Chicago Dermatological Society

October 2013
Monthly Educational Conference

Program Information
Continuing Medical Education Certification
and
Case Presentations

Wednesday, October 9, 2013

David Fretzin Lecture

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

Program

Conference Locations

Student Center West (SCW) – 828 S. Wolcott, 2nd Floor
Dermatology Clinic, 1801 W. Taylor St., Suite 3E

8:00 a.m.	**Registration Opens** *Student Center West, 2nd floor Foyer*
9:00 a.m. - 10:00 a.m.	**Resident Lecture** – *SCW Chicago Room A-C* "Laminins in the Skin" *M. Peter Marinkovich, MD*
9:30 a.m. - 10:45 a.m.	**Clinical Rounds** Patient & Poster Viewing *Dermatology Clinic, Suite 3E* Slide Viewing *Student Center West, Room 213 A/B*
11:00 a.m. - 12:00 p.m.	**General Session** - *SCW Chicago Room A-C* FRETZIN LECTURE: "New Insights into the Pathophysiology of Human Psoriasis" *M. Peter Marinkovich, MD*
12:00 p.m. - 12:40 p.m.	**Box Lunches & visit with exhibitors** *SCW - 2nd Floor Foyer*
12:45 p.m. - 1:00 p.m.	**CDS Business meeting** – *SCW Chicago Room A-C*
1:00 p.m. - 2:30 p.m.	**Case Discussions** – *SCW Chicago Room A-C*
2:30 p.m.	**Meeting adjourns**

Mark the Date!

Next CDS monthly meeting – Wednesday, November 13, 2013 at Northwestern University; James G. Krueger, MD, PhD from the Rockefeller University in New York City; and Emma Guttman, MD, PhD, Mount Sinai Hospital, New York

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

Guest Speaker

M. PETER MARINKOVICH, MD

Associate Professor of Dermatology
Director, Autoimmune Blistering Disease Clinic; Stanford University School of Medicine, Department of Dermatology; Redwood City, CA

Delivering the David Fretzin Lecture

Dr. Marinkovich has his clinical focus in cutaneous dermatologic oncology, autoiummune blistering diseases and epidermolysis bullosa. He earned his medical degree from the St. Louis University School of Medicine in 1988 and finished an Internship in 1989 at the University of California-San Francisco. He completed a fellowship at Shriner's Hospital in Portland, OR (1990) and his residency in dermatology at the Oregon Health Science University in 1994.

Current research and scholary interests include extracellular matrix of epithelial tissues. Dr. Marinkovich also is involved in a number of clinical trials, such as grafting of epidermolysis bullosa wounds using cultured revertant autologous keratinocytes. He has numerous scholarly publications to his credit.

Chicago Dermatological Society

"Chicago Dermatological Society Monthly Meeting Series"

October 09, 2013 *Chicago, IL*

OBTAINING YOUR CERTIFICATE OF CREDIT

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

JOINT SPONSORSHIP STATEMENT

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

GOAL / PURPOSE

To broaden the clinical knowledge of dermatologists.

TARGET AUDIENCE

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

FACULTY

M. Peter Marinkovich, MD
Associate Professor of Dermatology
Director Autoimmune Blistering Disease Clinic, Stanford University School of Medicine
Department of Dermatology
Redwood City, CA

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EDUCATIONAL OBJECTIVES

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

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

2. Describe the manifestation of skin cancers and the efficacy of treatments available to the dermatologist.

3. List the therapeutic options available to the dermatologist for a variety of skin diseases, both medical and surgical, and discuss how new emerging treatments can be successfully

PHYSICIAN ACCREDITATION STATEMENT

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

CFMC designates this live activity for a maximum of 4.5 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

OTHER HEALTHCARE PROFESSIONALS STATEMENT

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

DISCLOSURE STATEMENT

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

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

University of Illinois at Chicago
Department of Dermatology

FACULTY

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DERMATOPATHOLOGY

Marylee Braniecki, MD
David Fretzin, MD

DERMATOLOGY RESIDENTS

Third Year

Juliana Choi, MD, PhD
Patricia Dymek, MD
Steven Kahn, MD
Amanda S. LaReau, MD
David Smart, MD

Second Year

Sonoa Au, MD
Whitney Fancher, MD
Amanda Marsch, MD

First Year

Monique Boomsaad, MD
Rosemara Hughart, MD
Pauline Scott, MD
Drew Taylor, MD

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Case Presented by Patricia Dymek, MD, Lucy Park, MD and Iris K. Aronson, MD

History of Present Illness:
This 21 year old male presented in January 2013 with a history of firm nodules arising on the extensor surfaces of the fingers and forearms, along with multiple mildly pruritic firm papules on the extremities and neck.

Past Medical and Surgical History:
Common variable immunodeficiency, autoimmune thrombocytopenia treated with multiple courses of rituximab, autoimmune neutropenia, autoimmune hemolytic anemia, tuberculous mediastinal lymphadenitis treated in 2008, recurrent pneumonia and sinusitis since early childhood, reactive airway disease, Blount's disease treated by bilateral osteotomy of the tibiae.

Medications:
Intravenous immunoglobulin infusions every 4 weeks, fluticasone diskus as well as nasal spray, and albuterol

Allergies:
No known drug allergies

Family History:
There was no family history of immunodeficiency, recurrent infection, early death due to severe infection, or autoimmune disease.

Social History:
He was studying mechanics at a community college while working at his father's auto shop. He frequently visited his grandfather on his chicken farm. He denied tobacco, alcohol, or illicit drug use.

Review of Systems:
The patient reported symptoms of nasal and chest congestion, purulent nasal discharge, cough, fevers and chills, arthralgias, recurring diarrhea, and progressive weight loss over the past two years (over 20 kg) despite having a good appetite.

Physical Examination:
The patient was noted to have multiple firm subcutaneous nodules along the extensor forearms and on the dorsal joints of the fingers. On the arms, legs, and neck were multiple pink to violaceous firm papules with mild scaling.

Laboratory Data:
The following were positive or abnormal:

Immunoglobulin A < 6 mg/dl (66-436)
Immunoglobulin M < 25 mg/dl (43-279)
Lactate dehydrogenase 204 units/l (90-180)
Erythrocyte sedimentation rate 39 mm/hr (< 10)
C-reactive protein 1.6 mg/dl (< 0.8)
White blood cells 3.1 k/µl (3.9-12.0)
Absolute lymphocytes 0.4 k/µl (1.3-4.2)
Hemoglobin 12.1 g/dl (13.2-18.0)
Platelets 206 k/µl (150-450)
Prealbumin 11.3 mg/dl (18-38)

The following were negative or within normal limits:
Immunoglobulin G level, rheumatoid factor, intrinsic factor antibody, complete metabolic panel, QuantiFERON®-TB Gold test

Diagnostic Procedures and Tests:

03/13 **Radiograph, left forearm**: Osseous structures and soft tissue structures are within normal limits. There is no acute fracture or dislocation.

05/13 **Computed tomography, chest**: Compared to the prior study, there is an increase in mediastinal and axillary lymphadenopathy. There is interval development of lung parenchymal abnormalities including small airways disease in the left base and lingula. Nodular and ground glass opacities are scattered throughout the left lower lobe and lingula. Hepatosplenomegaly is noted.

07/13 **Sputum culture**: Normal respiratory flora, rare yeast, no acid-fast bacilli isolated.
Stool culture: No virus isolated.
Stool ova and parasites: No parasites.

Histopathology:

Left forearm, skin: The dermis demonstrates large confluent areas of necrobiotic collagen surrounded by a granulomatous infiltrate consisting of epitheloid histiocytes. Periodic acid-Schiff, acid-fast bacilli, and Fite stains are negative.

Diagnosis:

Common variable immunodeficiency with granulomatous disease

Treatment and Course:

The patient was prescribed triamcinolone 0.025% ointment and hydroxyzine for the relief of pruritus. He continues to be closely evaluated by allergy-immunology and receives intravenous immunoglobulin infusions every four weeks. A biopsy of one of the mediastinal or axillary lymph nodes is planned in order to rule-out malignancy or systemic granulomatous disease. If the granulomatous disease continues to spread or become symptomatic, treatment with a tumor necrosis factor-α inhibitor will be initiated.

Discussion:

Common variable immunodeficiency (CVID) is a primary immunodeficiency in which a variety of immunologic abnormalities have been identified, including defects in B-cell maturation and differentiation, impaired T-cell function, defects in monocytes/macrophages, and deficiency of natural killer cells. CVID results from a sporadic mutation in 80-90% of patients. Presentation is bimodal with a few patients presenting in mid-childhood and a majority presenting in early to mid-adulthood. Three key features are needed in the diagnosis of CVID: hypogammaglobulinemia in two or more immunoglobulin isotypes (IgG, IgA, or IgM), recurrent sinopulmonary infections, and impaired functional antibody responses to vaccinations. Genetic testing is not done as 75% of patients have no known defect.

CVID has a heterogeneous phenotype as it affects multiple organ systems. Most patients have recurrent bouts of bronchitis, sinusitis, otitis media, and pneumonia which can lead to anomalies of lung parenchyma including bronchiectasis, pulmonary fibrosis, and obstructive lung disease. Gastrointestinal symptoms are common and 50% of patients present with chronic diarrhea with malabsorption. Due to the underlying immune dysregulation, 20% of CVID patients develop autoimmune disorders, most commonly autoimmune thrombocytopenia and hemolytic anemia, affecting 5-8% of patients. Other autoimmune disorders include anti-IgA antibodies, pernicious anemia, autoimmune thyroiditis, rheumatoid arthritis, vitiligo, Crohn's disease, celiac sprue, and vasculitis. CVID patients have an increased risk for the development of malignancies, most commonly non-Hodgkin's lymphoma and gastric cancers.

Multisystem granulomatous disease occurs in 8-22% of CVID patients and can arise in the lungs, liver, spleen, skin, bone marrow, or lymph nodes. The granulomas are typically non-caseating and can be mistaken for sarcoidosis which may delay the diagnosis of CVID. Cutaneous granulomas typically present as nonpruritic and nontender discrete erythematous papules, plaques, or indurations with central scaling and atrophic scarring on the extremities and face. The etiology for granuloma formation remains unclear but patients with granulomatous disease have a higher morbidity, earlier mortality, and are more prone to autoimmune complications, especially cytopenias.

The mainstay of treatment for CVID is monthly infusion of intravenous immunoglobulin (IVIg) at 300-400 mg/kg body weight in order to maintain IgG concentrations above a minimum of 5 g/L. IVIg infusions reduce the incidence of pneumonia and serious bacterial infections, prevent chronic lung disease and enteroviral meningoencephalitis, and may serve as prophylaxis against autoimmune thrombocytopenia and autoimmune hemolytic anemia. However, IVIg has shown little effect in controlling granuloma formation. Treatment of granulomatous disease with immunosuppressive agents poses a therapeutic challenge given the underlying immunodeficiency. There are no guidelines for the treatment of granulomatous disease in CVID. Systemic corticosteroids are most often used and a majority of patients must remain on a low dose of 5-10 mg/day to maintain remission. Hydroxychloroquine can be used as an alternative for mild disease since it inhibits tumor necrosis factor-α (TNF-α) production which is a key cytokine in granuloma formation. Several case reports have demonstrated the effectiveness of TNF-α inhibitors such as infliximab or entanercept in the treatment of granulomatous disease of the lymph nodes, skin, liver, and lungs. Cyclophosphamamide, methotrexate, mycophenolate mofetil and rituximab may be useful in treatment of aggressive disease.

Essential Lessons:

- CVID is a heterogeneous disorder with 8-22% developing multisystem granulomatous disease.
- Treat granulomatous disease in CVID patients who are symptomatic or demonstrate organ dysfunction.
- TNF-α inhibitors are emerging as a treatment option for both cutaneous and systemic granulomatous disease.

References:

1. Agarwal S. and Cunningham-Rundles C. Autoimmunity in common variable immunodeficiency. *Curr Allergy Asthma.* 2009;9:347-352.
2. Aghamohammadi A, et al. Cutaneous granulomas in common variable immunodeficiency: a case report and review of literature. *Acta Dermatovenerol Croat.* 2010;18:107-13.
3. Ardeniz O. and Cunningham-Rundles C. Granulomatous disease in common variable immunodeficiency. *Clin Immunol.* 2009;133:198-207.
4. Boursiquot JN, et al. Granulomatous disease in CVID: retrospective analysis of clinical characteristics and treatment efficacy in a cohort of 59 patients. *J Clin Immunol.* 2013;33:84-95.
5. Cunningham-Rundles C. Autoimmune manifestations in common variable immunodeficiency. *J Clin Immunol.* 2008;28:S42-S45.
6. Lin JH, et al. Entanercept treatment of cutaneous granulomas in common variable immunodeficiency. *J Allergy Clin Immunol.* 2006;117:878-882.
7. Park MA, et al. Common variable immunodeficiency: a new look at an old disease. *Lancet.* 2008;372: 489-502.
8. Thatayatikom A, et al. Infliximab treatment for severe granulomatous disease in common variable immunodeficiency: a case report and review of the literature. *Ann Allergy Asthma Immunol.* 2005;95:293-300.

Case Presented by Juliana Choi, MD, PhD
and J. Thomas Landers, MD

History of Present Illness:
This 28 year old otherwise healthy female presented with acute onset facial swelling, diffuse itching and numerous red swollen bumps and pustules on her trunk and extremities. One day prior she had noted small red dots on her left volar wrist and was diagnosed with scabies. She applied permethrin 5% cream diffusely and 4 hours following this application she developed a severely pruritic whole body rash. She denied recent exposures to other medications, other topicals, and denied known allergies.

Past Medical and Surgical History:
None

Medications and Allergies:
None; >3 weeks prior she received an intramuscular penicillin injection and adenovirus, hepatitis A, influenza, meningococcal/diphtheria, and diphtheria/tetanus/pertussis immunizations as part of her routine clearance for military training; no known drug allergies.

Social History:
The patient was a military recruit who was one month into training. She denied tobacco and alcohol use.

Review of Systems:
She reported subjective fever, itch, and facial edema. She denied nausea, vomiting, oral erosions, dysphagia, shortness of breath, abdominal pain, diarrhea, dysuria, swollen glands, joint pains, and fatigue.

Physical Examination:
The patient was afebrile. There was diffuse edema and erythema with scattered pinpoint pustules on her face, some of which had progressed to desquamation. On the trunk and extremities, there were innumerable pinpoint non-follicular pustules, diffuse blanchable erythema and edematous papules and plaques. Her lower extremities also had edematous purpuric papules and plaques. No ocular or nasopharyngeal mucosal lesions were present. No linear burrows on the hands or feet suggestive of scabies were present.

Laboratory Data:
The following were positive or abnormal:
Neutrophil percentage 91.3% (40-80), absolute neutrophil count 20.1 k/μL (1.5-8.0)
Eosinophil percentage 3.2% (0-6), absolute eosinophil count 0.7 k/μL (0-0.4)

The following were negative or within normal limits:
Complete metabolic panel

Histopathology:
Right upper back, pustule from skin: The biopsy demonstrates moderate spongiosis and a mixed superficial perivascular infiltrate which includes a few eosinophils. Subcorneal pustules are scattered throughout the epidermis. A large neutrophilic abscess is found in a dilated follicular infundibulum. There is no evidence of bacterial or fungal organisms.

Diagnosis:
Acute generalized exanthematous pustulosis induced by permethrin

Treatment and Course:
Oral prednisone was initiated with taper over 16 days. She was also started on oral hydroxyzine and hydrocortisone 1%/pramoxine 1% lotion for itch. At a 10-day follow-up visit, she noted near resolution of her rash. The T.R.U.E. Test® patch test was administered 11 days after discontinuing the prednisone taper as the patient was soon to be transferred to a different military base. In addition, the patient was instructed to apply permethrin 5% cream twice daily for 5 days to her left inner arm as a repeat open application test. The patient did not react to any tested allergens.

Discussion:
Acute generalized exanthematous pustulosis (AGEP) is a pustular reaction associated with medications in over 90% of cases. It is characterized by an acute appearance of widespread edematous erythema on which dozens to hundreds of sterile non-follicular pinhead-sized pustules develop. The rash commonly begins in intertriginous areas or the face and can become widespread within a few hours. Burning or itching is often described. Additional skin symptoms include marked edema of the face, purpura especially on the legs, Stevens-Johnson-syndrome-like "atypical" targets, blisters, and vesicles. Mucous membrane involvement may occur in 20% of cases and is usually restricted to oral lesions. Pustules usually resolve spontaneously within a few days and this is followed by a characteristic post-pustular superficial desquamation.

In addition to skin findings, fever, neutrophilia, mild eosinophilia, and lymphadenopathy can be associated. A slight reduction of creatinine clearance and a mild elevation of aminotransferases can be observed, but usually internal organs are not involved.

The histopathological features of AGEP can be difficult to characterize as a wide range of features can be seen, likely from different stages being biopsied from skin lesions. Furthermore, AGEP is difficult to distinguish both clinically and histologically from generalized pustular psoriasis. In 2010, Halevy et al. characterized histopathological features in AGEP. All biopsies demonstrated superficial infiltrates and dermal neutrophils. The majority of cases featured sub/intracorneal or intraepidermal pustules, mild spongiosis, papillary edema, mid/deep-dermal infiltrates, interstitial infiltrates, few dermal eosinophils, necrotic keratinocytes, and neutrophilic exocytosis. Furthermore, 23% of cases demonstrated follicular pustules.

In 2001, Sideroff et al. developed an algorithm for AGEP validation based on results from the EuroSCAR study (a multinational epidemiological study on severe cutaneous adverse reactions) and a comprehensive review of the literature (Table 1). Based on this algorithm, our patient scored a 10 which is interpreted as a "definite" case of AGEP (our patient's findings are highlighted in Table 1).

To help determine the causative medication, drug patch tests can be used to reproduce AGEP. In a study conducted by Barbaud et al, 58% of patients with AGEP demonstrated a positive patch test. The European Society of Contact Dermatitis (ESCD) and the European Network on Drug Allergy (ENDA) previously devised guidelines for performing patch tests for the diagnosis of cutaneous adverse drug reactions. The ESCD recommends waiting 6 weeks to 6 months after complete healing of cutaneous adverse reactions prior to patch testing, and the ENDA recommends waiting 3 weeks to 3 months. It is also recommended that systemic glucocorticoids and immunosuppressive therapy should be stopped at least 1 month prior to drug patch testing, and topical glucocorticoids should not be applied to patch test sites for at least 2 weeks prior to testing.

AGEP is most strongly associated with use of pristinamycin, aminopenicillins (amoxicillin/ampicillin), quinolones, chloroquine, sulfonamides, terbinafine, and diltiazem. Rarely, AGEP has been reported

following the application of a topical medication. To our knowledge, this is the first reported case of AGEP induced by permethrin.

Table 1. Algorithm for AGEP validation from Sideroff et al.

Morphology		**Course**		**Histology**	
Pustules		Mucosal		Other disease	-10
Typical*	+2	involvement		Not representative/no histology	0
Compatible**	+1	Yes	- 2	Exocytosis of PMN	+1
Insufficient***	0	No	0	Subcorneal and/or intraepidermal *non* spongiform or NOS pustule(s) *with* papillary edema or subcorneal and/or intraepidermal *spongiform* or NOS pustule(s) *without* papillary edema	+2
Erythema		Acute onset (≤ 10 d)			
Typical	+2	Yes	0		
Compatible	+1	No	- 2		
Insufficient	0				
Distribution/pattern		Resolution ≤ 15 d		*Spongiform* subcorneal and/or intraepidermal pustule(s) *with* papillary edema	+3
Typical	+2	Yes	0		
Compatible	+1	No	- 4		
Insufficient	0				
Postpustular desquamation		Fever ≥ 38 °C			
Yes	+1	Yes	+1		
No/insufficient	0	No	0		
		PMN ≥ 7000/mm^3			
		Yes	+1		
		No	0		
Interpretation: ≤0: no AGEP, 1-4: possible, 5-7: probable, 8-12: definite					
* Typical: typical morphology as described in the discussion ** Compatible: not typical, but not strongly suggestive of other disease *** Insufficient: lesions cannot be judged (mostly because of late stage of the disease or poor quality of pictures) PMN = neutrophils, NOS = not otherwise specified					

Essential Lessons:

- Topical agents need to be considered as a potential rare cause of AGEP.
- The diagnosis of AGEP is mainly clinical and the histopathologic features of AGEP can be difficult to characterize.
- A minimum of 3-6 weeks after healing is recommended prior to drug patch testing to reproduce AGEP.

References:

1. Barbaud A, et al. A multicentre study to determine the value and safety of drug patch tests for the three main classes of severe cutaneous adverse drug reactions. *Br J Dermatol* 2013;168(3):555-562.
2. Cheng CE and Kroshinsky D. Iatrogenic skin injury in hospitalized patients. *Clin Dermatol*. 2011;29(6):622-632.
3. Halevy S, et al. The spectrum of histopathological features in acute generalized exanthematous pustulosis: a study of 102 cases. *Br J Dermatol*. 2010;163(6):1245-1252.
4. Romano A, et al. Patch testing in non-immediate drug eruptions. Allergy *Asthma Clin Immunol*. 2008;4(2):66-74.
5. Sidoroff A, et al. Acute generalized exanthematous pustulosis (AGEP)--a clinical reaction pattern. *J Cutan Pathol*. 2001;28(3):113-119.

Case #3

Case Presented by Drew Taylor, MD, Bharati Chittineni, MD, and Iris K. Aronson, MD

History of Present Illness:
This 72 year old Filipino female with a history of atopy and diabetes mellitus, presented with a five-month history of bilateral ear pain, swelling, and redness. She complained of ear pain while lying down at night. The pain alternated between her right and left ears and waxed and waned. She was initially treated by her primary care physician with two courses of ciprofloxacin with no reported improvement. She denied any previous trauma to ears, hearing loss or headaches.

Past Medical History:
Eczema, seasonal allergies, diabetes mellitus

Medications:
Metformin, ezetimibe, simvastatin, and vitamin B12

Allergies:
Penicillin - developed rash and pruritus

Family History:
No family history of autoimmune disorders. History of unknown arthritis in father.

Social History:
The patient denied any tobacco, alcohol, or illicit drug use.

Review of systems:
She denied any hearing changes, fever, chills, shortness of breath, hoarseness, cough, weight loss, headache, vision changes, epistaxis, or hematuria.

Physical Examination:
The patient had diffuse erythema and swelling of bilateral helices, antihelices, tragi and antitragi, with right-sided involvement greater than left. Bilateral lobules were not involved. No conjunctival erythema or other ocular changes were seen. No nasal septum erythema was noted. Gross neurological examination of cranial nerves II-XII was unremarkable. No oral or genital ulcers were present.

Laboratory Data:
The following were positive or abnormal:
Collagen Type II Antibody 27.5 EU/ml (<20 EU/ml)
Erythrocyte sedimentation rate 39 mm/hr (<20mm/hr)

The following were negative or within normal limits:
Antinuclear antibody titer, cryoglobulins, anti-neutrophil cytoplasmic antibodies, rheumatoid factor, C-reactive protein, complete metabolic panel, complete blood count, and urinalysis

Histopathology:
Right helix, skin: The epidermis demonstrates mild irregular psoriasiform epidermal hyperplasia. A mild superficial perivascular and interstitial infiltrate are observed in the dermis. No perichondrium or cartilage is observed in the biopsy.

Diagnosis:
Relapsing polychondritis

Treatment and Course:
The patient is presented for discussion of management.

Discussion:
Relapsing polychondritis (RP) is a severe and pleomorphic multisystem disease characterized by recurrent and progressive inflammation primarily of the auricular and nasal cartilage, with devastating ramifications when involving the pulmonary, neurological, and cardiovascular systems. Peak age of onset is the fifth decade with a female predominance of 3:1. RP is a rare disease with an estimated annual incidence of 3.5 cases per million, with around 600 reported cases worldwide.

The exact etiopathogenesis is still eluding the medical field, but is thought to involve both cellular and humoral immunity aberrancies. Current theory points towards autoimmunity against native and denatured collagen, specifically collagen type II as well as minor collagens, IX and XI, which form the major extracellular scaffolding in cartilage. Recent studies have shown that 33% of patients with RP have circulating antibodies against type II collagen, although this has a low specificity. Additionally, the presence of genetic susceptibility is further supported by an increased frequency of HLA-DR4 in patients with RP.

The development of statin-induced autoimmune diseases is currently being investigated. Twenty-eight cases of statin-induced autoimmune diseases have been published so far. Systemic lupus erythematosus development is reported in the majority of cases published. Although there are no reported cases of RP associated with statin use, this may be an inciting factor in a genetically vulnerable patient.

Relapsing polychondritis is a clinical diagnosis, with specific criteria outlined by Michet, Damiani, and McAdam. The clinical diagnosis can be further supported by both laboratory and histopathology findings, although no one specific finding is pathognomonic for RP. Commonly, patients will have both an elevated erythrocyte sedimentation rate and C-reactive protein; in addition to leukocytosis, thrombocytosis, and normocytic anemia. Histopathology may reveal loss of basophilia in the cartilage matrix, corresponding to loss of matrix proteoglycans.

To date, there is no consensus on the appropriate treatment of RP. All literature regarding treatment of RP is anecdotal, and data from clinical trials is lacking. Most patients described in literature were treated with a combination of high dose corticosteroids either alone or in combination with disease-modifying antirheumatic drugs, with the eventual goal of tapering corticosteroids while maintaining remission. Trentham and Le report on 31 patients with RP who received methotrexate therapy; 23 were able to taper their prednisone dosage from 19 to 5 mg daily, while continued on methotrexate 17.5 mg weekly. Recalcitrant RP tends to be managed with biologics. A recent review of biologic use in RP by Lepka et al revealed 62 cases of RP treated with biologic therapy reported in the literature. Several reports of infliximab (3-10 mg/kg every 4-8 weeks) yielded good or partial responses of chondritis and respiratory complications. The endpoint of treatment varied from one publication to the next, therefore, comparison of efficacy among the biologics is hard to determine given the current literature, and further investigation is needed.

Essential Lessons:
- Relapsing polychondritis is the result of both cellular and humoral immunity aberrancies. Statin therapy may augment these deviant immunoreactions in genetically predisposed patients.
- The severity and pleomorphic nature of RP make it difficult to manage often requiring a multidisciplinary approach.

References:

1. Kemta LF, et al. Biologics in relapsing polychondritis: a literature review. *Semin Arthritis Rheum.* 2012;41(5):712-719.
2. Mathew SD, et al. Relapsing polychondritis in the Department of Defense population and review of the literature. *Semin Arthritis Rheum.* 2012;42(1):70-83.
3. McCarthy EM, Cunnane G. Treatment of relapsing polychondritis in the era of biological agents. *Rheumatol Int.* 2010;30(6):827-828.
4. Noel B. Lupus erythematosus and other autoimmune diseases related to statin therapy: a systematic review. *J Eur Acad Dermatol Venerol.* 2007;21:17-24.
5. Rapini RP, Warner NB. Relapsing Polychondritis. *Clin Dermatol.* 2006;24(6):482-485.
6. Sharma A, et al. Relapsing Polychondritis: a review. *Clin Rheumatol.* 2013 [Epub ahead of print].
7. Trentham DE, Le CH. Relapsing polychondritis. *Ann Intern Med* 1998;129:114-122.

Case Presented by Amanda Marsch, MD,
and Iris K. Aronson, MD

Fast Break: Cicatricial Pemphigoid

Case #5

Case Presented by Whitney Fancher, MD
and Aleksandar Krunic, MD, PhD

UNKNOWN CASE

This 44 year old female presented with painful skin lesions.

Case #6

Case Presented by David Smart, MD
and Michelle Bain, MD

History of Present Illness:
This 4 year old male presented with a 2 year history of recurrent outbreaks of multiple violaceous and hyperpigmented papules scattered mainly on the trunk and proximal extremities. The papules were occasionally pruritic but otherwise asymptomatic, and many were found to have superficial erosions and scale. While each outbreak resolved after several weeks leaving areas of residual hypopigmentation, the outbreaks themselves also seemed associated with the onset of multiple hypopigmented macules and small ill-defined patches not present prior to the outbreaks.

Past Medical History:
No significant past medical history was reported

Medications:
None

Allergies:
No known drug allergies

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

Physical Examination:
The majority of the integument was affected with multiple scattered, ill-defined, hypopigmented macules and small patches with diffuse mild xerosis. Several scattered, 2mm to 6mm, erythematous to violaceous papules were found on the upper trunk, abdomen, and proximal extremities.

Laboratory Data:
The following were negative or within normal limits:
Complete blood count, complete metabolic panel

Histopathology:
Left upper back, skin: The dermis demonstrates a top-heavy polymorphous lymphocytic infiltrate with mild vacuolar interface changes. Scattered within the infiltrate are lymphocytes with enlarged, irregular, hyperchromatic nuclei with a coarse chromatin pattern. Mitotic figures are easily identified. The epidermis demonstrates mild spongiosis, irregular acanthosis, and exocytosis of lymphocytes with overlying mounds of parakeratosis. Approximately 30% of the atypical lymphocytes stain positive for CD30. The lymphocytes are CD15 negative.

Diagnosis:
Lymphomatoid papulosis in a young child

Treatment and Course:
Prior to diagnosis, the patient was started on oral erythromycin to treat suspected pityriasis lichenoides. A definitive histologic diagnosis was obtained and on follow up it was noted that the papules had improved, but the xerosis and dyschromia were unaffected. Erythromycin was subsequently discontinued and the patient was prescribed triamcinolone 0.025% ointment to treat the papules should they recur. The patient was also referred to pediatric hematology oncology for consultation.

Discussion:

Lymphomatoid papulosis (LyP) is a chronic, recurrent, self-healing dermatosis with features that mimic lymphoma. The condition is uncommon, but rare in childhood. It is most common in adults with a median age of 44. The initiating event and pathogenesis are unknown. Clinically the disorder manifests itself as a papulonodular skin disease with the primary lesion being a red-brown papule approximately 1 cm or less in size. The lesions typically appear in crops and evolve to papulovesicular, hemorrhagic, or necrotic papules that subsequently disappear spontaneously within 3 to 8 weeks. Although individual lesions do often disappear spontaneously, the entire course of the disorder may be prolonged and last for years. The disorder is generally asymptomatic, but will occasionally resolve with varioliform scars.

LyP is considered to be on the spectrum of lymphoproliferative disorders with pityriasis lichenoides and cutaneous T-cell lymphoma. Because of the overlapping clinical and histologic features between LyP and other cutaneous lymphomas, specifically cutaneous anaplastic large cell lymphoma, many authors suggest that LyP is best regarded as a low-grade variant of CTCL, although it most often follows a benign course and the prognosis is usually excellent.

The risk of malignant lymphoma developing in adult-onset LyP is cited at 10–20%, which may precede, coexist with, or follow other cutaneous lymphomas. The risk of malignant lymphoma in childhood LyP is estimated to be less than 10%. Risk factors for the development of a systemic lymphoma are unknown. No guidelines exist but current consensus suggests long term follow-up at regular intervals with additional testing performed when abnormalities are detected at routine evaluations. Histopathologically, LyP is divided into 3 separate subtypes (A, B, and C). The classic histopathologic picture in children is type A, and is characterized by a heavy infiltrate of large atypical CD-30^{+} cells with prominent nucleoli in a background of inflammatory cells. Type B lesions more closely resemble mycosis fungoides, while type C lesions overlap with anaplastic large cell lymphoma. Mixtures of these subtypes have also been described. Types A and B are associated with lymphoma.

Treatment may not be necessary, and there is no evidence to suggest that treatment of LyP prevents the development of lymphoma. Superpotent topical corticosteroids are beneficial and effective as monotherapy in many childhood cases. Other beneficial therapies include systemic steroids, systemic antibiotics, PUVA, and UVB light. Methotrexate in particular has been used with good responses reported in both adult and pediatric cases.

Essential Lessons:

- Lymphomatoid papulosis is an uncommon lymphoproliferative disorder that occasionally presents in childhood.
- While the prognosis is generally excellent, long-term follow up is recommended to monitor for the development of lymphoma.

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Case #7

Case Presented by Sonoa Au, MD
and Aleksandar Krunic, MD, PhD

History of Present Illness:
This 51 year old Hispanic female with a history of early-onset breast, renal and thyroid carcinomas presented for evaluation of numerous longstanding asymptomatic skin growths on her face, postauricular area, neck and axillae.

Past Medical and Surgical History:
Thyroid cancer status post total thyroidectomy at age 33, left breast cancer status post mastectomy and chemotherapy at age 49, chromophobe renal cell carcinoma of left kidney status post complete left laparoscopic nephrectomy at age 51, osteoarthritis.

Medications:
Levothyroxine, tramadol, and goserelin subcutaneous implant

Allergies:
No known drug allergies

Family History:
Daughter, age 26, with Neurofibromatosis Type I. Son, age 20, with a formal diagnosis of autism. A complete four-generation pedigree was obtained, with no family history of any type of cancer.

Social History:
She denied alcohol, tobacco and illicit drug use.

Review of Systems:
She denied nausea, vomiting, cough, or weakness.

Physical Examination:
The patient's head circumference was measured to be 60cm (>97% consistent with macrocephaly). In the periorbital regions and around the alar grooves, few 1-2mm skin colored, pedunculated papules were noted. In the postauricular region bilaterally, several small, firm, skin colored papules were seen. The buccal mucosa and hard palate demonstrated several papillomatous lesions, giving a cobblestoned appearance. Around the neck and in the axillae were numerous less than 5mm skin colored, pedunculated papules. A few 1-2mm firm, keratotic papules were noted on her palms, but her soles are spared.

Diagnostic Procedures and Tests:
11/11 **Mammogram, right breast**: The breast tissue is composed of scattered fibroglandular tissue.
08/12 **Genetic testing**: The patient is heterozygous for PTEN mutation c.493-2A>G.
10/12 **Computed tomography, chest**: Right middle lobe and right lower lobe pulmonary micronodules are seen but no cysts or pneumothorax.
10/12 **Ultrasound, transvaginal**: Two large masses in the body and fundus of the uterus are seen, which are likely consistent with fibroids.
02/13 **Colonoscopy**: Numerous polyps are seen throughout her colon, with one large polyp showing high-grade dysplasia but no malignancy was found.

Histopathology:
Mouth, left buccal mucosa: Low power magnification demonstrates a nodular proliferation of fibrocollagenous tissue with scattered thin-walled blood vessels and minimal inflammation. There are focal areas within the collagenous proliferation that appear hyalinized and almost keloidal in appearance. The overlying epidermis demonstrates hyperkeratosis as compared to the base which is non-keratinized.

Diagnosis:
Cowden Disease

Treatment and Course:
Given the patient's history of multiple malignancies, she is currently deciding on whether to pursue prophylactic mastectomy of her right breast and hysterectomy. She will continue follow up with oncology for her breast and renal cancers. Since her son has autism, it is recommended that he receives evaluation for genetic testing.

Discussion:
Cowden disease (CD), also known as multiple hamartoma syndrome, is characterized by multiple benign and malignant neoplasms affecting multiple organ systems including mainly the skin, breast, thyroid gastrointestinal and genitourinary systems. It is inherited in an autosomal dominant pattern with variable expressivity, affects an estimate of 1 in 200, 000 individuals and is reported predominantly in Caucasians. CD is most commonly caused by a mutation in the tumor suppressor gene PTEN, located on chromosome 10q22–23. Other diseases associated with PTEN mutations include Bannayan–Riley–Ruvalcaba syndrome (BRRS), Lhermitte–Duclos disease (LDD), and autism/macrocephaly syndrome.

Over 80% of affected individuals have cutaneous involvement, usually with lesions starting in the second and third decades. Trichilemmomas are skin-colored or yellow verrucous papules located on the face, that consist of smooth lobules of clear glycogenated cells extending from an epidermis that is outlined by a thick eosinophilic basement membrane on histology. As seen in our patient, there may also be nonspecific cutaneous papules located on the face, especially grouped around facial orifices and the ears. In the oral cavity, a characteristic finding is multifocal or extensive mucosal papillomatosis. Multiple palmoplantar keratoses are observed in more than half the patients. Other cutaneous and noncutaneous findings of CD, as well as the indications for PTEN gene testing are listed in Table 1 below.

Since patients with CD are at an increased risk for multiple malignancies, periodic surveillance is required. About one-third of affected women develop breast cancer, so annual mammograms or magnetic resonance imaging should be performed, along with clinical breast examinations twice a year. Prophylactic mastectomies are also an option. Thyroid ultrasound and thyroid function studies are recommended at baseline, with yearly ultrasound follow-ups. Surveillance for renal carcinoma and endometrial carcinoma by annual renal ultrasounds and urine studies, and annual blind endometrial biopsies respectively is recommended for those with a family history of these cancers. Patients with CD do not have an increased risk of colon cancer compared to the general population so patients should follow the standard guidelines for screening.

Table 1: Cowden Disease Criteria, National Comprehensive Cancer Network 2011.

Major criteria	Minor criteria
Mucocutaneous lesions • One biopsy-proven trichilemmoma, *or* • Multiple palmoplantar keratoses, *or* • Multifocal or extensive oral mucosal papillomatosis, *or* • Multiple cutaneous facial papules (often verrucous), *or* • Pigmented macules on the glans penis Macrocephaly (>97th percentile; 58 cm in adult woman, 60 cm in adult man) Breast carcinoma Thyroid carcinoma (non-medullary; especially follicular) Endometrial carcinoma Multiple gastrointestinal hamartomas or ganglioneuromas	Fibromas Lipomas Fibrocystic breast disease Other thyroid lesions (e.g. adenoma, nodules, goiter) Uterine leiomyomas (fibroids) Single gastrointestinal hamartoma or ganglioneuroma Renal cell carcinoma Mental retardation (IQ ≤75) Autism spectrum disorder
Indications for *PTEN* gene testing/provisional diagnosis (A, B, *or* C)	
A. Individual from a family with a known *PTEN* mutation B. Individual with a personal history of: Bannayan-Riley-Ruvalcaba syndrome (BRRS), *or* Adult Lhermitte-Duclos disease, *or* 2 or more biopsy-proven trichilemmomas, *or* 2 major criteria, including macrocephaly, *or* 3 major criteria, without macrocephaly, *or* 2 major criteria + 2 minor criteria, *or* 1 major criterion + 3 minor criteria, *or* 4 minor criteria C. Individual with a 1st degree relative with a clinical diagnosis of Cowden disease or BRRS plus a personal history of: 1 major criterion, *or* 2 minor criteria	

Essential Lessons:

- Cowden disease is most commonly caused by a mutation in the tumor suppressor gene PTEN.
- Cowden disease is characterized by multiple benign and malignant neoplasms affecting multiple organ systems including mainly the skin, breast, thyroid gastrointestinal and genitourinary systems.

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Case #8

Case Presented by Amanda S. LaReau, MD,
Aleksandar Krunic, MD, PhD, and J. Thomas Landers, MD

Fast Break: Innovative Treatments for Keloids

Case #9

Case Presented by Monique Boomsaad, MD
and Iris K. Aronson, MD

History of Present Illness:
This 50 year old female was transferred to the inpatient medicine service with a fever, altered mental status and rash. Her cutaneous symptoms appeared seven days prior to her initial presentation. She subsequently became confused, non-verbal and febrile and presented to an outside hospital emergency room with a diffuse maculopapular rash affecting her face, arms and legs. A lumbar puncture at that time demonstrated elevated lymphocytes. The patient was started on acyclovir for suspected herpes encephalitis and transferred to our facility. Upon arrival, MRI of the brain was normal.

Past Medical History:
Hypertension

Medications:
Famotidine

Allergies:
No known drug allergies

Family History:
Mother with rheumatoid arthritis. One daughter with systemic lupus erythematosus.

Physical Examination:
The patient was awake, non-verbal and did not follow commands. She had coalescing erythematous to violaceous blanchable patches on the proximal extremities, chest and abdomen. Her face was also affected with involvement of the nasal bridge, nasolabial folds, malar cheeks, and glabella.

Laboratory Data:
The following were positive or abnormal:
Cerebrospinal fluid white blood cell count 112/*u*L (0-5) with the following differential: Neutrophils 1/*u*L, Lymphocytes 74/*u*L, Monocytes 24/*u*L, Eosinophils 1/*u*L (0)

The following were negative or within normal limits:
Antinuclear antibody negative. Antibodies to dsDNA, RNP, Smith, SSA (Ro), SSB (La), Lyme and HIV are negative. QuantiFERON®-TB Gold test is negative. CSF culture, HSV, and VDRL are negative.

Histopathology:
Right upper arm, skin: Sections show compact hyperkeratosis and prominent foci of vacuolar change along the basal layer. Scattered necrotic keratinocytes are observed along the dermal-epidermal junction and within the epidermis. The dermis demonstrates mild edema and a mild perivascular mostly superficial lymphocytic infiltrate.
Right lateral upper arm, skin: Sections show similar changes to the above, with the additional findings of admixed neutrophils within the superficial dermal infiltrate, fragmented lymphocyte nuclei, and hematoxyphile bodies.

Direct immunofluorescence, right upper chest, skin: IgG demonstrates 3+ granular staining. IgM demonstrates 2+ granular staining, with granular staining of a blood vessel wall in the papillary dermis. Additionally, C3 is weakly positive in a granular pattern at the dermal-epidermal junction.

Diagnosis:
Neuropsychiatric lupus

Treatment and Course:
The patient was treated with intravenous methylprednisolone 500mg every 12 hours for five days while inpatient, and then discharged on prednisone 60mg daily. By discharge, she had returned to her baseline mental status. Her most recent regimen consisted of prednisone 20mg daily and hydroxychloroquine 200mg twice daily.

Discussion:
Neuropsychiatric lupus (NPSLE) is defined by the American College of Rheumatology as including a broad variety of syndromes: total spectrum of headache (39%–61%), seizures (8%–18%), cerebrovascular disease (2%–8%), psychosis (3%–5%), cranial neuropathy (1.5%–2.1%) and movement disorders (1%). It is estimated that 28%–40% of NPSLE manifestations develop before or around the time of the diagnosis of SLE; in particular, most psychiatric episodes occur within the first two years of disease onset.

This patient's negative serologic studies are not uncommon among those with NPSLE manifestations; small studies have estimated that up to 6-8% of NPSLE patients are ANA negative. Reliable serologic markers for NPSLE have yet to be defined, though several studies have demonstrated that NPSLE is associated with the presence of anti-phospholipid and, less often, anti-Ro antibodies. These associations are inconsistent, however, as they vary by a patient's ethnicity and the chronicity of the neuropsychiatric dysfunction.

Deposition of immunoglobulins at the dermoepidermal junction (DEJ) detected via direct immunofluorescence staining is a hallmark of LE. The exact mechanism of this deposition is unclear, but a common hypothesis is that these deposits partly represent circulating immune complexes of antinuclear antibodies and DNA that have become trapped in the DEJ. The deposits may also be due to antinuclear antibodies binding to DNA that has crossed the basement membrane zone after being released from ultraviolet-damaged keratinocytes. These mechanisms do not explain how the patient presented here can be ANA negative, but have IgG, IgM and C3 deposits at the DEJ.

This case was unusual in that the patient's lupus antibody panel was negative, yet her skin biopsy demonstrated findings diagnostic of lupus. To our knowledge, there are no reports detailing the frequency of this occurrence. This case suggests that we might consider skin biopsy in cases where lupus is suspected, even without the classic clinical findings or serologic markers of SLE.

Essential Lessons:
- Systemic lupus erythematosus can present with neuropsychiatric findings.
- If NPSLE is suspected, skin biopsy may be diagnostic even in the absence of classic SLE laboratory findings.

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Case #10

Case Presented by Steven Kahn, MD
and Aleksandar Krunic, MD, PhD

History of Present Illness:
This 28 year old otherwise healthy man presented with a nodule on the left nasal dorsum that had been present for 5-6 months. The lesion was tender and occasionally bled after it was lanced by the patient's primary care physician.

Past Medical History:
No significant past medical history

Medications:
None

Allergies:
No known drug allergies

Family History:
No history of skin conditions.

Review of systems:
The patient denied any cough, fevers, chills, night sweats, weight loss, joint pains, shortness of breath, chest pain, palpitations, dizziness, or fainting.

Physical Examination:
The patient had a 1.2 x 1.1 cm cystic nodule with yellow to clear drainage from the center of the nodule and surrounding erythema.

Diagnostic Procedures and Tests:
09/13 **Echocardiogram, Chest**: Pending.

Histopathology:
Left nasal dorsum, skin: The epidermis shows ulceration with underlying granulation tissue, fibrosis, and a background of inflammation. A proliferation of stellate and round spindled cells with relatively uniform nuclei and scant cytoplasm extends into the deep dermis, the subcutaneous fat and between skeletal muscle. Many of the nests show a myxoid appearance. These cells stain positively with CD68. There is some CD10 positivity noted within the neoplasm. S100, MelanA, MITF, digested PAS, gram, and acid-fast bacilli stains are all negative. Mitoses are rare, and significant cellular pleomorphism is not identified.

Diagnosis:
Superficial angiomyxoma

Treatment and Course:
An excision was performed with 2 mm margins and closed with an advancement flap. He had no signs of recurrence in the following 7 months after his excision. Cardiac workup is pending. The patient is presented for discussion of diagnosis.

Discussion:
Superficial angiomyxoma (SA), also called cutaneous angiomyxoma, is a rare benign yet locally aggressive myxoid-type neoplasm first described by Allen et al. and named angiomyxoma to stress its vascular component. Superficial angiomyxomas are distinguished from aggressive (recurrent, infiltrative) angiomyxomas, which affect the female genital region. SA are distinguished from other myxoid tumors by its superficial location, lack of atypia, stromal inflammatory infiltrate, and frequent association with an entrapped epithelial component. Clinically, SA presents as a skin nodule or polypoid lesion less than 5 cm and located most commonly on the trunk or lower limbs, followed by the head and neck, and least common on the upper limbs. In a retrospective review, only 28 cases of SA have been reported in the head and neck area. Males demonstrated a slightly higher prevalence than females, and the mean age of presentation was 36.45 years.

Histology of SA demonstrates a well-defined non-invasive lesion and shares characteristics of other myxomatous lesions with the presence of spindle, stellate, and oval cells within a myxoid stroma as in focal cutaneous mucinosis and aggressive angiomyoma. SA characteristically has a scattered distribution of thin-walled blood vessels and the presence of inflammatory cells, which are absent in other myxomatous lesions. This entity can be differentiated from cutaneous focal mucinosis by its well-defined border, presence of a reticular network, lack of fragmented collagen fibers, prominent vascular component, and tendency toward local recurrence. Epithelial components have been reported to be more frequently present than not in angiomyxomas. While non-specific, immunohistology may show variable positivity for CD34, S100, smooth muscle actin, muscle-specific actin, factor XIIIa, CD68, and pankeratin. Most reported cases of SA with immunohistological stains have been positive with vimentin and negative with desmin.

There is a known association of angiomyxomas with Carney complex. This autosomal dominant syndrome, which includes the presence of cardiac and cutaneous myxomas, skin hyperpigmentation, and endocrine overactivity, should be ruled out in a patient with SA presenting in the external ear. To date, there are 7 reports of cutaneous emboli from myxomatous tissue fragments, with findings including splinter hemorrhages, livedoid macules, acral erythematous papules, livedo reticularis, ulcerative lesions of the feet, annular and serpiginous lesions of the fingers, acral petechiae, cyanosis, and a violaceous malar flush. Local recurrences of angiomyxomas have been reported in 38% of cases but SA have no propensity to metastasize. A lower recurrence rate has been described from SA in the head and neck region. This tendency for recurrence emphasizes the need for deep excision and thorough postoperative surveillance.

Essential Lessons:
1. Angiomyxomas are rare benign yet locally aggressive myxoid-type neoplasms most commonly presenting on the trunk or lower limbs.
2. There is a known association of angiomyxomas with Carney complex, and Carney complex should be ruled out in a patient with an angiomyxoma located in the external ear.
3. Though superficial angiomyxomas have not been shown to metastasize, they do have a tendency to recur, emphasizing the need for deep excision and postoperative surveillance.

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Case #11

Case Presented by Pauline Scott, MD,
Sonoa Au, MD and Aleksandar Krunic, MD, PhD

History of Present Illness:
This 53 year old Caucasian female presented with a five year history of a nail deformity of her left thumbnail. The nail was tender and the deformity had gradually worsened over the years. She denied any preceding trauma or inciting event.

Past Medical and Surgical History:
None

Medications:
None

Allergies:
Penicillin

Social History:
She quit smoking 15 years ago. She denied alcohol and illicit drug use.

Review of Systems:
She denied fever, chills, weight change, nausea, vomiting, cough, fatigue, dyspnea, or weakness.

Physical Examination:
The left thumbnail demonstrated transverse curvature and pincer deformity. Upon nail avulsion, a softened matrical area with gelatinous transformation of the submatrical tissue was seen along with cavitation of the dorsal phalangeal bone.

Diagnostic Procedures and Tests:
8/13 **Radiograph, left thumb**: The distal phalanx of the thumb demonstrates an expansile, well-defined, lytic lesion.
8/13 **Magnetic resonance imaging, left thumb**: The T1-weighted precontrast image demonstrates near complete replacement of the bone marrow of the distal phalanx of the thumb with cortical destruction along the dorsal surface. Post-contrast imaging demonstrates heterogeneous abnormal enhancement throughout the marrow extending into the soft tissues of the nail bed.
9/13 **Radiograph, chest**: There is no evidence of metastases.

Histopathology:
Soft tissue and bone, left thumb distal phalanx: Lobules of hypercellular cartilage with foci of reactive bone are present. Mitotic activity is not appreciated and the proliferation index (Ki-67) is low.

Diagnosis:
Chondrosarcoma, Grade I

Treatment and Course:

Orthopedic surgery performed an excisional curettage and bone biopsy, followed by a bone graft. Given the diagnosis of a low grade chondrosarcoma, this conservative approach was preferred over resection or amputation. The patient will have a bone scan to rule out any other bony tumors. She will follow up with orthopedic surgery and orthopedic oncology regularly to monitor for recurrence.

Discussion:

Chondrosarcomas account for approximately 4% of malignant hand tumors. It is most commonly found in bones of the pelvis and proximal extremities. Involvement of the distal phalanx of the hand is rare with less than 10 cases reported in the literature. Patients can present with pain and swelling of the involved digit. There has also been one reported case of metastatic chondrosarcoma presenting with onycholysis. Phalangeal chondrosarcomas are characterized as locally aggressive tumors with low metastatic rates. In contrast, chondrosarcomas found in other locations are associated with increased metastatic potential and mortality rate.

Plain radiographs can be used to diagnose hand chondrosarcomas. The radiologic characteristics most commonly seen include matrix calcifications, endosteal erosions, cortical destruction, bone expansion, soft tissue mass, and indistinct margins. A few cases demonstrated benign appearing results on radiographs, which must be interpreted with caution when clinically suspicious for more aggressive lesions. Other tests to confirm the diagnosis are magnetic resonance imaging and soft tissue and bone biopsy.

The most common histologic features of the soft tissue and bone include hyaline cartilage, myxoid or mucoid changes, ossification, nuclear pleomorphism, calcification, necrosis, cortical destruction, and soft tissue invasion. Furthermore, immunohistochemistry analysis with Ki-67 revealed a lower mean Ki-67 index for phalangeal chondrosarcomas than chondrosarcomas in other locations. The diagnosis of chondrosarcoma can be difficult to make, and therefore it is prudent to collectively analyze the clinical, radiological, and histological presentations to elicit the diagnosis.

Treatment options of chondrosarcomas of the hand include curettage with bone grafting, digital ray resection, and amputation. As these tumors have low metastatic potential, it has been recommended to treat Grade I chondrosarcomas with curettage and close follow-up.

Essential Lessons:

- Chondrosarcoma of the distal phalanx is rare and can present as a pincer nail deformity.
- Although chondrosarcomas are histologically aggressive tumors, minimal metastatic potential has been observed in phalangeal chondrosarcomas.
- Conservative treatment with curettage and regular follow-up is the preferred management of Grade I chondrosarcoma.

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