispanic female who presented at age 3 months for evaluation of a split pigmented nevus over her left eyelid, present since birth. The nevus involves her medial canthus, but does not appear to affect her conjunctiva. She has had surveillance examinations every six months. The nevus has been growing commensurate with growth of the head and has become darker over time. She has been evaluated by ophthalmology and has no obvious visual complications. She is otherwise healthy and meeting developmental milestones.

PAST MEDICAL HISTORY, MEDICATIONS & ALLERGIES
None relevant

FAMILY HISTORY
History of congenital nevus in father's cousin. Patient's one year old brother has congenital nevus on left forearm. No family history of melanoma.

SOCIAL HISTORY
Lives with parents.

PHYSICAL EXAM
Left upper/lower eyelid: 38 mm x 20 mm light brown macule with central dark brown plaque. Decreased eyelash density over left medial portion of eyelids

HISTOPATHOLOGY, LABORATORY RESULTS & RADIOLOGY
No biopsy or diagnostic tests were performed.

DIAGNOSIS
Split Congenital Nevomelanocytic Nevus of the Eyelid

TREATMENT AND COURSE
The patient's family was advised to continue surveillance examinations with dermatology every 6 months and to continue ophthalmology follow-up at least once a year.

Case B
The patient is a 5-year-old Hispanic male who presented at 2 years of age for evaluation of a split pigmented nevus over his left eyelid, involving the medial canthus and sparing the conjunctiva. He returned to clinic for surveillance at 6 and 12 month intervals, at which time growth of the lesion appeared commensurate with growth of the head. He has since been lost to follow-up.

DISCUSSION
Split congenital nevus of the eyelid, also known as "divided nevus," "kissing nevus" and "panda nevus," is a rare congenital neoplasm that occurs on opposing margins of the upper and lower eyelids. Fewer than 150 cases have been reported in the English literature, with most cases categorized as medium-sized intradermal melanocytic nevi. Split congenital nevi may rarely occur on the penis and between fingers.

Precursors of congenital nevomelanocytic nevi likely develop between the ninth and twentieth weeks of gestation. Progenitor melanoblasts can be found in fetal epidermis as early as the 50th day of gestation. The eyelids form as ectodermal folds between the sixth and eighth week of development. By the ninth to tenth week, the two eyelids meet, and the epidermal layer fuses. Melanocytes first appear in the head and neck at approximately 10 weeks gestation. The eyelids begin to separate at the twentieth week and are fully separated between twenty seven to thirty weeks of gestation. It is presumed that abnormal melanoblasts give rise to nevomelanocytic nevi that are apparent at birth, and the split nevus of the eyelids is present before 20 weeks gestation.

Congenital nevi occur in 1% of newborns. The prevalence rate of congenital nevi in siblings of patients with congenital nevi is 12%. In other words, congenital nevi demonstrate familial aggregation. Reports on malignant transformation of congenital nevi vary widely, partially due to variables such as lesion size and length of follow-up. It is generally accepted that people with congenital nevi have an estimated 5% risk of developing melanoma, but such an estimate is based on the congenital nevus as a risk factor. Skin occupied by a small congenital nevus has an observed 10,000-fold increased risk of developing melanoma, compared to the expected risk based on body surface area and chance alone. There was a recent report of malignant transformation of a split congenital nevus of the eyelid in a 57 year old male in the Nepal Journal of Ophthalmology, and a search of the literature revealed two other possible cases of malignant transformation in split congenital nevi of the eyelids.

Other potential complications of split nevi include ptosis due to a heavy nevus burden on the upper eyelid, exophytic growths that may lead to ectropion, disordered ciliary growth causing corneal irritation, and epiphora due to involvement of puncta in the lesion. Nonsurgical treatments for eyelid nevi include dermabrasion, cryotherapy, and laser therapy, but all have high rates of recurrence. Most authors recommend early surgical intervention to prevent any functional problems and avoid potential teasing at school. In a series of 73 cases, the authors recommended that defects involving just the eyelids should be reconstructed with a 1-stage reconstruction with skin flap, musculocutaneous flap and/or skin graft. If the lesion involves the cheek, a 2-stage reconstruction with skin flap and/or musculocutaneous flap is generally required. Specific care must be taken to maintain the integrity of the tarsal plate for eyelid contour and to maintain patency of the puncta for lacrimal function.

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

HISTORY OF PRESENT ILLNESS

A 29-year-old white male with no significant past medical history was referred for the evaluation of intermittent red bumps on his hands. The lesions started 2.5 years prior and were associated with pruritus and a burning sensation. Since the onset of the lesions, the patient was managed by an allergist from an outside facility who was treating the patient with chronic systemic glucocorticoids. The patient's current regimen included prednisone 10 mg daily with higher doses, up to 50 mg daily, for flares. He reported daily treatment with prednisone for at least one year. The patient also had a history of irregular use of fexofenadine and cetirizine during flares.

PAST MEDICAL HISTORY

None relevant

MEDICATIONS

Prednisone 10 mg po daily
Fexofenadine 180 mg po PRN flares
Cetirizine 10 mg po PRN flares

ALLERGIES

No known drug allergies

FAMILY HISTORY

There was no family history of thyroid disease, atopy, angioedema or urticaria.

SOCIAL HISTORY

The patient is a non-smoker and reports social consumption of alcohol.

PHYSICAL EXAM

Bilateral wrists: scattered red non-scaling papules
Lateral trunk: few 1-3 cm wheals

DIAGNOSIS

To be discussed

TREATMENT AND COURSE

To be discussed

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

HISTORY OF PRESENT ILLNESS
A 47-year-old Caucasian male presented to clinic with a 10-12 year history of an enlarging cluster of firm nodules on the left vertex scalp, recently biopsied at an outside institution, which demonstrated dermatofibrosarcoma protuberans. The lesions were tender to palpation, but otherwise asymptomatic. The site had never bled, and he denied any prior trauma to the area. There was no prior personal or family history of any skin cancer or melanoma. The patient denied any fevers, chills, night sweats, unintentional weight loss, abdominal pain, nausea, vomiting, headaches, chest pain, or shortness of breath.

PAST MEDICAL HISTORY
Hypertension

MEDICATIONS
Atenolol

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 or smoking. Patient reported occasional alcohol consumption, rarely on the weekends and in social settings.

PHYSICAL EXAM
On the left vertex scalp, there was a cluster of three subcutaneous skin-colored, firm, non-pulsatile nodules comprising a 2 cm by 3 cm mass. The nodules were fixed to the overlying skin, but freely movable over the deeper structures. There was no palpable cervical lymphadenopathy.

HISTOPATHOLOGY
The original punch biopsy performed at an outside institution was reviewed and found to be consistent with a diagnosis of dermatofibrosarcoma protuberans. The spindle cell proliferation stained positively for CD34 and was negative for actin, desmin, S-100, and Melan A, supporting the diagnosis. Subsequent Mohs debulking demonstrated invasion of the periosteum.

LABORATORY RESULTS
Complete metabolic panel, complete blood count with differential, and a urine analysis were normal.

RADIOLOGY
CT scans of the chest, abdomen, and pelvis were negative.

DIAGNOSIS
Dermatofibrosarcoma Protuberans of the Scalp with Pericranial Involvement

TREATMENT AND COURSE

After review of the patient's initial punch biopsy demonstrating dermatofibrosarcoma protuberans, the patient's case was extensively discussed at tumor board conference, with input from dermatology, oncology, pathology, plastic surgery, and neurosurgery. The consensus was that although there was a high potential for local recurrence, there was no indication for a metastatic workup at the time due to the low-grade nature of the patient's tumor. The patient underwent Mohs surgery. The peripheral margins were clear after the second stage, however the deep margins revealed involvement of the periosteum. We obtained an additional 1 cm margin for permanent sections, which were clear. Due to involvement of the periosteum on Mohs sections, neurosurgery removed multiple sections of the outer table of the skull in the center of the surgical wound. No evidence of malignancy was found in the skull biopsies or granulation tissue. A split thickness skin graft from the left anterior thigh was placed to close the final defect. Over 1 year later, the patient has healed well and is followed every 3 months by dermatology.

DISCUSSION

A rare soft tissue tumor that tends to be locally aggressive, dermatofibrosarcoma protuberans (DFSP) accounts for less than 5% of adult soft tissue sarcomas, and less than 1% of all malignant tumors of the head and neck. The tumor has been described in all age groups, including a number of congenital cases, but is commonly diagnosed between age 30 and 50. The literature suggests a slight male predominance, and multiple reports have indicated that it tends to be more common in blacks than whites. The translocation t(17;22)(q22;a13), which results in fusion of the collagen 1A1 gene with the platelet-derived growth factor B (PDGFB) gene, has been demonstrated in 90% of DFSP tumors and is thought to cause tumor formation.

Clinically, DFSP typically presents as an asymptomatic, slow-growing, skin-colored plaque that eventually becomes nodular. The overlying skin may demonstrate atrophic changes. While the tumor tends to be adherent to overlying skin, it is usually freely mobile over deeper structures. The trunk is the most commonly involved site, seen in approximately 50% of cases, followed by the proximal extremities (20-35%). Involvement of the head and neck is rare, accounting for only 10-15% of cases. Specifically, DFSP of the scalp accounts for less than 5% of all cases. The differential diagnosis of DFSP is broad and includes neurofibroma, leiomyoma, epidermal cyst, melanoma, morpheaform basal cell carcinoma, keloid, desmoid tumor, Kaposi's sarcoma, fibrosarcoma, dermatofibroma, nodular fasciitis, and sarcoidosis. The slow-growing nature of these tumors, combined with clinical misdiagnosis of early lesions often results in delayed definitive diagnosis.

Diagnosis is based on histologic analysis, often from an incisional biopsy. On histology, DFSP demonstrates a storiform or cartwheel proliferation of dermal spindle cells that extends into the subcutaneous fat via tentacle-like projections, resulting in a honeycomb appearance. The mitotic index is low, with little pleomorphism. Immunohistochemical stains can help differentiate DFSP from other benign spindle cell neoplasms. Specifically, CD34 is strongly expressed in DFSP, with a sensitivity of 84-100%, whereas factor XIIIa and Stromolysin-3 are positive in benign dermatofibromas.

In patients with the diagnosis of DFSP, history, review of systems, and physical examination largely determine the extent of work-up required. Although locally aggressive, DFSP rarely metastasizes, with estimated rates between 0.5% and 5%. The lungs are the most common site of metastasis, with an estimated rate of around 1% of cases. Lymphatic spread is rare, thus physical examination with special attention to the regional lymph node basin is often sufficient to evaluate for lymphatic metastases. In cases of long-standing tumors or extensive locally invasive disease, a chest radiograph or CT scan should be considered.

The mainstay of treatment is complete surgical eradication, with most authors advocating 3-5 cm margins. Of note, head and neck tumors demonstrate higher rates of recurrence (50-75%) compared to those on the trunk (10-60%), primarily because it can be difficult to achieve wide margins in these locations. Because of this, Mohs micrographic surgery is the preferred method of treatment for head and neck DFSP. Mohs provides more complete surgical clearance, allows for the most preservation of normal tissue, and has demonstrated lower recurrence rates (1%). It is important to remember that due to the locally invasive nature of DFSP scalp tumors, bony erosion and even invasion into the brain may occur, thus the periosteum should be removed and analyzed. In our case, there was involvement of the periosteum, leading to removal of the outer table of the skull to avoid tumor recurrence. For cases of locally advanced or metastatic DFSP that are not amenable to surgical resection, the PDGF receptor inhibitor, imatinib, has emerged as a potential therapeutic option.

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Presented by Blake Troiani, MD, and Sheetal Mehta, MD
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HISTORY OF PRESENT ILLNESS

A 79-year-old white female with past medical history significant for rheumatoid arthritis and hypertension presented for Mohs micrographic surgery consultation with a recurrent basal cell carcinoma of the right lower eyelid, which had been biopsied 1 month ago due to spontaneous bleeding and pruritus. The primary basal cell carcinoma was excised eight years ago, followed by four subsequent re-excisions for recurrences. After the most recent recurrence, the patient was evaluated by otolaryngology for possible right globe exenteration, which was considered the patient's only option for surgical treatment. However, given the patient's near-total loss of vision in the non-affected left eye, exenteration was determined not to be in the best interest of the patient. Given the clinical extent of the disease, the patient was deemed an inappropriate candidate for Mohs. The patient was presented at a multidisciplinary tumor conference and treatment with vismodegib 150 mg po daily was recommended.

PAST MEDICAL HISTORY

Rheumatoid arthritis
Hypertension
Anemia

MEDICATIONS

Methotrexate
Folic acid
Prednisone
Lisinopril
Vitamin D/Calcium
Multivitamin

ALLERGIES

Penicillin
Sulfa
Morphine
Nitrofurantoin

FAMILY HISTORY

No family history of skin cancer, melanoma, or other malignancies.

SOCIAL HISTORY

Patient denied alcohol and illicit drug use. Patient smoked a half pack of cigarettes per day for approximately 10 years; last use approximately 50 years ago.

PHYSICAL EXAM

The tumor involved 3/4 of the lower eyelid margin with extension onto the infraorbital cheek, right lateral canthus, and upper eyelid. An 8 mm pink papule was noted on the lower medial conjunctival margin.

HISTOPATHOLOGY

12/21/2011: Right lower eyelid, superficial basal cell carcinoma

2/3/2012: A) Bulbar conjunctiva next to canthus, basal cell carcinoma involving margins
B) Inferior fornix bulbar conjunctiva, basal cell carcinoma involving margins
C) Bulbar conjunctiva medial to A, basal cell carcinoma involving margins

11/12/2012: A) Right inferior fornix, negative for basal cell carcinoma
B) Right conjunctiva canthal angle, negative for malignancy

1/23/2013: A) Right lateral eyelid, negative for malignancy
B) Right medial eyelid, negative for malignancy
C) Right mid eyelid, negative for malignancy

LABORATORY RESULTS

The following were positive or abnormal:
Creatinine 1.2, Hemoglobin 9.3

The following were negative or within normal limits:
WBC, Platelets, Hepatic Function Tests

RADIOLOGY

MRI (2/1/2012) demonstrated unremarkable orbits without visualized evidence of basal cell carcinoma.

DIAGNOSIS

Recurrent Basal Cell Carcinoma Involving the Bulbar Conjunctiva

TREATMENT AND COURSE

The patient tolerated the initiation of vismodegib well, noting only mild muscle cramps of the bilateral legs that did not require pharmacologic intervention at her initial follow up with oncology one month later. Coordination with the patient's ophthalmologist led to a planned treatment course of nine to twelve months. After a total of 5 months on treatment, the patient noted decrease in size of visible involvement of the skin and a significant reduction in associated local symptoms of irritation and pruritus. However, the bilateral leg muscle cramps continued, leading to the initiation of gabapentin. After 7 months of therapy, the patient began to note decreased appetite. After 11 months of therapy, the patient discontinued vismodegib secondary to loss of appetite and significant weight loss. At that time, there was no clinical evidence for tumor in the distribution of previously affected skin. Scout biopsies of the right lower eyelid performed were negative for malignancy. After discontinuation of vismodegib, the patient experienced resolution of muscle cramps, and her appetite returned to normal. Two months post-discontinuation of the vismodegib, the patient continues to do well without clinical evidence of basal cell carcinoma recurrence. The 8 mm papule on the mid lower eyelid remained stable throughout the patient's course and is thought to represent scar tissue from previous procedures. The patient will be closely monitored and vesmodegib will be considered if recurrence occurs.

Cutaneous basal cell carcinoma (BCC) accounts for approximately 25% of cancers diagnosed in the United States, making it the most common malignancy among individuals of European descent. Moreover, the incidence of BCC continues to rise. Cumulative damage to DNA caused by exposure to UV radiation has long been implicated in its pathogenesis. Multiple treatment modalities are available and may be chosen based on lesion location, size, and histologic features. Such options include surgical excision, Mohs micrographic surgery,

cryosurgery, electrodessication and cautery, and topical therapies, such as imiquimod, 5-fluorouracil, and photodynamic therapy with aminolevulinic acid. When chosen appropriately, treatments of BCC have demonstrated high success rates.

In rare cases, standard treatment modalities have little chance of achieving acceptable cure rates secondary to advanced local growth (depth, size, or extent) or metastasis. Patients with the rare genetic disorder basal cell nevus syndrome (also known as Gorlin syndrome) develop multiple, in some cases hundreds, of BCCs in addition to medulloblastomas, making treatment of individual lesions by conventional methods clinically impractical. Although rare, with a reported median survival of 8 months, metastatic BCC represents a challenging clinical entity to treat. While traditionally there has been no standard accepted treatment for locally advanced or metastatic disease, promising results in the blockade of the sonic hedgehog (SHH) pathway have provided evidence to suggest its utility as an effective treatment modality.

Study of hedgehog genes, first discovered in the 1970s, has revealed much about the normal development of embryonic cells. Research has demonstrated the importance of SHH pathways in the development and maintenance of multiple structures, including the skin, hair, and stem cells. In normal adult tissue, SHH pathways lay dormant except in the case of limited activity in hair growth, spermatogenesis and tissue repair. Intact SHH pathways begin with the binding of SHH to patched-1 (PTCH1), a 12-transmembrane receptor, which prevents PTCH1-mediated inhibition of signaling through smoothened (SMO), a seven-transmembrane protein. Removal of inhibition of SMO allows for the downstream activation of glioma-associated oncogene family zinc finger (GLI), a transcription factor, which then moves to the nucleus where transcription of genes responsible for cell growth is activated.

Aberrant activation of the SHH pathway has been implicated in several malignancies, such as colon, pancreas, prostate, and BCC. First implicated in the pathogenesis of basal cell nevus syndrome, mutations in the SHH pathway have also been shown in sporadic BCCs, resulting in unchecked basal cell proliferation in the skin. Many BCCs demonstrate an activating mutation of PTCH1, leading to continued activation of SMO and, subsequently, downstream regulators of transcription. Alternatively, mutations causing constitutive activation of SMO have also been described.

In January 2012, the FDA approved vismodegib, an inhibitor of SMO, for the treatment of locally advanced and metastatic BCC. The FDA's decision for this approval was based primarily on a multicenter open-label trial of 96 patients with locally advanced BCC (laBCC) or metastatic BCC (mBCC). The overall response rate for mBCC was 30.3% (95% CI 15.6, 48.2) with all mBCC responses representing partial responses. In the case of laBCC, the overall response rate was 42.9% (95% CI 30.5, 56.0). Of these, 13 (20.6%) were complete responses and 14 (22.2%) were partial responses. The median progression-free survival for both groups was 9.5 months, and the median duration of response was 7.6 months. The median duration of drug exposure was 10 months in both groups, and the most common reasons for discontinuation of vismodegib were disease progression in the mBCC group (18%) and patient preference in the laBCC group (25%).

At least one adverse event was experienced by every participant. The most commonly encountered adverse events were muscle spasms (68%), alopecia (63%), dysgeusia (51%), weight loss (46%), and fatigue (36%). The majority of these cases represented grade 1 or 2 reactions. Seven fatalities were reported during this study, 1 in the mBCC group and 6 in the laBCC group. In these cases, patients had clinically significant risk factors or coexisting conditions at baseline, and no relationship to vismodegib could be established. Phase III trials are currently in progress, and combination of vismodegib with other chemotherapeutic agents is being investigated. Recently, case reports of new onset keratoacanthomas after the onset of vismodegib in patients without history of squamous cell neoplasm have been reported.

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Presented by Mark Romanelli, MD, and Michael D. Tharp, MD
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Unknown

Presented by Conor Dolehide, MD and Arthur R. Rhodes, MD
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HISTORY OF PRESENT ILLNESS

The patient is a 38-year-old African American female who presented with bilateral inguinal, vulvar, and perianal bumps for three years. Before this presentation, she had similar lesions seven years ago, which resolved with an unknown topical treatment. The lesions are associated with continual pruritus. She denies shaving or using hair removal products. She does not have a personal history of genital warts. Her mother and two of mother's brothers are said to have Hailey-Hailey disease.

PAST MEDICAL HISTORY

No other significant past medical history.

MEDICATIONS

No medications prior to presentation.

ALLERGIES

No known drug allergies.

FAMILY HISTORY

Family history of Hailey-Hailey disease in mother and two of mother's brothers.

SOCIAL HISTORY

Lives with family. No history of sexually transmitted diseases.

PHYSICAL EXAM

Bilateral medial upper thighs and vulva: dozens of scattered 2-3 mm skin-colored and hyperpigmented flat-topped papules with a surrounding rim of hyperpigmentation.
Perianal: dozens of 3mm hypopigmented flat-topped papules
Axillae: Clear
Chest: Clear

HISTOPATHOLOGY

Left groin, saucerization biopsy (12/12/2006): acantholysis of the epidermal keratinocytic cells present in the lower two-thirds of the epidermis and suprabasil clefting. Overlying the acantholytic area is a compact stratum corneum with trapped dyskeratotic cells.

Right and left groin, punch biopsies (2/7/2013): hyperkeratosis, suprabasal clefting, extensive acantholysis, and dyskeratosis with the formation of corps ronds and grains.

DIAGNOSIS

Papular Acantholytic Dyskeratosis

TREATMENT AND COURSE

The patient began treatment with hydrocortisone 2.5 % ointment daily and tretinoin 0.025% cream nightly. She continued treatment for two months without improvement.

DISCUSSION

Papular acantholytic dyskeratois (PAD) belongs to the spectrum of focal acantholytic dyskeratoses. Focal acantholytic dyskeratosis was first described by Ackerman in 1972 to refer

to the histological findings including focal acantholysis, suprabasal clefts, hyperkeratois, parakeratosis, and dyskeratosis with corps ronds and grains. At that time, the differential diagnosis for focal acantholytic dyskeratosis included Haily-Hailey disease (HHD), Darier's disease, Grover's disease, warty dyskeratoma, and acantholytic acanthoma. In 1984, Chorselski reported the first case of a genital variant of focal acantholytic dyskeratosis and named the disease "PAD of the vulva." There are fifteen cases of PAD reported in the literature.

PAD usually involves women, but has also been reported in a male patient. It is characterized by skin colored to white keratotic papules in the genital and/or perianal area. Patients may be asymptomatic or exhibit intense pruritus. It is not known if this is a variant of another disease or a unique clinical entity. There is one case report of a familial inheritance of PAD in a mother and her daughter. This case was remarkable for a novel mutation in ATP2C1, which encodes the Golgi hSPCA1 pump, which is also defective in HHD. This suggests a possible link between HHD and PAD. However, unlike HHD, PAD has never been reported to cause erosions, crusts, or involve the axillary, inframammary, or cervical folds.

PAD should be distinguished from the other focal acantholytic dyskeratoses. There is less acantholysis in PAD when compared to HHD. PAD has less hyperkeratosis than Darier's disease. Darier's disease has been reported to involve the genitocrural region, but these may actually represent PAD. A warty dyskeratoma usually presents as a solitary papule or nodule. Histologically, warty dyskeratomas appear as cup-shaped invaginations with more prominent villi, clefting, and corps ronds than PAD. Grover's disease usually occurs on the trunk, neck, and proximal limbs, and has never been reported to arise in the genital area.

Several treatments have been reported with varying success. These include tacrolimus 0.1% ointment, topical and systemic steroids, topical and oral retinoids, and ablation with cryotherapy, electrocautery, or excision.

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Presented by Jill C. Anderson, MD, and Jessie Cheung, MD
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HISTORY OF PRESENT ILLNESS

A 36-year-old male with history of natural killer cell lymphoma presented to Rush with altered mental status and fevers. Upon admission, he was started on broad-spectrum antibiotics (vancomycin, cefepime, levofloxacin, fluconazole, and acyclovir) and intravenous fluids. He became increasingly confused, tachycardic, and hypotensive. He was transferred to the MICU for further management of septic shock. He developed diffuse alveolar hemorrhage and was intubated. Due to his history of adrenal insufficiency and chronic corticosteroid use, stress dose corticosteroids were initiated. Infectious Disease was consulted. Amphotericin B, oseltamivir, sulfamethoxazole-trimethoprim, and doripenem were added for coverage of possible aspergillosis, influenza, pneumocystis pneumonia, and hospital-acquired pneumonia, respectively. Cefepime was discontinued.

Dermatology was consulted on the third day of admission for a new onset eruption primarily over the abdomen and upper extremities. The family denied any sick contacts, pets in the home, or recent travel. The family reported that the patient complained of mild cough, fatigue, and decreased appetite prior to admission.

PAST MEDICAL HISTORY

Natural killer cell lymphoma [diagnosed in June 2012, s/p chemotherapy (8 cycles of EPOCH, most recent chemotherapy in 12/2012)]
Hemophagocytic lymphohistiocytosis
Epstein-Barr viremia
Cytomegalovirus viremia
Positive galactomannan antigen
Adrenal insufficiency
Zinc deficiency

MEDICATIONS

Amphotericin B
Doripenem
Fentanyl
Insulin
Levofloxacin
Methylprednisolone
Midazolam
Norepinephrine
Oseltamivir
Sulfamethoxazole-trimethoprim
Vancomycin

ALLERGIES

No known drug allergies

FAMILY HISTORY

Non-contributory

SOCIAL HISTORY

No tobacco or illicit drug use. Former alcohol use (last drink 2 years ago). Born in Mexico, but has lived in the United States for 20 years. Last trip to Mexico was at least 10 years ago.

PHYSICAL EXAM

Initial examination on the third day of hospitalization revealed numerous petechiae (too numerous to count) over abdomen and scattered petechiae over the bilateral upper extremities. Palms and soles were notable for erythema.

Subsequent examination on the fourth day of hospitalization revealed “thumbprint” purpura over the abdomen and slightly increased petechiae over the bilateral upper extremities.

HISTOPATHOLOGY

Punch biopsy, abdomen: *Strongyloides* organisms identified within the dermis.

LABORATORY RESULTS

The following were positive or abnormal:

Sodium	132	(normal 137 – 147)
Chloride	109	(normal 99 – 108)
Bicarbonate	15	(normal 22 – 29)
Creatinine	0.52	(normal 0.75 – 1.20)
Glucose	215	(normal 60 – 99)
Total Protein	3.2	(normal 6.0 – 8.2)
Albumin	1.7	(normal 3.5 – 5.0)
Calcium	7.0	(normal 8.7 – 10.7)
Total Bilirubin	1.6	(normal 0.2 – 1.3)
Direct Bilirubin	1.20	(normal 0.00 – 0.35)
Alkaline Phosphatase	163	(normal 30 – 125)
AST	124	(normal 3 – 44)
ALT	152	(normal 0 – 40)
Lactate Dehydrogenase	568	(normal 110 – 240)
GGT	323	(normal 12 – 64)
Uric Acid	2.2	(normal 3.5 – 7.7)
Magnesium	1.5	(normal 1.6 – 2.7)
Fibrinogen	138	(normal 190 – 395)
Hemoglobin	6.8	(normal 13.5 – 17.5)
Platelet Count	75	(normal 150 – 399)
Neutrophil %	87.3	(normal 46.0 – 78.0)
Immature Granule %	1.9	(normal 0.0 – 1.5)
Lymphocyte %	4.8	(normal 18.0 – 52.0)
CMV DNA Quantification	1367	(normal <300)
EBV DNA Quantification	32,922	(normal < 250)
Galactomannan Antigen	1.39	(normal <0.5)

Peripheral and Catheter Blood Cultures positive for *Staphylococcus Epidermis*
Bronchoalveolar lavage demonstrated presence of *Strongyloides*

The following were negative or within normal limits:
Potassium, Phosphorus, BUN, PT, INR, PTT, White Blood Count, MCV, Monocyte %, Eosinophil %, Basophil %, Cryptococcal Antigen, Hepatitis A Antibody, Hepatitis B Surface Antibody, Hepatitis B Surface Antigen, Hepatitis B Core Antibody, Hepatitis C Antibody, HIV

RADIOLOGY

Chest X-Ray: Diffuse bilateral parenchymal ground-glass opacities in both lungs. Rounded focus of consolidation in retrocardiac region
CT Brain: No acute intracranial abnormality

DIAGNOSIS

Strongyloides Hyperinfection Syndrome

TREATMENT AND COURSE

Upon punch biopsy results significant for *Strongyloides* infection, the patient was started on ivermectin, and systemic steroids were discontinued. Patient continued to have fevers despite

treatment with ivermectin. Amikacin was added for concern for gram negative meningitis. A lumbar puncture was not attempted due to hemodynamic instability. The patient's condition continued to deteriorate with massive hemoptysis, worsening shock, increasing oxygen requirements on mechanical ventilator, and development of disseminated intravascular coagulation (DIC). Despite continued supportive care, the patient expired on the fifth day of admission.

DISCUSSION

Strongyloides stercoralis is an intestinal nematode that affects millions of individuals and is endemic in tropical and subtropic regions, but is also found in the southeastern United States. Humans act as the definitive host, in which *Strongyloides* has the unusual ability to autoinfect. Infected individuals may subsequently develop latent infection that persists for many years without symptoms.

Clinical presentation of *Strongyloides* is variable, depending on the acuity of the infection and the host's immune system. Acute infection is characterized by gastrointestinal and pulmonary symptoms, such as diarrhea, constipation, abdominal pain, and dry cough. A pneumonitis that resembles Loeffler syndrome may develop. Dermatologic manifestations may occur locally at the site of skin penetration (often the feet, but may occur on any site that is in contact with infected soil) and present as pruritic papulovesicles, commonly referred to as ground itch.

Chronic infections are often asymptomatic, but may present with gastrointestinal or cutaneous symptoms. Frequently, patients will report epigastric pain, episodic diarrhea and constipation, and heartburn. Other less common presentations include fecal occult blood or massive gastrointestinal hemorrhage. Dermatologic manifestations include larva currens, which presents with a recurrent, pruritic serpiginous eruption that progresses quickly (up to 10 cm/hour) and is often overlying the buttocks, perineum, and thighs. Larva currens is due to repeated auto-infection. Chronic *Strongyloides* may also present as chronic urticaria. Three-fourths of patients may have a mild peripheral eosinophilia or elevated IgE levels. Rarely, chronic infections may present with arthritis, cardiac arrhythmias, nephrotic syndrome, and asthma.

A severe manifestation of *Strongyloides* infection is hyperinfection syndrome, which usually presents in immunocompromised patients. Hyperinfection syndrome can present in patients with HIV or HTLV-1 infections, severe malnutrition, hematologic malignancies, and organ transplantation. Corticosteroids and anti-TNF receptor therapy have also been reported to precipitate disseminated strongyloidiasis. Manifestations of *Strongyloides* hyperinfection syndrome include: fever, nausea, vomiting, diarrhea, anorexia, abdominal pain, dyspnea, wheezing, hemoptysis, and cough. Translocation of gut bacteria into the blood stream may lead to gram negative bacteremia and meningitis. Patients may develop shock, DIC, diffuse alveolar hemorrhage, and renal failure, leading to death.

A clue to the diagnosis of hyperinfection syndrome is the pathognomonic thumbprint periumbilical purpura. This sign is associated with intubation and positive pressure ventilation, which are thought to cause retrograde migration of larvae into the periumbilical portosystemic anastomoses. The larvae then are able to cross the endothelium in the dermal vascular plexus, leading to red blood cell extravasation and the characteristic purpura. The distribution of lesions is reminiscent of the caput medusa seen in patients with portal hypertension.

The diagnosis of strongyloidiasis may be difficult, especially in chronic cases. Diagnostic techniques include: stool tests (serial stool examination, the Baermann method, and the agar culture method); enzyme-linked immunosorbent assay (ELISA), which may cross react with other infections; serum indirect fluorescent antibody test (IFAT); polymerase chain reaction (PCR); endoscopy; aspiration of duodenojejunal fluid; and the string test. Hyperinfection

syndrome may be confirmed with skin biopsy or examination of nasogastric aspirates and bronchopulmonary lavage specimens.

The treatment of choice for strongyloidiasis is ivermectin. Albendazole may be used as an alternative. For patients with hyperinfection syndrome, immunosuppressive therapy should be reduced or stopped and antimicrobials against enteric pathogens should be given.

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HISTORY OF PRESENT ILLNESS

A 56-year-old female previously presented at CDS in 2001 with unilateral sclerotic-type chronic graft-versus-host disease (cGVHD) after a matched related donor allogeneic stem cell transplant (SCT) in February 1999 subsequent to multiple myeloma. At her previous visit in 2001, she was offered treatment with psoralen plus ultraviolet A light therapy (PUVA) as well as extracorporeal photophoresis, but declined. She did not return and was lost to follow up until recently, when she presented with lesions on the right buttock x 1 year. They were tender and intermittently extruded white material. Mometasone cream was applied without improvement.

PAST MEDICAL HISTORY

Multiple myeloma in remission s/p SCT
Sclerotic-type chronic graft-versus-host disease (cGVHD)
Avascular necrosis of the right hip (steroid related)
Osteoporosis (steroid related)
Restrictive lung disease
Diabetes (steroid related)

MEDICATIONS

Mycophenolate mofetil
Penicillin V potassium
Calcium carbonate-vitamin D
Budesonide/formoterol inhaler
Acyclovir
Metformin
SMX-TMP
Sertraline

ALLERGIES

No Known Drug Allergies

FAMILY HISTORY

No family history of kidney disease or parathyroid disease

SOCIAL HISTORY

Married; lives with husband.
Denies alcohol, tobacco, or recreational drugs

PHYSICAL EXAM

Right lower extremity, upper extremity, and trunk: hyperpigmented slightly firm plaques
Right buttock: less than 10 white hard papules 2-5 cm
Right lower extremity: diffuse atrophy

HISTOPATHOLOGY

4 mm punch biopsy of right buttock nodule: intraepidermal calcium nodules with surrounding multinucleate giant cells.

LABORATORY RESULTS

The following were negative or within normal limits:
CBC with differential, Magnesium, Phosphorus, Calcium

RADIOLOGY

None

DIAGNOSIS
Unilateral Sclerotic-Type GVHD with Calcinosis Cutis

TREATMENT AND COURSE
Excision of the larger calcinosis cutis lesions was discussed with the patient. She has not yet followed up.

DISCUSSION
Chronic GVHD occurs in the majority of post hematopoietic stem cell transplant (HSCT) patients. The most commonly affected organs are mucocutaneous (90%) and less frequently gastrointestinal, pulmonary, and lymphoid tissues. Sclerotic-type GVHD describes a group of skin changes that can resemble lichen sclerosus, morphea, panniculitis, or eosinophilic fasciitis. The frequency of this type of cGVHD reported in one large cross sectional study by Martires et al was approximately 53% and significantly associated with reduced intensity total body radiation. Occurring at a mean onset of over 1 year after transplantation, dermal inflammation and subsequent fibrosis can result in significant functional disability.

There are several reports of segmental GVHD. Some occur in dermatomal distributions while others are Blaschkoid or unilateral with variable body area involvement. Several of these report lesions that occur on the same side, but not always in the same site as previous varicella zoster reactivation (shingles). The proposed etiologies of these incomplete forms of cGVHD include viral triggering of a previously innocuous self-antigen, or a postzygotic clone of keratinocytes that creates a mosaic pattern of skin antigens to which the patient generated tolerance during fetal development, but became antigenic after HSCT.

Calcinosis cutis, the subcutaneous deposition of insoluble calcium salts, has multiple subtypes: metastatic calicification, dystrophic calcification, iatrogenic calcification, idiopathic calcification, and calciphylaxis. Our patient most likely developed her condition via dystrophic calcification given their restriction to areas of skin inflammation and normal calcium and phosphorous levels. Usually the depositions are localized and encountered in connective tissue diseases, especially CREST syndrome (Calcinosis, Reynaud syndrome, Esophageal dysmotility, Sclerodactyly, and Telangiectasias) and less commonly dermatomyositis and systemic lupus erythematosus. Rarely, the deposition is widespread (calcinosis cutis universalis), and this form is most frequently described in juvenile dermatomyositis. The lesions are tender and may ulcerate, increasing the possibility of infection. There exists one report of calcinosis cutis universalis arising in sclerotic type cGVHD. There are no reports of calcinosis cutis developing within unilateral GVHD.

Treatment of calcinosis cutis is supported by case reports and case series; no randomized placebo controlled trial exists. Medical therapies reported to be effective include calcium channel blockers, colchicine, minocycline, ceftriaxone, probenecid, bisphosphonates, warfarin, intravenous immunoglobulin, and sodium thiosulfate. Procedural treatments attempted have included excision, extracorporeal shock wave lithotripsy, carbon dioxide and Erbium: YAG lasers, and intralesional corticosteroid injections.

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Presented by Andrew Nesterovitch, MD, and Arthur R. Rhodes, MD, MPH
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HISTORY OF PRESENT ILLNESS

A 64-year-old white male attorney presented in December 2012 with asymptomatic skin lesions on the right chest present for 10-15 years, without changes in size or color. There had been no treatment.

PAST MEDICAL HISTORY

End stage renal disease, s/p kidney transplant in 2005 (on immunosuppressive therapy)
Acute myeloblastic leukemia, s/p chemotherapy in 1987
Hepatitis C
Tubular adenoma of colon
Multiple nonmelanoma skin cancers:
- Squamous cell carcinoma in-situ, right eyebrow
- Squamous cell carcinoma, invasive, left mastoid
- Basal cell carcinoma, fibrosing infiltrative, left elbow
- Basal cell carcinoma, left cheek

MEDICATIONS

tacrolimus
mycophenolate mofitil
lisinopril
rosuvastatin
metoprolol
amlodipine
allopurinol
glipizide
pioglitazone
famotidine
tramadol
hydrocodone-acetaminophen
vitamin D2

ALLERGIES

Penicillin and amoxicillin

FAMILY HISTORY

No family history of melanoma
Family history of multiple basal cell carcinomas (brother)
Family history of colon cancer

SOCIAL HISTORY

Married. 20-year history of smoking, quit in 2005

PHYSICAL EXAMINATION

Right breast superior: 6 mm x 6 mm (raised 2 mm) red multilobular plaque
Right breast lateral: 12 mm x 10 mm (raised 1 mm) multilobular heart shaped plaque
Right upper chest: 4 mm x 4 mm (raised 2 mm) red papule with central erosion/crust

HISTOPATHOLOGY

Right breast superior, incisional saucerization: The epidermis is variable in thickness but shows sudden transition to uniformly sized small basaloid cells within which are occasional well-defined ducts. Consistent with eccrine poroma.
Right breast lateral, incisional saucerization: same as above
Right upper chest, incisional saucerization: same as above

DIAGNOSIS
Multiple Eccrine Poromas

TREATMENT AND COURSE
Excisions are planned for all lesions.

DISCUSSION
The term “poroma” refers to a group of benign adnexal neoplasms with “poroid” or tubular (usually distal ductal) differentiation. Like syringoma, poroma has been interpreted historically as a neoplasm of eccrine lineage. More recently, it has been suggested that poromas can be a proliferation of either eccrine or apocrine lineage. The difficulty in differentiating both lineages of poromas occurs because the sweat ducts of the two are histologically and immunohistochemically identical. The term acrospiroma is used by some authorities as a synonym for poroma and is used by others as a broad designation that includes both poroma and hidradenoma.

First reported by Pinkus et al in 1956, the eccrine poroma (EP) is believed to comprise 10% of all sweat gland tumors. Sweat gland tumors represent 1% of all primary cutaneous tumors. The pathogenesis of EP is unknown, although it has been associated with possible precipitating factors of scarring, trauma, and radiation. There is no predilection according to race or sex. EP tends to be diagnosed in patients aged 40-70 years. The most common location is on the foot (47%), but reports are not always clear if plantar or dorsal surfaces are involved. Cases have also been described on the head, trunk, and upper limbs.

Multiple EP have been associated with radiation and polychemotherapy. The clinical diagnosis of EP is often difficult because lesions exhibit a polymorphic gross appearance and may mimic capillary hemangioma, nevus sebaceous, intradermal nevus, acrochordon, pyogenic granuloma, wart, cyst, amelanotic melanoma, squamous cell carcinoma, pyogenic granuloma-like Kaposi sarcoma, and porocarcinoma. Although usually presenting as skin-colored papules, plaques, or nodules less than 2 cm in diameter, pigmented EP (from melanin) and erythematous lesions (from dilation or proliferation of blood vessels) have been reported. Surface erosion or ulceration, presumably secondary to trauma, are occasionally reported.

It has been suggested that a significant proportion of cases of eccrine porocarcinoma (EPC) arise from a preexisting EP. In a study of 69 cases of EPC, only 18% had residual foci of EP, but the proportion may be even higher due to posible destruction of the potential precursor lesion (EP). The most common location of EPC is the lower extremity in 44% (thigh 20%, foot 10%), trunk in 24%, and head in 18%. In one clinicopathologic study of 35 EPC, tumors showed predilection for the trunk or head and neck, in contrast to EP which showed predilection for palms and soles.

Given the possible risk of malignant transformation of EP, modest excisions of all remaining lesions are planned.

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Presented by Jessica Hsu, MD, and Brian Bonish, MD, PhD
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HISTORY OF PRESENT ILLNESS

A 21-year-old male with no significant past medical history, transferred from an outside hospital to Rush University Medical Center, presented for further evaluation of a 3 day history of fevers, polyarthralgias and rash. Patient had a cough and sore throat 1 week earlier, followed by eruption of an asymptomatic rash over the legs, forearms, plantar feet and dorsal hands. He also developed diarrhea, in addition to arthralgias of the bilateral wrists, knees, and ankles. He denied any sick contacts, recent travel, tick bites, or outdoor exposures. Patient was sexually active with males and females. One month prior, he had dysuria which resolved after treatment with azithromycin. He reported a recent STD work-up 3 weeks ago, which was negative. Patient denied any new medications prior to this. He went to an outside hospital for evaluation of these symptoms, and was treated with antibiotics (ceftriaxone, azithromycin, and doxycycline) for possible meningitis with mild improvement in symptoms before being transferred to Rush. Patient denied any weight loss, photophobia, headaches, neck stiffness, dysuria, hematochezia, chest pain, shortness of breath, or abdominal pain.

PAST MEDICAL HISTORY

There was no significant past medical history.

MEDICATIONS

Tramadol
Acetaminophen

ALLERGIES

There were no known drug allergies.

FAMILY HISTORY

The patient's family history was significant for hypertension in his mother and hyperthyroidism and fibromyalgia in his father.

SOCIAL HISTORY

Patient denied smoking or illicit drug use. He reported rare alcohol consumption only in social settings.

PHYSICAL EXAM

At the time of initial exam, there were several purpuric macules and minimally raised papules, some with dusky centers, scattered over the bilateral plantar feet and legs, more so than on the dorsal hands and forearms. No lesions were seen on the oral mucosa or conjunctiva. Patient had bilateral wrist effusions with swelling of the MCP, PIP, and DIP joints, in addition to bilateral knee effusions with diminished range of motion. There was no warmth or erythema over any of the joints.

The following day, the patient developed a few pustular lesions, including one overlying the PIP joint of the right fourth toe.

HISTOPATHOLOGY

None

LABORATORY RESULTS

Complete blood count with differential demonstrated a leukocytosis of 12.33 with an elevated proportion of monocytes. Patient's CRP and ESR were elevated at 159.8 and 71, respectively.

Negative or normal studies included complete metabolic panel, coagulation studies, ANA screen, complement levels, HIV, RPR, MHA-TP, Urine analysis, Hep B, Hep C, HLA B27, rheumatoid factor, Lyme antibody.

Left knee synovial fluid analysis was consistent with infection, demonstrating elevated WBC count of 66,364 with 92% polymorphonuclear cells, 3+ turbidity, and intracellular and extracellular bacteria. There were no crystals. Synovial fluid culture demonstrated few intracellular gram negative cocci in pairs. Peripheral blood cultures were negative. Rectal and pharyngeal Neisseria gonorrhea cultures were negative. Urine PCR for chlamydia and gonorrhea was negative.

RADIOLOGY

CT of the chest was normal.

DIAGNOSIS

Disseminated Gonococcal Infection

TREATMENT AND COURSE

The patient was evaluated by rheumatology, who performed arthocentesis of the left knee, confirming the diagnosis of disseminated gonococcus. The patient was started on IV ceftriaxone and received one dose of azithromycin 1g for empiric Chlamydia treatment. He improved with appropriate antibiotic therapy and was discharged with a PICC line to receive a total of 4 weeks of IV ceftriaxone 2 grams daily per infectious disease.

DISCUSSION

Disseminated gonococcal infection (DGI) is reported to develop in 1-3% of the 600,000 Americans infected with *N. gonorrhoeae* each year. It may develop in sexually active persons of any age, but is four times more common in women than men in the United States, and many of the men that are affected are homosexual or bisexual. DGI results from bacteremic dissemination of *N. gonorrhoeae* and usually develops within 2-3 weeks of the primary infection. The bacteria are transmitted by sexual or perinatal contact with the mucous membranes of the urethra, cervix, rectum, oropharynx, or conjunctivae. Dissemination has been associated with menstruation, the post-partum period, pelvic operation, and intrauterine devices. Patients with late complement component deficiencies are particularly at risk.

Classic manifestations are a combination of dermatitis (60%), tenosynovitis (60%), and migratory polyarthralgia (85%), or purulent arthritis without skin lesions. Patients typically have no urogenital symptoms. Skin lesions are commonly few in number and limited to the extremities. They start out as papules or petechial lesions, which progress into hemorrhagic pustules. Most cutaneous manifestations are thought to result from bacterial embolization followed by microabscess formation. Multiple tendons can be simultaneously inflamed, particularly the wrist, fingers, ankle and toes. Rarely, severe cases can result in meningitis or endocarditis.

Although presumptive diagnosis can be made on clinical grounds, culture of the bacteria remains the gold standard for definitive diagnosis. This can prove difficult since initial aspiration of synovial fluid is typically negative, and only half of patients with DGI present with positive blood cultures. There is a wide range (25-100%) of positive mucosal surface cultures from

urethral, cervical and rectal samples quoted in the literature. Cultures from skin lesions are usually negative.

In terms of management, the consensus is that multiple-dose regimens using cephalosporins or fluoroquinolones are the most effective, though no randomized controlled trials on this topic have been published since 1981. Resistance to single-dose antimicrobials develops frequently, and clinicians need to be aware of the local resistance profile when making appropriate treatment choices. Studies in the US and UK have found concurrent *Chlamydia trachomatis* in 7-14% of homosexual men with gonorrhea, in 20-30% of heterosexual men, and in 40-50% of women. Thus, treatment for potential coexistent chlamydia is advised whenever treating gonorrhea.

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