New England Dermatological Society Meeting
Saturday, October 21, 2023
Hosted by the Department of Dermatology at the Warren Alpert Medical School of Brown University and the Brown University Dermatology Residency Program
October 21, 2023

Dear Attendee:

I would like to take this opportunity to invite you to become a member of the New England Dermatological Society (NEDS). A key benefit to membership in the Society is complete and full access to the NEDS website. This access allows members to view cases presented at past clinical meetings. These cases provide a valuable database of unusual dermatological disorders and their treatment. NEDS membership dues cover attendance at up to four NEDS meetings during the membership year, which runs October through September.

The New England Dermatological Society offers a 50% discount on the first year’s membership dues for any person who applies within one year of completing their residency or fellowship training. NEDS members who refer a new member to the Society receive $50 from NEDS.

Initiate your application by applying online at www.nederm.org. You’ll find our membership application and other helpful information in the ‘Membership’ section of our website. Your application will be reviewed at the next scheduled NEDS Council meeting once all required application materials have been received.

If you have any further questions, please contact Gayle Sommer, NEDS Administrator at 781-434-7731 or NEDS@mms.org.

With best regards,

Gabriela Cobos, MD
Secretary
New England Dermatological Society
www.nederm.org
FUTURE MEETINGS OF THE NEW ENGLAND DERMATOLOGICAL SOCIETY

December 2, 2023 – Dermoscopy Course
Course Instructor: Dr. Ashfaq A. Marghoob
Embassy Suites . Waltham, MA

February 10, 2024 – Virtual Didactic Meeting
Hosted by Geisel School of Medicine

April 6, 2024 – Clinical Meeting
UMass Chan Medical School
Worcester, MA
NEDS Awards

Case of the Year
The Case of the Year Award is given to the best clinical case presented during the academic year. Each program submits their “best” case at the conclusion of each academic year so that the Council can vote and decide on the award recipient. If the winner then presents the case at the American Academy of Dermatology (AAD) in the gross and microscopic session he/she will be awarded $ 500 to help with travel expenses. $ 500 will also be presented to the recipient’s residency program’s educational fund.

Century Scholar Award
The Century Scholar Award is given to the dermatology resident or trainee in their dermatology rotation who wrote up the winning case. He or she is awarded a $ 500 Amazon gift card towards the purchase of medical textbooks.

If the case is accepted for presentation at a conference and the trainee travels to present it, $ 500 is awarded to the trainee to help with travel expenses. Their write up must specify that the case was presented at a New England Dermatological Society Conference and the case must be accepted within two years to receive the travel funding.

Book Award
The New England Dermatological Society will award a $ 500 gift card towards the purchase of a medical textbook to any dermatology resident at a member institution who satisfies the following requirements:

1. The resident is a first author* of a report based on a case presented at a meeting of the New England Dermatological Society (*if the first author is a medical student, then the resident who is the second author is eligible for the award)

2. The report is accepted for publication by a peer-reviewed journal within two years of the NEDS meeting and contains language indicating that the “this case was presented at a meeting of the New England Dermatological Society held at (institution) on (date).”

3. The resident supplies the Society’s Secretary with a copy of the final journal acceptance letter and a receipt for their purchased medical textbook. The recipient is then awarded a gift card in the amount of $500 towards the purchase of their medical textbook.
October 21, 2023
NEDS Clinical Meeting hosted by
Warren Alpert Medical School at Brown University
Division of Dermatology

7:30 – 8:00 AM  Check-In, Continental Breakfast and Exhibits Open*
222 Richmond Street, Providence, RI. (1st floor)

8:00 – 9:30 AM  (live) Patient and Pathology Viewing and Casebook Review
222 Richmond Street, Providence, RI. (2nd and 3rd floors)

The remainder of the meeting will be held in the first floor auditorium of 222 Richmond Street, Providence, RI

9:30 – 10:10 AM  Case Discussion 1-8
Moderators: Su-Jean Seo, MD, PhD, Elnaz Firoz, MD

10:10 – 10:30 AM  Guest Speaker: Oliver Wisco, DO
RI Skin Cancer Risk Assessment

10:30 – 11:10 AM  Case Discussion 9-15
Moderators: Su-Jean Seo, MD, PhD, Elnaz Firoz, MD

10:10 – 11:25 AM  Guest Speaker: Cathy Massoud, MD
Lessons Learned from the Wards: Tour of Reticulated & Retiform Morphologies

11:25 – 11:40 AM  Mid-Morning Break / Exhibits Open*

11:40 – 11:55 AM  NEDS Business Meeting*

11:55 AM – 12:10 PM  Preceptorship Awardee Speakers*
Project Summaries

12:10 – 12:30 PM  Case Discussion 16-20
Moderators: Su-Jean Seo, MD, PhD, Elnaz Firoz, MD

12:30 – 12:45 PM  Guest Speaker: Christopher DiMarco, MD
The Devil Is in the Details: Updates on Coding

12:45 – 1:00 PM  Final Comments and Meeting Adjourns

Box Lunch Provided

*ineligible for CME credit
Acknowledgements

Welcome to the New England Dermatological Society Clinical Meeting hosted by the Warren Alpert Medical School of Brown University. We would like to take this opportunity to thank the following individuals, without whom this meeting would not have been possible:

Our faculty mentors in the Department of Dermatology and community, whose support and contributions to our case presentations were invaluable.

Our faculty planning committee: Leslie Robinson-Bostom, MD, Lionel Bercovitch, MD, Gladys Telang, MD, and Christopher DiMarco, MD.

Our dermatopathologists, Leslie Robinson-Bostom, MD, Gladys Telang, MD, and Christopher DiMarco, MD, for their assistance with the preparation and presentation of the histopathology associated with each case.

Our guest speakers, Cathy Massoud, MD, Christopher DiMarco, MD, and Oliver Wisco, DO, for sharing their knowledge and expertise with us.

Our program moderators, Su-jean Seo, MD, PhD, and Elnaz Firoz, MD, for their facilitation of the case discussion.

Our resident NEDS coordinators, Leila Shayegan, MD, Fatima N. Mirza, MD, MPH, Mayra Buainain de Castro Maymone, MD, DSc, and Laura Burns, MD, for their organization of the casebook.

NEDS administrator, Gayle Sommer, who has been integral in planning this meeting.

Erika Abou Kelila, our administrator in the Department of Dermatology, for all of her assistance.

Our dermatology residents, who prepared the written cases presented in the program booklet.

Our New England Dermatological Society member colleagues for their attendance and participation in the conference today.

Above all, we are grateful to our patients and their families for the generous donation of their time and contribution to our education.

We hope you enjoy this clinical meeting today. We look forward to seeing you at future meetings.

On behalf of the Brown Dermatology NEDS planning committee,

Leslie Robinson-Bostom, MD
Professor of Dermatology
The Warren Alpert Medical School of Brown University
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CASE 1
A newborn female with missing skin

**Presenters**
Esther B. Henebeng, MD
Leila Shayegan, MD
Svetlana Shapiro, PA
Arya Batta, MD
Monique De Paepe, MD
Lionel Bercovitch, MD

**History**
A monoamniotic monochorionic twin female infant, born at 39 weeks via vaginal delivery, was noted at birth to have localized absence of skin on her back. Pediatric dermatology was consulted on day 1 of life.

Pregnancy was complicated by pre-eclampsia with severe features and HELLP syndrome, as well as intrauterine fetal demise of the patient’s twin at week 12 of gestation. At birth, the deceased twin was noted to be embedded in the placenta.

Past medical history: Velamentous cord insertion

Family history: No family history of similar congenital absence of skin

Medications: None

**Physical Examination**
At birth, on the lower back was an angulated 3 cm x 1 cm full thickness skin defect.
At 5 weeks of age, the patient was also noted to have a 2 cm faintly lighter linear patch on the left lateral abdomen continuous with the previous scar.

**Labs and Imaging**
Labs: None.
Imaging: None.

**Histopathology**
No biopsy of the patient’s skin was performed. The patient’s deceased twin was sent for pathology and was found to be a severely macerated, partially mummified and compressed fetus. The placenta was unfortunately not sent for pathology.
Aplasia Cutis Congenita with Fetus Papyraceus (Type V)

Treatment
- The patient’s skin was treated with wound care consisting of daily petrolatum ointment covered by gauze and transparent skin dressing until healed.
- After 5 weeks of treatment, the patient’s skin had fully healed with residual stellate scars.

Discussion
- Aplasia cutis congenita (ACC) is defined as localized or widespread absence of skin at birth. It is localized to the scalp or extremities in 70-85% of cases and has an incidence of ~3 in 10,000 births.\(^1,2\) The classification system for ACC was originally published by Ilona Frieden in 1986 (see table).\(^1-3\)
- Type V ACC occurs in multiple gestation pregnancies following in utero twin demise resulting in fetus papyraceus or mummification. As in our case, twin demise is most common in the late 1st or early 2nd trimester.\(^4\) The rare entity presents with erosions or depressed scars over the trunk or extremities, sometimes occurring in a symmetric distribution resembling the letter “H” on the neonate’s back.\(^2,4\) Our patient’s faint scar on the left lateral abdomen is contiguous with the area of aplasia, suggesting the possibility of partial intrauterine healing.
- While the exact mechanism of type V ACC is unknown, a disruption in the shared blood flow between the deceased and surviving twin’s anastomotic vessels has been suggested. In the setting of ischemia, the areas farthest from the vascular supply are considered most likely to undergo damage resulting in skin necrosis.\(^3\) This may be why the trunk and extremities are so commonly affected in Type V ACC.
- The diagnosis of type V ACC is clinical. In the prenatal period, ultrasound may show an elevated amniotic fluid index, and labs may be remarkable for increased maternal alpha-fetoprotein levels.\(^1\) Biopsy is not typically performed but may show absence of epidermis, dermis, or subcutaneous fat.\(^3\) Placental studies may demonstrate signs of diminished blood flow including reduced placental thickness and thrombosis.\(^1,2,4\)
- To achieve the best outcome, neonatal intensive care and specialists such as dermatology and plastic surgery should be consulted early. Conservative management involves application of petrolatum followed by an absorbent dressing to promote granulation. In the setting of large areas of absent skin, grafting may be indicated given the risk of infection and fluid imbalance. Contractures may develop during re-epithelialization and can be treated with rigorous massage, physical therapy, or surgical release.\(^4\)

Aplasia cutis congenita (ACC) classification \(^1-3\)

<table>
<thead>
<tr>
<th>Type</th>
<th>Presentation</th>
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<tbody>
<tr>
<td>I</td>
<td>ACC on the scalp with no other anomalies</td>
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<tr>
<td>II</td>
<td>ACC on the scalp with concomitant limb anomalies</td>
</tr>
<tr>
<td>III</td>
<td>ACC on the scalp with epidermal nevi, neurological, and ophthalmic abnormalities</td>
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<tr>
<td>IV</td>
<td>ACC on any site* with embryologic deformities</td>
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<tr>
<td>V</td>
<td>ACC on any site* associated with fetal papyraceus or placental infarction</td>
</tr>
<tr>
<td>VI</td>
<td>ACC on any site* with epidermolysis bullosa</td>
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<tr>
<td>VII</td>
<td>ACC on any site* without epidermolysis bullosa</td>
</tr>
<tr>
<td>VIII</td>
<td>ACC on any site* associated with teratogens, varicella or herpes virus</td>
</tr>
<tr>
<td>IX</td>
<td>ACC on any site* with congenital malformations</td>
</tr>
</tbody>
</table>

*usually the trunk and/or extremities

Teaching Points
- Type V aplasia cutis congenita is associated with fetus papyraceus and is clinically diagnosed by a stellate congenital absence of skin over the trunk and/or extremities.
- Many infants respond well to conservative therapy, but subspecialist involvement and surgical intervention should be considered to prevent long-term complications.

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CASE 2
A 2-month-old male with scalp alopecia

Presenters
Jasmine Gibson, BA
Esther B. Henebeng, MD
Brea Prindaville, MD

History
A 2-month-old male ex-full-term infant presented with skin tags on the right upper eyelid and birthmarks on the scalp associated with alopecia. According to his family, these findings were first noticed at birth. There were no birth complications. Developmental milestones were appropriate. He had been seen by an ophthalmologist and a dilated eye exam was normal.

Review of systems was negative for seizures, visual problems, or poor feeding.

Past medical history: Parents denied significant past medical history

Family history: Unremarkable

Medications: None

Physical Examination
Extending from the right frontal scalp to the temporal region was a salmon-colored soft flat plaque with overlying alopecia. A similar well-demarcated plaque with overlying alopecia was noted on the vertex scalp. Three discrete skin-colored to white 1-2 mm papules were present—two on the right upper eyelid and one on the right lateral canthus.

Neurologic examination was notable for non-sustained clonus in the bilateral lower extremities and brisk deep tendon reflexes.

Labs and Imaging
Imaging: Brain MRI/MRA revealed a large right anterior temporal arachnoid cyst, right cerebral hemiatrophy, enlargement of the right atrium and occipital horn of the lateral ventricle, defective insular opercularization, leptomeningeal angiomatosis, and an anomalous pial venous plexus in the subarachnoid space without evidence of arteriovenous fistula.

Spine MRI showed subtle enhancement of the cauda equina nerve roots, otherwise no abnormalities of the cervical and thoracic spine. EEG was unremarkable.

Abdominal ultrasound was normal, without evidence of Wilms tumor.

Histopathology
None

Clinical Images
Nevus Psiloliparus as part of Encephalocraniocutaneous Lipomatosis

Treatment
• The patient was referred to neurology and genetics.
• The patient was encouraged to continue following with ophthalmology.

Discussion
• Encephalocraniocutaneous lipomatosis (ECCL) is a rare, sporadic, neurocutaneous disorder characterized by skin, ocular, and central nervous system (CNS) anomalies.¹
  o Nevus psiloliparus (NP), a skin condition characterized by alopecia and fatty tissue on the scalp, is the dermatologic hallmark of ECCL.¹ ²
  o The predominant ocular finding in ECCL is a choristoma, which is a benign ocular tumor.¹
  o CNS findings include ventriculomegaly, atrophy, calcifications, arachnoid cysts, intracranial and spinal lipomas, leptomeningeal angiomatosis, and abnormal insular opercularization, which is a brain structure involved in neurologic and cognitive processes.¹ ³ ⁴
  o ECCL is also associated with seizures, developmental delay, intellectual disability, and an increased risk for brain, Wilms, and jaw tumors.¹
• One of the major diagnostic criteria of ECCL includes the presence of biopsy-proven NP.¹
  o NP presents as a unilateral yellowish or skin-colored slightly raised plaque with well-defined or occasionally irregular borders on the scalp.⁵ Characteristic histopathological findings include mature adipose tissue, arrector pili muscles, and sparse or absent mature hair follicles.⁵
• Though the etiology of ECCL is not well understood, it is believed to be related to activating mosaic mutations in the fibroblast growth factor receptor 1 (FGFR1) and KRAS genes.¹
• There is no standard treatment for ECCL. Management includes addressing the clinical features of ECCL, which include follow-up with dermatology, ophthalmology, neurology, and oncology.¹ Recommendations include assessing for lipomas and tumors with routine brain and spinal MRI/MRAs, odontomas with dental examinations, and Wilms tumor with renal ultrasounds until age 8.¹

Teaching Points
• ECCL is a rare neurocutaneous disorder thought to be related to mosaic-activating mutations in the FGFR1 and KRAS genes.
• Nevus psiloliparus can be the presenting feature of ECCL in an otherwise healthy-appearing child.

CASE 3
A 35-year-old female with recrudescence of a blaschkoid vesicular eruption

Presenters
Mayra B. C. Maymone, MD, DSc
Blake Brooks, MD
Leslie Robinson-Bostom, MD
Cathy Massoud, MD

History
A 35-year-old female presented to the emergency department with epigastric pain, fatigue, and a new pruritic vesicular eruption overlying cutaneous hyperpigmentation on the right leg, left arm, and left breast. She reported a similar blistering eruption when she was 13 years old. Of note, she had been treated for H. pylori infection with a triple antibiotic course two months prior to this presentation. During the present admission, she was diagnosed with gastric adenocarcinoma (pT3N3aMx).

Past medical history: Incontinentia pigmenti (IP), epilepsy, migraines, varicella, enucleation of left eye, C-section, tubal ligation

Family history: Mother, sister, and daughter with incontinentia pigmenti; mother with breast cancer

Review of systems: Abdominal pain, fatigue, decreased appetite, weight loss of 10 pounds, tinnitus, and headaches

Medications: All stopped due to healthcare insecurity

Physical Examination
Oral cavity: conical teeth.
Integumentary: several reticulated hyperpigmented patches in a blaschkoid distribution on left upper extremity, trunk, abdomen, and lower extremity. Grouped vesiculobullae on an erythematous base overlying hyperpigmented patches. Right first toe with subungual hyperkeratosis.

Labs and Imaging
Labs: CBC revealed anemia (Hgb 5.9 g/dL) and leukocytosis. BMP, LFTs negative or within normal limits. HSV/VZV PCR cutaneous swab negative.

Imaging: Esophagogastroduodenoscopy with biopsy positive for gastric adenocarcinoma. Staging brain MRI with contrast with no evidence of intracranial metastatic disease. CT chest/abdomen/pelvis negative for metastatic disease.

Genetics: Not performed.

Histopathology
A punch biopsy of the right abdomen showed eosinophilic spongiosis, dyskeratosis, and a perivascular lymphocytic infiltrate with many eosinophils and dermal melanophages. Biopsy of the left forearm showed vacuolar interface dermatitis, hyperkeratosis, papillomatosis, and dyskeratosis with a perivascular lymphocytic infiltrate with many eosinophils and dermal melanophages.

Clinical Images
Incontinentia Pigmenti Recrudescence as a Paraneoplastic Syndrome

Treatment

• The patient was started on clobetasol 0.05% ointment to active skin lesions.
• The patient's gastric adenocarcinoma was initially managed with neoadjuvant FOLFOX chemotherapy (folinic acid, fluorouracil, oxaliplatin). Five months post-admission, the patient underwent gastrectomy with lymphadenectomy. Surgical pathology revealed residual gastric adenocarcinoma with lymphovascular/perineural invasion and positive lymph nodes.
• The patient is now status-post adjuvant chemotherapy and without evidence of disease. Notably, cutaneous symptoms persisted until after gastrectomy and lymphadenectomy.

Discussion

• Incontinentia pigmenti (IP) is an X-linked dominant genodermatosis due to mutation in the nuclear essential modulator (NEMO)/IKKy gene leading to dental, ocular, neurologic, and cutaneous abnormalities.¹
• IP generally affects young children and is rarely reported in adults. Skin lesions follow Blaschko lines and present in four stages: vesiculobullous, verrucous, hyperpigmented, and hypopigmented, which evolve over months to years. Of note, not all stages may be present.²
• Normally, the NEMO/IKKy gene is required for activation of nuclear factor-kB, which is implicated in cell adhesion, immune and stress responses, inflammatory reactions, and protection against TNF-induced apoptosis. In unstimulated cells, NF-kB remains inactive and sequestered in the cytoplasm due to interaction with IkB family. When cells are stimulated (such as by viruses and other cytokine-inducing states), IkB undergoes phosphorylation by IKK, causing rapid degradation of IkB and release of NF-kB.³
• In patients with IP, mutations in NEMO/IKKy encode a non-functional protein, which cannot activate the NF-kB pathway, making the cells more sensitive to apoptosis and hyperproliferation. NEMO-mutated keratinocytes expressing X chromosomes are often destroyed during the first acute episode; however, residual mutated keratinocyte IKKy-deficient cells remain in IP-affected individuals.³
• Reactivation occurs when these cells are exposed to TNF alpha through vaccine, infection, fever, or laser procedures; without NF-kB activation, the cells undergo apoptosis. Repeat cycles of inflammation and apoptosis can occur until all cells with the mutant X chromosome are eliminated.¹,⁴
• To our knowledge, this is the first report of IP reactivation as paraneoplastic syndrome in the English medical literature.
• We hypothesize the mechanism involved in recurrence of IP in the setting of malignancy is based on elevated TNF alpha levels present in H. pylori-associated gastric adenocarcinoma and expression of chemokines implicated in metastasis, leading to stimulation of residual cells with a mutant X chromosome, inability to activate NF-kB, and subsequent apoptosis.⁵

Teaching Points

• Incontinentia pigmenti may demonstrate recrudescence in the setting of illness, vaccines, inflammatory disorders, and Behçet syndrome; malignancy should be added to the list of possible triggers.
• IP recurrence occurs typically in the areas of hyperpigmentation or prior involvement without extra-cutaneous involvement. Multiple episodes may occur.

**CASE 4**  
A 31-year-old female with keratitis-ichthyosis-deafness syndrome

**Presenters**
Leila Shayegan, MD  
Blake Brooks, MD  
Hayley Goldbach, MD  
Christopher DiMarco, MD  
Gladys Telang, MD  
Leslie Robinson-Bostom, MD

**History**
A 31-year-old female presented with a tender growth on the right buttock. The patient had been diagnosed with keratitis-ichthyosis-deafness syndrome as an infant in the setting of sensorineural hearing loss, palmoplantar keratoderma, and mucocutaneous candidiasis, with confirmatory genetic testing demonstrating a G12R mutation in GJB2. She subsequently developed multiple superficial infections, ocular vascularizing keratitis, and porokeratotic eccrine duct and hair follicle nevi. The patient ultimately was found to have a moderately to poorly differentiated squamous cell carcinoma (SCC) of the buccal mucosa metastatic to local lymph nodes with extranodal extension (pT2N2aM0), treated with wide local excision, lymph node dissection, and radiation therapy which was complicated by acute radiation dermatitis and recurrence.

Past medical history: KID syndrome, chronic mucocutaneous candidiasis, hidradenitis suppurativa, Stevens-Johnson Syndrome from fluconazole, SCC of the buccal mucosa

Family history: No family history of genetic disorders

Medications: clindamycin phosphate, hydrocortisone 2.5% cream, mupirocin, ophthalmologic cyclosporine 0.05%, otofloxacin 0.3%, diphenhydramine, gabapentin, hydroxyzine, methadone, ondansetron, pantoprazole, prednisone, sertraline

**Physical Examination**
Several pink hyperkeratotic plaques and papules, some with a collarette of scale, in the perineal region. Exam was otherwise notable for chronic findings associated with known KID syndrome, including scarring alopecia with scattered keratotic nodules, madarosis, generalized xerosis with ten nail dystrophy.

**Labs and Imaging**
Labs: CBC, BMP within normal limits  
Imaging: MRI brain demonstrated an exophytic enhancing mass arising from the right buccal soft tissue and extending through the cutaneous tissue of the right face, with deep invasion of the right maxilla, through the walls of the maxillary sinus, palate, and mandibular angle and body. PET-CT demonstrated avidity in the above regions as well as level 1 and 2 lymph nodes, without avidity in the inguinal or pelvic.

Genetic testing: GJB2 (G12R) Connexin 26 mutation

**Histopathology**
Shave biopsy of the right perineal region demonstrated well-differentiated SCC measuring 2mm in depth with adjacent coronoid lamella consisting of vertical columns of parakeratosis with diminished granular layer and dyskeratosis below. Biopsies of adjacent additional lesions demonstrated coronoid lamellae diagnostic of porokeratosis.

**Clinical Images**
Keratitis-Ichthyosis-Deafness Syndrome Associated with Squamous Cell Carcinoma and Porokeratoses

Treatment

• The patient’s perineal SCC was treated with Mohs surgery and left to heal by secondary intention.
• Cholesterol-lovastatin cream to the groin led to significant improvement in porokeratoses.
• Unfortunately, after treatment with surgery and adjuvant radiation, the patient declined trial of pembrolizumab and succumbed to her oral squamous cell carcinoma.

Discussion

• Keratitis-ichthyosis-deafness syndrome is a rare multisystem disorder due to mutations in connexin 26, a gap junction protein that normally permits intercellular ion flux.1
• Though KID syndrome may be inherited in autosomal dominant or autosomal recessive pattern, the disorder is most commonly sporadic, as in our case.1
• While the hallmark features of KID syndrome include ocular vascularizing keratitis, erythrokeratoderma, and congenital sensorineural deafness, other associated features include the follicular occlusion triad, alopecia, and mucocutaneous candidiasis and other recurrent infections.1
• KID syndrome patients are also at high risk of malignancy, with SCC arising in an estimated 20% of KID patients.1
• Predilection of KID patients to mucosal and cutaneous SCC may be due to impaired integrity of gap junctions leading to increased cellular proliferative potential.2,3,4
• Aberrant gap junctions may also contribute to impaired keratinocyte immune function.4 As in other conditions associated with chronic infections, prolonged inflammation may be implicated in carcinogenesis.
• These same mechanisms may be responsible for the development of multiple porokeratoses, which have been associated with immunosuppression or immunodeficiency and are widely recognized as premalignant lesions.5
• Although porokeratotic eccrine duct and hair follicle nevi (PEHFN) and mosaic forms have been reported in patients with connexin 26 mutations,6,7,8 classic porokeratoses without follicular and eccrine adnexal extension are not commonly seen in KID syndrome.
• Our patient experienced improvement in perineal porokeratoses following topical cholesterol-lovastatin. The mechanism of this drug is to prevent the accumulation of toxic metabolites in the mevalonate pathway, which is typically disrupted in familial porokeratoses but is not known to be affected in KID syndrome.5,9

Teaching Points

• Keratitis-ichthyosis-deafness (KID) syndrome is a rare genetic disorder defined by a classic triad of ocular keratitis, erythrokeratoderma, and deafness and is associated with an increased risk of infection and malignancy.
• Although PEHFN is a well-recognized feature of connexin-26 mutations and KID syndrome, classic porokeratoses are not commonly seen.

References

CASE 5
A 58-year-old female with skin-colored papules in a blaschkoaid distribution

Presenters
Michelle Mai, BS
Scott Bukoski, MD
Leila Shayegan, MD
Keith Choate, MD, PhD
Leslie Robinson-Bostom, MD

History
A 58-year-old female with a known personal history of segmental basaloid follicular hamartoma (BFH) and multiple basal cell carcinomas (BCCs) presented for continued dermatologic care and management. She reported undergoing more than 30 excisions for suspected BCCs since age 19.

Past medical history: Hypothyroidism, depression

Family history: Later reported that her mother had similar papules in a generalized distribution

Medications: Niacinamide, Vitamin D

Physical Examination
On the left hand, forearm, arm, shoulder, neck, back, flank, and thigh were innumerable 1-2 mm clustered, shiny, skin-colored comedo-like papules in a blaschkoaid distribution. There were small pits noted on the palm of the left hand.

Pertinent negatives: No overt skeletal or jaw abnormalities and no alopecic patches.

Labs and Imaging
Labs/Imaging: None

Genetics: Paired whole exome sequencing of both saliva and pathologic cutaneous tissue revealed post-zygotic SMO (smoothened) p.L412F mutations.

Histopathology
A biopsy from a characteristic lesion on the patient’s neck demonstrated anastomosing basaloid strands and horn cysts within a CD34-positive fibrotic stroma. A separate biopsy from a clinically similar lesion also on the patient’s left neck revealed basaloid islands with clefting within a CD34-negative mucinous stroma, consistent with basal cell carcinoma.

Clinical Images
Blaschkolinear Follicular Hamartoma with Associated Basal Cell Carcinomas

Treatment
- The patient is currently taking niacinamide 500 mg twice daily.
- Imiquimod was used in the past but was not well tolerated.
- Future treatment considerations instead of surgery include liquid nitrogen or intralesional fluorouracil or smoothened inhibitors.

Discussion
- BFH is a rare follicular malformation that gives rise to benign skin tumors. Clinical presentations include solitary or multiple small, skin-colored to brown papules in generalized and segmental linear unilateral forms. Palmar pits are commonly described. While BFH is most commonly an acquired condition, autosomal dominant inheritance has also been described.¹²
- While blaschkoid distribution of skin lesions is the most common form of cutaneous mosaicism, linear unilateral BFH is a rare occurrence.³ Blaschkolinear BFH has been reported in patients with Happle-Tinschert syndrome (HTS) and Curry-Jones syndrome (CJS). However, these syndromes tend to involve skeletal, dental, and cerebral abnormalities in addition to cutaneous findings.⁴
- A molecular pathogenic mechanism for BFH has been linked to a post-zygotic SMO p.L412F mutation. Interestingly, this is an identical mutation to that seen in HTS and CJS; however, the delayed embryonic timing of the mutation in BFH limits clinical findings to the epidermis.⁴
- SMO encodes the smoothened (Smo) protein within the sonic hedgehog (Shh) pathway. The typical inactive state of the Shh pathway involves Ptch1 inhibition of Smo, thus preventing downstream proliferative effects. Activating mutations in SMO lead to unrestricted cell growth through GLI-1 transcription factor upregulation as seen in BFH. In addition to HTS, CJS, and BFH, SMO mutations have been described in BCCs, meningiomas, and medulloblastomas.
- Our patient developed numerous BCCs within her unilateral follicular hamartoma. While classically considered a benign condition, multiple subtypes of BCC have been described in the setting of BFH.⁵
- BFH closely mimics infundibulocystic BCC clinically and histologically. Histopathologic patterns favoring BCC include basaloid cells in a mucinous stroma with clefting. Identification of follicular bulbs and papillary mesenchymal bodies are more characteristic of BFH.⁶
- Notably, the stroma in BFH is typically CD34-positive, while it is negative in BCC. Increased expression of Bcl-2 and Ki-67 in BCCs compared with BFH can further aid in the challenging histologic distinction between the two entities.⁴
- Accurate diagnosis of BFH prevents unnecessary resection of benign lesions. Appropriate treatment options include regular clinical monitoring of BFH for malignant transformation and preventative therapies such as niacinamide, imiquimod, or intralesional fluorouracil. Cosmetic procedures such as surgical excision, laser ablation, or dermabrasion may be important to patient satisfaction. If the BFH is associated with an autoimmune condition, corresponding autoimmune disease treatment may improve BFH outcome.¹

Teaching Points
- Because the SMO-mutated field of blaschkolinear BFH can induce both BFH and BCCs, immunohistochemical studies including CD34 and Ki-67 may be diagnostically helpful.
- No standardized treatment exists for BFH. However, frequent monitoring and preventative measures for BCC development should be considered.

CASE 6
A 59-year-old female with multiple pigmented scalp lesions

Presenters
Zaim Haq, BA
Sara Yumeen, MD
Lionel Bercovitch, MD
Oliver Wisco, DO

History
A 59-year-old female presented for evaluation of multiple non-healing scalp lesions. She had been recently diagnosed with triple negative invasive ductal carcinoma of the right breast, for which she underwent genetic screenings to evaluate for possible BRCA mutations. While BRCA mutations were not found, she was found to have a pathogenic variant in PTCH1 (C.448G>T[p.E150]), consistent with basal cell nevus syndrome. Of note, when she enlisted in the military reserve, she was told after getting an X-ray that an area of her jaw was fragile. She had never been diagnosed with skin cancer.

Past medical history: Breast cancer, peripheral neuropathy associated with paclitaxel therapy

Family history: No family history of skin cancer, jaw cysts, or other skin diseases

Medications: None

Physical Examination
There was diffuse alopecia involving the scalp with scattered dark brown to black papules and plaques, with multiple black spicules within them. There were two discrete palmar pits on the left fourth digit and left palm, mild plantar hyperkeratosis, and hyperpigmentation of the proximal nail beds of all fingers.

There were no other lesions of concern on the face, neck, mucous membranes, chest, back, or abdomen.

Labs and Imaging
Genetics: Pathogenic variant in PTCH1 (C.448G>T[p.E150])

Histopathology
Shave biopsies from the right anterior temporal and parietal scalp as well as the left anterior and posterior parietal scalp revealed basal cell carcinoma of superficial, nodular, and pigmented type.

Clinical Images
Gorlin Syndrome (Basal Cell Nevus Syndrome)

Treatment

• The patient was prescribed imiquimod 5% cream to apply daily to the entire scalp for 6 weeks. Additional lesions were found on the patient’s shin and confirmed to be superficial basal cell carcinomas which were also subsequently treated with topical imiquimod for 8 weeks.

• Upon follow-up three months later, lesions were found to have regressed on both scalp and shins and the patient was counseled to continue semi-annual skin exams given the increased risk of skin cancer.

Discussion

• Basal cell nevus syndrome (BCNS) syndrome, also known as Gorlin syndrome, is a rare autosomal dominant genetic disorder primarily characterized by multiple basal cell carcinomas. It is a multisystemic disease that can impact nervous, cardiovascular, and skeletal systems.1

• The age of onset for BCNS can vary, with some patients presenting with BCCs as early as 3 years of age. However, most individuals do not show noticeable symptoms until later in life, with a median age of onset of 25 years.2

• Diagnosis of BCNS requires meeting varying combinations of major, minor, or molecular criteria. These include either one major criterion and molecular confirmation, two major criteria, or one major and two minor criteria.2

• Pathogenesis of this syndrome involves mutations in the tumor suppressor gene PTCH1 which encodes a protein called " Patched-1." The mutated PTCH1 gene fails to properly inhibit the Sonic Hedgehog signaling pathway, resulting in uncontrolled activation and the characteristic clinical features of the syndrome.3

• Identifying mutations in PTCH1 or other related genes, like SUFU, can confirm the presence of Gorlin syndrome and differentiate it from similar conditions. Differential diagnosis includes Bazex syndrome, trichoepithelioma papulosum multiplex, basaloid follicular hamartoma, and Muir-Torre syndrome.1

• Gorlin syndrome requires multidisciplinary care. Although not obligatory for diagnosis, genetic testing for PTCH1 mutations is advised in cases of diagnostic uncertainty or as part of prenatal genetic counseling and presymptomatic diagnosis of siblings.4

• Individuals with Gorlin syndrome should avoid unnecessary X-ray exposure and radiation for basal cell carcinomas or medulloblastomas as the exposed area can develop additional basal cell carcinomas.

• Additionally, due to the heightened susceptibility for skin cancer, adult patients and those who have already been diagnosed with BCC are advised to undergo skin examinations every 4-6 months.1

Teaching Points

• Basal cell nevus (Gorlin) syndrome is a rare genetic disorder involving numerous basal cell carcinomas and multisystemic manifestations.

• Recognition of BCNS in patients with skin of color may be clinically challenging, leading to a delay in diagnosis and treatment.

• Comprehensive treatment for basal cell nevus syndrome may involve regular screenings by dermatologists and medical geneticists.

• Genetic testing should be considered for patients who have a first-degree relative with Gorlin syndrome.

1 Lo Muzio L. Neviod basal cell carcinoma syndrome (Gorlin syndrome). Orphanet J Rare Dis. 2008; 3:32.
# CASE 7

**A 67-year-old male with diffuse eruption, fever, and pulmonary symptoms**

## Presenters

Ogechi Ezemma, BA  
Daniella Reimann, MD  
Laura Burns, MD  
Christopher DiMarco, MD  
Abrar Qureshi, MD

## History

A 67-year-old male presented with an 8-month history of a painful eruption accompanied by fevers, fatigue, shortness of breath, and dry cough. He had previously been evaluated by rheumatology and was prescribed prednisone 30 mg daily and hydrocortisone cream with mild improvement of both cutaneous and systemic symptoms. Within this timeframe, the patient also developed superficial thrombophlebitis and saphenous vein thrombosis. Upon presentation to dermatology, the patient was unable to taper below 10 mg prednisone without recurrence of his eruption and fevers. He denied any new medications or recent sick contacts.

Past medical history/Family history: Unremarkable

Medications: Prednisone 30 mg daily and topical hydrocortisone

## Physical Examination

Tender, erythematous papules coalescing into plaques on the chest and upper back in a V-shaped distribution. Scattered edematous pink papules and plaques symmetrically distributed on the bilateral upper extremities.

No nail, oral mucosal or scalp findings.

## Labs and Imaging

**Labs:**

Positive: CRP 102.9 [0-10], ESR 44 [0-20], Hb 12.1 [13.5-16.0], MCV 100.8 [80.0-98.0]


**Imaging:** Chest X-ray revealed a right lower lobe opacity most suggestive of atelectasis or scarring.

**Genetics:** *UBA1* gene mutation

**Flow cytometry:** Flow cytometry of peripheral blood showed macrocytic anemia and toxic changes within neutrophils (granulation and occasional vacuoles).

## Histopathology

Shave biopsy of the right upper chest showed superficial perivascular and mildly interstitial dermatitis composed of lymphocytes and neutrophils. Shave biopsy of the right arm showed superficial perivascular dermatitis composed of lymphocytes and rare eosinophils consistent with urticaria (not pictured below). PAS-D stain negative for yeast or hyphal elements.

**Clinical Image**
VEXAS Syndrome
(Vacuoles, E1 Enzyme, X-linked, Autoinflammatory, Somatic)

Treatment
- While attempting to taper off systemic steroids, the patient failed dapsone and etanercept monotherapy.
- He is currently well controlled on methylprednisolone 16mg daily, canakinumab 150mg/mL q4 weeks, and colchicine 0.6mg BID.

Discussion
- VEXAS syndrome is a newly described adult-onset autoinflammatory disease predominantly affecting males. It is caused by a somatic mutation in the UBA1 gene on chromosome Xp11.23, leading to elevated IL-1 levels, among other proinflammatory cytokines.¹

Presentation of VEXAS Syndrome²

<table>
<thead>
<tr>
<th>Systemic Manifestations</th>
<th>Cutaneous Findings</th>
<th>Laboratory Abnormalities</th>
</tr>
</thead>
</table>

- **Recurrent fever** (most common)
- **Pulmonary infiltrates / pleural effusion**
- **Thromboembolism / venous thrombosis**
- **Myocarditis / pericarditis**
- **Myositis / arthritis / polychondritis**
- **Uveitis / scleritis / episcleritis**

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neutrophilic dermatoses</strong> (most common)</td>
<td>Neutrophilic dermatosis with myeloid cell infiltration</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>Small to medium vessel LCV</td>
</tr>
<tr>
<td>Erythema nodosum</td>
<td>Mixed perivascular infiltrate with interstitial edema³,⁴</td>
</tr>
<tr>
<td>Urticaria</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Serum</th>
<th>Bone marrow</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrocytosis and macrocytic anemia</td>
<td>Cytoplasmic vacuolization in erythroid and myeloid precursors³</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td></td>
</tr>
<tr>
<td>Elevated ESR/CRP</td>
<td></td>
</tr>
</tbody>
</table>

- VEXAS is commonly associated with hematologic abnormalities, as listed above, leading to myelodysplastic disorders in as many as 50% of patients.⁴
- Systemic steroids are the current first-line treatment. Monotherapy with dapsone, colchicine, and hydroxychloroquine generally do not provide adequate symptom control. **Bone marrow or allogeneic stem cell transplantation is the only definitive treatment** for VEXAS syndrome.³

Teaching Points
- VEXAS syndrome is a multi-system autoinflammatory disease caused by a mutation in the UBA1 gene, leading to elevation in the proinflammatory cytokine IL-1.⁵
- The clinical presentation is highly variable, with neutrophilic dermatoses, vasculitis, recurrent fever, thrombosis, and macrocytic anemia among the most common findings.
- Systemic steroids are the mainstay of treatment; however, there are no standardized consensus guidelines. Canakinumab, an IL-1 inhibitor, has shown early success.⁴

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CASE 8
A 32-year-old female with hidradenitis suppurativa and lower extremity ulcers

Presenters
Isabelle Moseley, AB
Laura Burns, MD
Leslie Robinson-Bostom, MD

History
A 32-year-old female presented for evaluation of a suspected wound infection on her right dorsal foot. She was being treated for hidradenitis suppurativa (HS) of the bilateral inguinal folds and axillae with oral doxycycline and topical clindamycin. The foot ulcer had initially been treated in the emergency department as an abscess with I&D and antibiotics. She developed similar lesions on the lower legs, subsequently receiving multiple courses of oral antibiotics and ultimately was admitted for IV treatment despite negative cultures.

Past medical history: Poorly controlled type 2 DM, obesity, PCOS, acne as a teenager
Family history: No family history of acne or HS
Medications: Insulin, oral contraceptive

Physical Examination
On the bilateral inguinal folds, there was extensive linear cribriform scarring with deep seeded cysts, nodules, double comedones, and sinus tracts with purulent drainage. Bilateral axillae demonstrated hyperpigmented fibrotic plaques studded with papules and pustules. Inframammary skin was unaffected. On the bilateral lower extremities were hyperpigmented plaques with erythematous borders, including on the dorsal right foot where there were three deep, punched-out ulcers with undermined edges and yellow granulation tissue. No nail, oral, mucosal, or scalp findings.

Labs and Imaging
Labs: CBC, CMP, hepatitis panel, and IGRA negative or WNL, except for elevated blood glucose levels (186 – 343)
Wound cultures negative for bacteria and fungi. Bacterial, mycobacterial, and fungal tissue cultures were negative.

Imaging: No imaging

Histopathology
Punch biopsy of an edematous, hyperpigmented plaque with central fluctuance on the right calf demonstrated dermal fibrosis, dense neutrophilic inflammation, and hemorrhage. PAS, Gram, and AFB stains were negative for microorganisms.

Clinical Images
PASH Syndrome
(Pyoderma Gangrenosum, Acne, Suppurative Hidradenitis)

Treatment

- The patient was planning to become pregnant and was started on certolizumab. She demonstrated improvement at a loading dose of 400 mg q2 weeks for 3 doses.
- After decreasing to a maintenance dose of 200 mg q2 weeks, she experienced a severe flare with multiple new draining abscesses. Her course was complicated by several hospital admissions with incision and drainage of abscesses. Two separate wound cultures grew coagulase negative *Staphylococcus aureus*. She improved with prednisone taper and doxycycline.
- She was subsequently switched to secukinumab at a loading dose of 300 mg weekly for 5 doses with a plan for a maintenance dose of 300 mg q4 weeks. She was given a 3-week prednisone taper with initiation of secukinumab and started on spironolactone 50 mg BID due to reported flaring with menses.

Discussion

- PASH syndrome is a rare autoinflammatory syndrome characterized by the triad of *Pyoderma gangrenosum* (PG), Acne, and *Suppurative Hidradenitis*.¹
- PASH is included in a spectrum of disorders defined by clinical presentation and specific genetic mutations, as detailed in the table below.²

<table>
<thead>
<tr>
<th>Definition</th>
<th>Gene mutations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PAPA</strong></td>
<td>Autosomal dominant autoinflammatory disorder</td>
</tr>
<tr>
<td>Pyogenic arthritis</td>
<td></td>
</tr>
<tr>
<td>Pyoderma gangrenosum</td>
<td></td>
</tr>
<tr>
<td>Acne</td>
<td></td>
</tr>
<tr>
<td><strong>PASH</strong></td>
<td>No known gene mutations identified</td>
</tr>
<tr>
<td>Pyoderma gangrenosum</td>
<td></td>
</tr>
<tr>
<td>Acne</td>
<td></td>
</tr>
<tr>
<td>Suppurative hidradenitis</td>
<td></td>
</tr>
<tr>
<td><strong>PAPASH</strong></td>
<td>Not fully elucidated</td>
</tr>
<tr>
<td>Pyogenic arthritis</td>
<td></td>
</tr>
<tr>
<td>Pyoderma gangrenosum</td>
<td></td>
</tr>
<tr>
<td>Acne</td>
<td></td>
</tr>
<tr>
<td>Suppurative hidradenitis</td>
<td></td>
</tr>
</tbody>
</table>

- Treatment of PASH syndrome is challenging as classic immunosuppressive agents often fail to achieve adequate control. More recently, treatment focus has shifted towards biologics.
- The pathogenesis of PASH is thought, in part, to be mediated by aberrant release of IL-1β. This results in increased chemokines including TNF-α and IL-17, which synergistically recruit and activate neutrophils.³
- Thus, medications targeted against both TNF-α and IL-17 have been used in treatment of PG and HS with mixed success. IL-17 inhibitors specifically have demonstrated cases of clearance as well as paradoxical PG and HS exacerbations.⁴ Further studies will be required to establish the success in PASH patients.

Teaching Points

- PASH is a hereditary autoinflammatory syndrome characterized by the triad of *Pyoderma gangrenosum*, Acne, and *Suppurative Hidradenitis*.
- Specific guidelines for the treatment of PASH syndrome are lacking, although evidence is beginning to accumulate in favor of medications targeting TNF-α and IL-17.

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CASE 9
A 6-year-old female with vascular plaques, bleeding, and thrombocytopenia

Presenters
Lindsey (Lou) Gaghan, MD
Leila Shayegan, MD
Christopher Elco, MD
Lionel Bercovitch, MD
Leslie Robinson-Bostom, MD

History
At birth, an ex-full term female neonate was noted to have more than 15 vascular plaques distributed over the trunk, extremities, and neck. A preliminary diagnosis of neonatal hemangiomatosis was made.

At 2 weeks of age, the patient was admitted with hematemesis, melena, and thrombocytopenia. Hospitalization was complicated by gastrointestinal bleeding with anemia requiring repeated platelet and red cell transfusions and endoscopic sclerotherapy of actively bleeding lesions. Sirolimus therapy was initiated, eventually leading to stabilization without the need for further transfusions.

At 23 months, the patient contracted adenovirus and rhinovirus and developed acute respiratory distress syndrome (ARDS) requiring intravenous corticosteroids, antibiotics, and extracorporeal membrane oxygenation (ECMO). She recovered, and sirolimus was discontinued.

Prenatal history: Maternal history of cerebral venous sinus thrombosis at 28 weeks treated with enoxaparin

Family history: No additional family history of vascular anomalies or hematologic abnormalities

Physical Examination
July 2017, Birth: Well-circumscribed 3.5cm violaceous vascular plaque extending from the right mastoid process to inferior ramus of the mandible and 17 blanching purple 2-4mm papules scattered over the extremities, buttocks, and trunk.

August 2023, 6 years old: Focally faded vascular plaques on the neck and trunk.

Labs and Imaging

<table>
<thead>
<tr>
<th>Age</th>
<th>Date</th>
<th>Hgb</th>
<th>Plt</th>
<th>Other results</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 weeks</td>
<td>August 2017</td>
<td>7.7</td>
<td>47</td>
<td>CXR and CT chest: numerous bilateral pulmonary nodules. EGD: 6 actively bleeding gastric vascular lesions.</td>
</tr>
<tr>
<td>27 months</td>
<td>Oct 2019</td>
<td>12.0</td>
<td>48</td>
<td>Pelvic X-rays: new lytic and sclerotic pelvic bone lesions.</td>
</tr>
<tr>
<td>31 months</td>
<td>Jan-Feb 2020</td>
<td>10.4</td>
<td>107</td>
<td>EGD: 6 non-active vascular lesions, smaller than prior. Whole body MRI without contrast: numerous muscular nodules and extensive abnormal bone marrow signaling in pelvis and femurs.</td>
</tr>
<tr>
<td>3 years</td>
<td>July 2020</td>
<td>11.2</td>
<td>86</td>
<td>Pelvic MRI with contrast: decreased size and hyperintensity of bone marrow and nodules.</td>
</tr>
<tr>
<td>6 years</td>
<td>August 2023</td>
<td>12.9</td>
<td>333</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Histopathology
At 2 weeks of age, three punch biopsies from vascular plaques on left thigh, right neck, and right buttock demonstrated complex vascular channels in the reticular dermis and subcutis with mural projections and endothelial redundancy. Lesional endothelial cells stained positive for ERG and CD34. D2-40 staining was focally positive. GLUT-1 staining was negative.
Clinical Images

2 weeks

6 years
Multifocal Lymphangioendotheliomatosis with Thrombocytopenia

Treatment

• The patient was initiated on oral sirolimus starting at 0.1mg/kg/day (titrated to serum level 10-13 ng/mL) from 8/2017 to 6/2019. She was prophylaxed with sulfamethoxazole-trimethoprim and pentamidine.
• Sirolimus was discontinued in the setting of ARDS in 2019. The subsequent four years after discontinuation have remained uncomplicated. She has had regular follow up with hematology/oncology and vascular anomalies clinic. She remains stable without systemic treatment and with observation of her bony lesions. Most of her cutaneous vascular lesions have gradually faded. Platelet count has normalized.
• Gastric lesions were treated initially with endoscopic sclerotherapy when actively bleeding, then with electrocautery two years later given improvement. There have been no further episodes of GI bleeding.

Discussion

• Multifocal lymphangioendotheliomatosis with thrombocytopenia (MLT) is a condition defined by congenital vascular proliferations involving the skin and gastrointestinal tract with associated thrombocytopenia. MLT typically presents in the first weeks of life with cutaneous plaques with or without gastrointestinal bleeding. First described in 2004, MLT is a relatively new diagnosis with little known about long-term prognosis and complications for those patients that survive infancy.\(^1,2\)
• Cutaneous and gastrointestinal lesions are most commonly reported, though central nervous system, pulmonary, and musculoskeletal involvement (including lytic bone lesions) can occur.\(^3\) Little information is available regarding the symptomatology, effect on physical functioning, and clinical course of associated lytic bone lesions. In our patient, they presented late in her course, were asymptomatic, and improved without treatment by three years of age.
• Histology classically demonstrates dilated dermal and subcutaneous vessels with hobnailed, proliferative endothelial cells and intraluminal papillary projections. These may be positive for LYVE or D2-40.\(^1\)
• Previously reported systemic treatments include sirolimus, bevacizumab, vincristine, propranolol, and corticosteroids.\(^2,4\) Sirolimus, an mTOR inhibitor, has been a popular choice for MLT given its antiangiogenic properties and favorable risk profile for use in pediatric patients. The most common adverse effects include hyperlipidemia, mucositis, hypogonadism, and myelosuppression.\(^5\)
• Sirolimus-induced pulmonary toxicity is a rare complication that has been primarily reported in the adult solid organ transplant literature. To date, fewer than 10 pediatric cases of sirolimus-induced pulmonary toxicity have been reported, all of which occurred within one year of initiating therapy.\(^6\) Given concomitant adenovirus infection in our patient, pre-existing pulmonary nodules, and two years of treatment with sirolimus, it is unclear what role sirolimus may have played in the development of ARDS.

Teaching Points

• MLT is a rare vascular disorder that can result in life-threatening anemia and thrombocytopenia. While cutaneous and gastrointestinal involvement are most common, lesions can also arise in the bones, muscle, and nervous system. Multidisciplinary follow-up is warranted.
• Sirolimus is an mTOR inhibitor and an effective treatment option for many vascular tumors and malformations. Pulmonary toxicity is an uncommon but potentially severe side effect.

CASE 10
A 59-year-old female with red pruritic plaques on the back

Presenters
Taylor E. Arnoff, BA
Pavane L. Gorrepati, MD
Gladys H. Telang, MD

History
A 59-year-old female presented with a one-year history of red plaques on the back and episodic pruritic eczematous dermatitis on the neck and right axilla. She had rapid resolution of the neck and axillary rash with topical steroids, but minimal improvement of the plaques on her back. The patient developed the back plaques one week after a seven-week course of daily radiation for right-sided breast cancer one year prior. Three biopsies from the back were performed over a two-year period. The patient had no upper extremity lymphedema.

Past medical history: Invasive ductal carcinoma of the right breast (clinical stage IIB: T2 multifocal, N1, M0 Grade 2, ER>90% positive, HER2/neu-3+ positive, PR-negative). She received six cycles of neoadjuvant chemotherapy (docetaxel, carboplatin, pertuzumab, trastuzumab). She underwent right mastectomy with right axillary sentinel lymph node biopsy (four negative nodes) and prophylactic left mastectomy. She received 52 weeks of herceptin and a total dose of 5000 cGy in 25 fractions to the right chest. Breast reconstruction was done. Anastrozole was initiated after radiation, but discontinued after two weeks due to hot flashes.

Family history: Unremarkable
Medications: No medications

Physical Examination
On the anterior neck extending to the superior chest was an ill-defined pink plaque with fine xerotic scale. Along the right scapular region and mid-back was a 25 cm x 8 cm pink plaque with overlying fine scale. The left mid-back exhibited a 5 cm pink scaly plaque. Greater severity was noted on the right side. There was no hair, mucosal, or nail involvement.

Labs and Imaging
Labs: Negative HepB sAg, Hep C Ab, HIV Ag/Ab, RPR, IGRA, ANA, and RF. HbA1c, ESR, ACE, and calcium levels were within normal limits.

Imaging: Chest X-ray showed no hilar adenopathy and no interstitial or granulomatous lung disease.

Histopathology
A punch biopsy of the right back demonstrated a well-formed epithelioid granulomas and a few admixed eosinophils in the superficial, mid, and deep dermis. D2-40 and CD-31 stains highlighted the endothelial lining of dilated vessels and lymphatics. Lichenoid and spongiotic features were also focally present. C-myc stain was negative on the prominent vasculature.

Clinical Images
Isoradiotopic Granulomatous, Lichenoid, and Spongiotic Dermatitis with Angiectasias in a Radiation Field

Treatment

- The patient was treated with several courses of clobetasol propionate 0.05% ointment, hydrocortisone valerate, and betamethasone dipropionate 0.05% ointment which all resulted in modest initial improvement. However, the patient continually relapsed when off therapy. The left mid-back plaque improved while the right-sided plaque persisted.
- Given the incomplete response, repeat biopsies were performed to rule out an atypical lymphoproliferative condition. Biopsy demonstrated a persistent lichenoid and granulomatous dermatitis with angiectasias.
- Patient declined a trial of oral hydroxychloroquine, preferring topical treatments.

Discussion

- Isoradiotopic responses are a rare phenomenon associated with radiotherapy and describe unrelated secondary dermatoses occurring in a prior site of radiation.
- Reports in the literature of isoradiotopic responses have depicted cases of discoid lupus erythematosus, lichen planus, pemphigus vulgaris, lichen planopilaris, bullous pemphigoid, morphea, hidradenitis suppurativa, and prurigo nodularis arising within areas of prior radiation. Most of these reported histopathologic changes have been localized to the radiation field.
- It is hypothesized that radiation increases the expression of pro-inflammatory molecules, driving an influx of CD8+ cytotoxic T-cells that damage the dermal-epidermal junction. This leads to a cycle of increased lymphocytic infiltrates, resulting in a persistent dermatitis.
- The patient’s initial punch biopsy demonstrated granulomatous, lichenoid, and spongiotic dermatitis. Lichenoid granulomatous dermatitis (LGD) is associated with infectious processes, drug eruptions, hepatobiliary disorders, endocrinopathies, systemic lupus erythematosus, rheumatoid arthritis, systemic vasculitis, cutaneous T-cell lymphoma, and other lymphoproliferative disorders.
- Repeat biopsy three months later demonstrated granulomatous dermatitis with dilated superficial capillaries and lymphatics, but lichenoid inflammation was not present. Given persistent granulomatous dermatitis and angiectasia in a radiation field, evaluation for atypical lymphoproliferative conditions, post-radiation angiosarcoma, and lymphangiosarcoma, was performed. C-myc staining was negative in the angiectasia.
- Many types of primary cancers have been reported in cases of radiation-induced dermatoses, including breast cancer, and prior cases have reported that post-radiation dermatoses typically occur up to four months following treatment. This aligns with our patient’s timeline of symptom onset one week after completing radiation.
- Given the patient’s history of radiation therapy and negative work-up, her findings were attributed to radiation scatter leading to a case of isoradiotopic granulomatous, lichenoid, and spongiotic dermatitis within a radiation field and extending focally to the periphery of the treatment zone.
- To our knowledge, this is the first case to demonstrate LGD following radiation therapy.

Teaching Points

- Isoradiotopic responses are a rare phenomenon associated with radiotherapy and describe dermatoses that develop within a prior radiation field.
- In patients with persistent granulomatous dermatitis, surveillance biopsies are recommended to rule out an underlying lymphoproliferative condition.

CASE 11
A 70-year-old female with firm vulvar papules and red-purple papules on the bilateral medial thighs

Presenters
Megan Tran, BS
Yostina Farid, MD
Laura Burns, MD
Leila Shayegan, MD
Gladys Telang, MD
Leslie Robinson-Bostom, MD

History
A 70-year-old female presented with a 28-year history of nontender, pink papules on the mons pubis and labia majora following radiation therapy for cervical cancer. Several of her vulvar lesions had been biopsied or removed. She was told that the lesions were angiokeratomas without further work-up. The patient also reported a more recent 6-year history of asymptomatic red-purple papules on the right medial thigh. Involvement of the left medial leg began four years later. The patient had extensive imaging performed of the right lower extremity for possible lymph node transplant near the time of thigh papule appearance. She was told that these lesions were vascular without further detail.

Past medical history: Radical hysterectomy, bilateral salpingo-oophorectomy with lymph node dissection and radiation for Stage 1B carcinoma of the cervix (1994)

Family history: Unremarkable

Medications: No medications

Physical Examination
On the right mons pubis and bilateral labia majora, there were several semi-firm and translucent to pink 7-10 mm papules. On the bilateral medial thighs, there were clustered round, dull red-purple, smooth papules. There was symmetric chronic lymphedema of the bilateral lower extremities.

Labs and Imaging
Labs: Within normal limits.

Imaging: No Imaging.

Histopathology
a) Biopsy of the right mons pubis and left labia majora showed mild epidermal acanthosis with widely ectatic and dilated lymphatic vessels filling and expanding the papillary dermis. Lesional cells stained positive with D2-40 and ERG. Staining for C-myc and HHV-8 was negative.

b) Biopsy of the right medial thigh demonstrated angiectasia with perivascular lymphocytic inflammation and scattered angulated multinucleated giant cells.

Clinical Images
Post-Radiation Acquired Lymphangioma and Multinucleate Cell Angiohistiocytoma

Treatment

• The patient was advised to continue use of compression stockings and home lymphatic massage machine.

Discussion

Acquired vulvar lymphangioma

• Acquired vulvar lymphangioma, also known as lymphangiectasia, is a rare, benign disease typically secondary to pelvic lymphatic obstruction.
• This may occur in the setting of prior radiotherapy, such as in our patient, post-pelvic surgery adhesions, lymphadenectomy, Crohn disease, or tuberculosis. It often presents years after radiation or surgery.
• Treatment of acquired vulvar lymphangioma aims to reduce underlying lymphedema, reduce infection risk, and address discomfort and cosmetic concerns. Options include carbon dioxide lasers, sclerotherapy, cryotherapy, cauterization, and surgical excision. Recurrence is common.
• Surgical excision may be considered for extensive disease or failure to respond to other treatments.

Multinucleate cell angiohistiocytoma

• Multinucleate cell angiohistiocytoma is also a rare, benign condition that typically follows a progressive course without tendency for spontaneous regression. The average age of onset is 50, with a strong female predominance.
• As seen in this patient, multinucleate cell angiohistiocytoma classically presents as red-brown to violaceous dome-shaped smooth papules which can clinically resemble Kaposi sarcoma. Lesions are most frequently found on the extremities, often in a random, linear, or annular pattern.
• Histopathology demonstrates dilated capillaries and small vessels in the dermis, mid-dermal fibrosis with thickened collagen bundles, and the presence of angulated multinucleated cells.
• The pathogenesis is not fully understood but is hypothesized to be an inflammatory response to intravascular macrophage migration and increased dermal vascularity. Affected areas have been shown to overexpress estrogen receptor-α as supported by the fact that estrogen signaling is linked to angiogenic effects. Fibrosis and atrophy are also hypothesized to play a role in the pathogenesis, especially regarding the progression to multiple lesions.
• In this patient who presented with multiple lesions, we suspect the development of multinucleate cell angiohistiocytoma was a reactive process secondary to radiation-induced skin injury as well as lymph node dissection induced lymphedema.
• Treatment is not necessary but may be considered for cosmetic reasons or due to pruritus. Options include intralesional corticosteroids, surgical excision, cryotherapy, laser, and intense pulsed light.

Teaching Points

• Acquired vulvar lymphangiomas can be seen in patients with chronic pelvic lymphatic obstruction, which commonly occurs in the setting of prior pelvic surgeries or radiation therapy.
• Multinucleate cell angiohistiocytoma is a rare, benign diagnosis that can resemble Kaposi sarcoma clinically and may occur in association with radiation-induced skin injury and lymphedema.

CASE 12
A 69-year-old female with purple and brown nodules on the left leg

Presenters
Idowu Olugbade, BS
Benjamin Gallo Marin, MD
Fatima N. Mirza, MD, MPH
Ronald Bukoski, MD
Gladys H. Telang, MD

History
A 69-year-old Hispanic female with rheumatoid arthritis presented with a six-month history of purple-red nodules and brown lesions on the left lower leg, ankle, and foot. The patient denied precedent trauma. The lesions were slowly increasing in size. Notably, the patient was taking long term hydroxychloroquine. Tofacitinib was also started for her rheumatoid arthritis one year prior to her presentation. There was no history of organ transplant.

Past medical history: Rheumatoid arthritis, erosive osteoarthritis s/p bilateral knee replacements, asthma, heart failure with preserved ejection fraction (HFpEF), insulin-dependent T2DM, hypothyroidism, and HSV

Family history: No family history of autoimmune disease

Medications: tofacitinib, insulin, hydroxychloroquine

Physical Examination
On the dorsal left foot, left lateral ankle, and left calf were multiple firm purple-red nodules and brown plaques ranging in size from approximately 2 mm to 10 mm. On the right medial calf, there was one 4 mm round dull red-purple macule. There was no mucosal involvement.

Labs and Imaging
Labs: CBC, TSH, and lipid panel within normal limits. HIV negative

Imaging: No Imaging

Histopathology
Biopsy of a nodule revealed marked vascularity, inflammation, and extravasated erythrocytes. There was a dense dermal proliferation of small, well-formed, endothelial-lined blood vessels, highlighted by a CD31 stain, irregular slit-like vascular spaces with interspersed interstitial spindle cells, and a brisk background lymphohistiocytic infiltrate with occasional plasma cells. HHV-8 immunostaining showed few scattered immunoreactive cells supporting a diagnosis of Kaposi sarcoma. Biopsy of a brown patch revealed brown and grey pigment throughout the dermis (Prussian Blue+ and Fontana Masson+ stains, HHV8-), supporting drug deposition, likely hydroxychloroquine.

Clinical Images
JAK Inhibitor Induced Kaposi Sarcoma

Treatment

- Tofacitinib was discontinued. The patient was started on alitretinoin 0.1% gel to the left leg and foot lesions BID. Lesions began to diminish. She experienced one episode of irritation at two months of therapy and was decreased to once daily application to all lesions with continued improvement.

Discussion

- Kaposi sarcoma (KS) is vascular endothelial neoplasm associated with KS-related herpesvirus/human herpesvirus-8 (KSHV/HHV-8) infections.
- There are 4 described clinical variants of KS:\textsuperscript{1,2}
  - Classic KS: Indolent purple or reddish-brown patches or nodules that occur on the lower extremities; common in older males of Mediterranean, Eastern European, or Middle Eastern descent.
  - Endemic/African KS: Commonly affects individuals in Sub-Saharan African; typically found in younger individuals. Locally aggressive and invasive compared to the classic variant.
  - Epidemic/AIDS-Related KS: Associated with HIV infection and AIDS.
  - Iatrogenic/Immunosuppression-Related KS: Associated with immunosuppressive drugs, most commonly after organ transplantation.
- A retrospective study of 137 patients with KS reported 37 cases of iatrogenic KS: 10 organ transplant patients on various immunotherapy medications and 16 cases reported following systemic corticosteroid use for various conditions.\textsuperscript{2} A subset of these were on concomitant immunosuppressive therapies such as cyclosporine, mycophenolate mofetil, leflunomide, or methotrexate.
- Tofacitinib is a small-molecule immunomodulator that inhibits Janus kinases (JAK1, JAK3, and lesser interaction with JAK2), surface protein mediators of intracellular cytokine-dependent inflammatory signaling pathway, thereby interfering with lymphocytic activation, proliferation, and function to modulate the immune response in diseases such as rheumatoid arthritis, alopecia areata, psoriatic arthritis, and ulcerative colitis.\textsuperscript{3}
- Tofacitinib has been associated with serious adverse events related to immunosuppression including infections and reactivation of latent viruses (e.g. varicella zoster, herpes simplex, and cytomegalovirus).
- There is one reported case of tofacitinib-associated iatrogenic KS in a 61-year-old HIV-negative male patient on two years of tofacitinib therapy for treatment-resistant ulcerative colitis.\textsuperscript{4}
- Treatment options include local therapies (such as radiation and cryotherapy) and systemic therapies (such as anthracycline, paclitaxel, vinblastine, vincristine, or interferon-α).\textsuperscript{5}
- Alitretinoin, a vitamin A derivative, is a topical therapy that has shown promise in the treatment of KS.
  - The proposed mechanism of action is via the modulation of cell growth, differentiation, and apoptosis by binding to specific retinoic acid receptors (RAR-α, RAR-β, RAR-γ) and retinoid X receptors (RXR-α, RXR-β, RXR-γ).\textsuperscript{5} In a randomized controlled trial of 134 patients, alitretinoin 0.1% gel was shown to be effective at treating AIDS-related KS. Local irritation was reported as the most common adverse event (32%).\textsuperscript{5}
  - Residual brown plaques exhibited drug deposition on biopsy, staining positive for Fontana Masson and Prussian Blue. The brown plaques did not change with either oral or topical treatment.

Teaching Points

- Iatrogenic immunosuppressed patients presenting with new skin lesions, especially on the lower extremity, should be closely monitored for KS.
- Alitretinoin is a topical patient-administered therapy effective at treating KS with minimal side effects.

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CASE 13
A 45-year-old female with a pruritic, blaschkoid rash after a COVID-19 infection

Presenters
Seungmin (Mina) Woo, BA
Lindsey (Lou) Gaghan, MD
Leslie Robinson-Bostom, MD
Elnaz Firoz, MD

History
A healthy 45-year-old female presented with a six-month history of a pruritic eruption that began suddenly 10 days after a COVID-19 infection. The rash started on the right abdomen and then progressed to the same side of the back. Over the next few months, the eruption spread to hermons and anteromedial thigh, eventually crossing the midline to the left thigh. Given the initial dermatomal distribution, the patient was treated empirically for herpes zoster with valacyclovir by her primary care provider without improvement. The eruption was also recalcitrant to triamcinolone acetonide and betamethasone creams prior to presenting to our clinic. Of note, the patient had received her first Pfizer-BioNTech COVID-19 vaccine booster 4 months prior to COVID-19 infection. She did not receive nirmatrelvir/ritonavir during her COVID-19 infection.

Review of systems was negative for systemic complaints, oral lesions, or other skin rashes.

Past medical history: None
Family history: No family history of autoimmune disease or cutaneous disorders
Medications: Supplemental oral iron, norethindrone, multivitamin, ibuprofen

Physical Examination
In a blaschkoid distribution over the right flank, hip, abdomen, and thigh were violaceous papules coalescing into plaques with surrounding erythema. No vesicles were appreciated. There were no nail, oral, or mucosal findings.

Labs and Imaging
Labs: ANA 1:180 and low total 25-OH vitamin D at 20.8 ng/mL (ref range: 30.0-100.0 ng/mL).

Histopathology
Punch biopsy from the right lateral abdomen demonstrated lichenoid interface dermatitis with eosinophils.

Imaging: No imaging
Blaschkoid Lichen Planus after a COVID-19 Infection

Treatment

- Given the disfiguring nature of the eruption and the patient’s concern, therapy with metronidazole 500mg BID, doxycycline 100mg BID, and hydroxychloroquine 200mg BID was initiated. For the pruritic component, hydroxyzine 10mg QHS was initiated.
- The patient noted slowing of disease spread and improvement in pruritus soon after starting treatment, but due to gastrointestinal side effects of vomiting and diarrhea, the patient self-decreased the frequency of all medications to once daily.
- After 2 months of therapy, there was significant clinical improvement. Metronidazole was discontinued while doxycycline was decreased to 50mg BID to help with GI side effects. Hydroxychloroquine was recommended at a frequency of 200mg BID.
- After 4 months of doxycycline, the patient self-discontinued due to persistent GI discomfort but was able to continue hydroxychloroquine without side effects.
- Current treatment also includes topical skin lightening agents to help with hyperpigmentation associated with her condition.

Discussion

- Lichen planus (LP) is an inflammatory condition which typically presents with pruritic violaceous papules and coalescent plaques frequently distributed on the distal extremities. Oral, genital, and nail involvement is common. Post-inflammatory hyperpigmentation is also common.  
  1
- Blaschkoid LP, sometimes referred to as “linear” or “zosteriform” LP, is rare, comprising less than 0.5% of LP cases. It is thought to be due to post-zygotic antigenic mosaicism of keratinocytes, resulting in a collection of cells along epidermal migration pathways that are more prone to development of LP.  
  2
- Histopathology of LP classically shows a band-like lymphocytic infiltrate. Eosinophils are typically scarce or absent in classic LP in contrast to hypertrophic LP and lichenoid drug eruptions.  
  3
- LP activation is a rare complication of COVID-19 infection and vaccination. Just over 200 initial presentations of LP have been reported in the literature with onset within 30 days of infection or vaccination.  
  4
- Current hypotheses of the pathogenesis of disease focus on induction of apoptosis of basal keratinocytes. Possible mechanisms include general activation of B-cells, CD8+ cytotoxic T-cells, and CD4+ helper T-cells, as well as molecular mimicry caused by cross-reactivity of the SARS-CoV-2 antigen with ACE2 receptors on basal keratinocytes.  
  4
- Vitamin D deficiency has been associated with LP activation after COVID-19 infection. However, limited evidence supports the efficacy of vitamin D supplementation in the treatment of LP.  
  4
- Oral corticosteroids can be considered for the treatment of diffuse cutaneous LP. In recalcitrant cases, hydroxychloroquine and metronidazole have shown to be effective steroid-sparing treatment options for cutaneous LP. Oral antihistamines may also be prescribed to control itch associated with cutaneous LP.  
  5

Teaching Points

- LP is a rare complication following COVID-19 infection and vaccination.
- Antigenic mosaicism in individuals may lead to a blaschkoid distribution of LP and pose a diagnostic challenge.

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CASE 14
A 59-year-old female with multiple spiny follicular papules after renal transplant

Presenters
Mayra B. C. Maymone, MD, DSc
Fatima N. Mirza, MD, MPH
Reginald Gohh, MD
Christopher DiMarco, MD
Leslie Robinson-Bostom, MD

History
A 59-year-old female with a past medical history of a renal transplant secondary to biopsy-proven ANCA-associated vasculitis presented with a generalized eruption on the face, trunk, and upper extremities. The eruption developed seven months after renal transplant.

A skin biopsy was performed at an outside office, and the patient had been trialed on topical acyclovir and discontinued mycophenolate mofetil without improvement. She was referred to this dermatology service and had two biopsies performed of the left shoulder and nose.

Past medical history: Renal transplant secondary to ANCA-associated vasculitis and glomerulonephritis
Family history: No relevant family history
Review of systems: Unremarkable
Medications: Tacrolimus, rosuvastatin, rivaroxaban, famotidine

Physical Examination
There were multiple 1-2 mm skin-colored follicularly-based papules with fine white spicules on the face, trunk, and upper extremities.

Pertinent negatives: There was no hair loss on the trunk or extremities.

Labs and Imaging
Labs: Tacrolimus level: 8.6 ng/mL

Histopathology
Punch biopsy of the left shoulder revealed a dilated and plugged follicle with parakeratosis replacing the hair shaft. Punch biopsy of the right nasal bridge revealed a distorted and enlarged follicle with a widened inner root sheath, large eosinophilic trichohyalin granules, and hair matrix with abortive hair shaft keratin formation.
Viral-Associated Trichodysplasia

Treatment

- The patient was treated with oral valganciclovir 450 mg twice daily for 4 months and was later decreased to 450mg daily for 10 months with significant improvement.
- Topical cidofovir was prohibitively expensive and tazarotene resulted in extensive xerosis.
- She continued topical acyclovir twice a day for maintenance.

Discussion

- Viral-associated trichodysplasia is a rare follicular disorder also known as trichodysplasia of immunosuppression and has previously been reported as trichodysplasia spinulosa, follicular spicules of the nose, pilomatrix dysplasia, and cyclosporine-induced follicular dystrophy.\(^1,2\)
- This condition was first reported in 1995 in a renal transplant recipient and described in 1999 in patients with solid organ transplants on immunosuppressive therapy. It has also been seen in patients with pre-B cell leukemia, acute and chronic lymphocytic leukemia, and non-Hodgkin lymphoma.\(^3,4\)
- Viral-associated trichodysplasia is caused by trichodysplasia spinulosa associated polyomavirus (TSPyV), also known as human polyomavirus (HPyV8), a small double-stranded DNA virus discovered in 2010. Seroprevalence in healthy individuals ranges from 63-80%. The virus appears to have low infectivity in immunocompetent hosts.\(^1\)
- The pathogenesis is not fully understood, and it is unclear if this is a reactivation of latent infection or a primary infection.
- Clinically, the lesions are skin colored to pink follicular papules that may coalesce into plaques primarily involving the face, specifically the nose and nasolabial folds, but may affect the trunk and extremities.\(^3\)
- Histopathology is characterized by dilated hair follicles without hair shafts, keratin plugging of the follicular infundibulum, a dystrophic inner root sheath, or enlarged trichohyalin granules.
- The diagnosis is based on clinical and histological findings in addition to PCR for TSPyV. Pull test of a spicule for microscopic evaluation of inner root sheath keratinization may be a useful non-invasive diagnostic tool.\(^1\)
- There is no standard treatment for viral-associated trichodysplasia, and while reduction of immunosuppressive therapy has been shown to improve disease, this is not always possible.\(^1,5\)
- Other treatment options described in the literature with variable success include topical cidofovir, tazarotene gel, imiquimod, oral valganciclovir, and photodynamic therapy.\(^5\) The reported side effects of valganciclovir may include nausea, emesis, retinal detachment, peripheral neuropathy, and pancytopenia. Laboratory monitoring with at least CBC with differential and renal function is recommended, and closer monitoring in patients receiving other nephrotoxic medications such as tacrolimus, cyclosporine, aminoglycosides, and amphotericin B is indicated.\(^6\)

Teaching Points

- Viral-associated trichodysplasia is a rare disorder among solid organ transplant recipients.
- Although trichodysplasia has a characteristic histopathology, some biopsies may only show dilated and plugged follicles with parakeratosis replacing the hair shaft. Dermatopathologists and clinicians should be aware that multiple biopsies may be required to appreciate the classic histopathologic findings.
- When reduction of immunosuppression is not feasible or effective, treatment with oral valganciclovir is a well-tolerated and efficacious option.

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CASE 15
A 30-year-old male with hypopigmented verrucous papules on the oral mucosa

Presenters
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Mohamed Omer, MD, MHA, MSc
Sara Yumeen, MD
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Hayley S. Goldbach, MD
Sook-Bin Woo, DMD
Gerard J. Nuovo, MD
Leslie Robinson-Bostom, MD
Deep Joshipura, MD

History
A 30-year-old male of North Haitian descent presented with white papules on the lips that had been present for one year and were asymptomatic; however, the patient was bothered by associated dyspigmentation and rough texture. The patient admitted to picking the lesions as well as a history of cheilitis worsened by manipulation. He also reported a papule on the right third digit that had been present for many years. He did not have a known history of immunosuppression. He self-reported negative HIV testing.
Past medical history: Unremarkable
Family history: Unremarkable
Medications: No medications

Physical Examination
There were multiple soft, light pink to white verrucous, exophytic papules on the upper and lower mucosal lip and gingival mucosa. On the right third digit of the upper extremity, there was a firm, skin-colored hypertrophic papule consistent with verruca vulgaris.

Pertinent negatives: There was no genital involvement.

Labs and Imaging
Labs: Initial in situ hybridization (ISH) testing for low-risk and high-risk HPV was negative. Testing for the HPV L1 capsid protein using a consensus antibody (Biocare Medical, Pacheco, CA) was positive. Further ISH testing yielded positivity for HPV-13.

Imaging: No Imaging

Histopathology
Biopsy from midline lower lip mucosa showed epithelial hyperplasia, elongated rete ridges, and parakeratosis with three karyorrhectic cells, two of which appeared “mitosoid” but were located away from the basal layer.
Heck Disease (Focal Epithelial Hyperplasia)

Treatment

- The patient was initially treated with cryotherapy and subsequently elected for the removal of the remaining lesions with excision due to greater clearance with biopsy than cryotherapy.

Discussion

- This patient was diagnosed with focal epithelial hyperplasia (FEH), also known as Heck Disease or multifocal epithelial hyperplasia.

- FEH is a benign mucosal proliferation strongly associated with the low-risk human papillomavirus (HPV) subtypes HPV-13 and HPV-32.  

- FEH is clinically characterized by multiple asymptomatic exophytic white to mucosal-colored papules or nodules on the oral mucosa, gingiva, tongue, and lips, and histopathologically by epithelial hyperplasia with parakeratosis and acanthosis, ballooning degeneration, mitosoid bodies, koilocytosis, and thickened rete ridges.  

- Most reported cases of FEH are in children or in immunocompromised adults. FEH is endemic in some communities in Greenland and North Canada, Colombia, Brazil, and South Africa. Only one other case has been reported in a person of Haitian descent. In that case, HPV-32 was detected (as opposed to HPV-13 in our case), and the patient was an immunosuppressed child (as opposed to a healthy adult in our case).

- Initial HPV *in situ* hybridization testing was negative in our study; however, HPV-13 and HPV-32 are not usually included in low-risk panels. Therefore, a negative ISH result may not rule out FEH. It is important to differentiate FEH from other oral verrucae that may be acquired due to sexual contact, particularly as some HPV high-risk subtypes may lead to squamous cell cancer. In children, this is particularly important to identify sexual abuse.

- Treatment for FEH is optional, and modalities include imiquimod 5% cream, 80% trichloroacetic acid, topical or systemic interferon, cryotherapy, electrocoagulation or electrodesiccation, surgical resection, and laser therapy. Some lesions resolve without treatment, and recurrence is possible.

Teaching Points

- Focal epithelial hyperplasia is strongly associated with HPV-13 and HPV-32 and manifests with multiple asymptomatic exophytic white to mucosal-colored papules or nodules on the oral mucosa, gingiva, tongue, and lips.

- HPV-13 and HPV-32 are often not included in commercially available low-risk HPV tests.

- Differentiating FEH from other oral verrucae is important as some HPV subtypes are associated with malignant transformation and/or are sexually transmitted.

- Treatment is optional, and modalities include imiquimod 5% cream, 80% trichloroacetic acid, topical or systemic interferon, cryotherapy, electrocoagulation or electrodesiccation, surgical resection, and laser therapy.

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CASE 16
An 81-year-old female with a three-year history of skin fragility

Presenters
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Thinh Chau, MD
Joseph Wu, PhD
Benjamin Kahn, MD
Christopher Elco, MD
Leslie Robinson-Bostom, MD
Elnaz Firoz, MD

History
An 81-year-old female with a three-year history of skin fragility suffered a right femoral neck fracture due to a mechanical fall. She underwent a right hip hemiarthroplasty and was observed to have easy skin tearing upon contact with medical adhesives. Post-operatively, she developed shallow erosions in areas where tape was applied and direct contact with operating room equipment occurred. Despite careful wound care, her skin fragility persisted, leading to a dermatology consultation.

Past medical history: No personal history of solid organ cancers. Colonoscopy q5 years with polyps. Normal mammogram 4 years. Smoked 1 pack per week x 10 years - stopped over 55 years ago
Family history: Mother died of colon cancer at age 83 years
Medications: metoprolol, paroxetine, pravastatin, valsartan

Physical Examination
Examination revealed geometric erosions ranging from 1 to 5 cm on her trunk and extremities. Additionally, a tense bulla of 2 cm was noted on her left wrist where she had rested her arm on a hospital chair. Skin biopsies were taken from the intact bulla for hematoxylin and eosin (H&E) staining and from perilesional skin for direct immunofluorescence (DIF).

Pertinent negatives: There was no mucosal involvement.

Labs
- SPEP: monoclonal IgM lambda paraprotein
- IIF studies for IgG, IgA, and IgM Ab at the cell surface and BMZ were negative.
- ELISA negative for IgG BP 180 Ab, IgG BP 230 Ab, and IgG collagen VII Ab
- CA19-9 elevated at 44.5; negative 24-hour urine porphyrins

Imaging
- CT Scan: 1.7 cm enhancing exophytic lesion in the right kidney later found on partial nephrectomy to be an oncocytoma
- CT Scan: Multiple pancreatic cystic lesions later found on abdominal MRI to be intraductal papillary mucinous neoplasms

Histopathology
Punch biopsy of the left wrist showed cell-poor subepidermal split with minimal inflammatory infiltrate on H&E. DIF on perilesional skin revealed 3+ linear IgA, 2+ linear IgM, and patchy weak 0-1+ IgG along the basement membrane zone.

Clinical Images
IgA- & IgM-Mediated Epidermolysis Bullosa Acquisita

Treatment

- Treatment for IgA- and IgM-mediated EBA includes dapsone, corticosteroids, mycophenolate mofetil, or cyclophosphamide.
- Our patient’s milder mechanobullous presentation without mucosal involvement aligns more closely with IgM-EBA clinical characteristics rather than IgA-EBA.

Discussion

- Most commonly, epidermolysis bullosa acquisita (EBA) is a noninflammatory blistering disorder affecting acral and dependent body surfaces, as well as trauma-prone areas, leading to scarring and milia during healing. It is primarily caused by circulating autoantibodies targeting type VII collagen, usually of the IgG subtype, which localize to the dermal side in salt-split skin.\(^1,2\)
- IgA-EBA lesions clinically mimic those seen in linear IgA bullous dermatosis (LABD) and tend to also involve mucosal surfaces; however, lesions heal without scarring.\(^3\) Even less common is the IgM subtype of EBA (IgM-EBA); only two cases demonstrating linear IgM deposition along the dermal side of the BMZ have been reported.\(^4,5\)
- Diagnosing EBA accurately can pose a considerable challenge due to its clinical similarities with other subepidermal and immunobullous disorders characterized by autoantibodies targeting BMZ components. These disorders include porphyria cutanea tarda, bullous pemphigoid, bullous lupus erythematosus, and LABD. In our patient, the absence of positive urine porphyrin studies and the lack of perivascular antibody deposition on DIF effectively ruled out the possibility of porphyria cutanea tarda. Additionally, the mechanobullous nature of the disease, the absence of significant neutrophilic infiltration on hematoxylin and eosin staining, and negative results in enzyme-linked immunosorbent assays provided strong evidence against bullous pemphigoid, bullous lupus, and LABD.
- The etiology of EBA remains unclear, but associations with autoimmune, infectious, and neoplastic conditions have been proposed. In our patient's case, she had an underlying monoclonal gammopathy of uncertain significance, and incidental findings of renal oncocytoma and pancreatic intraductal papillary mucinous neoplasms were noted, though a definitive link to EBA has not been established.

Teaching Points

- Diagnosing immunobullous eruptions can be challenging due to overlapping clinical presentations and autoantibody subtypes.
- It is crucial to identify the target antigen and carefully correlate clinical and pathological findings to guide proper diagnosis and treatment.

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CASE 17
Three females with skin tightening

Presenters
Rachel K. Lim, BA
Sara D. Ragi, MS
Yostina Farid, MD
Neha Kinariwalla, MD
Abrar A. Qureshi MD, MPH

Case A: History
A 42-year-old female presented with a one-year history of muscle weakness and aches, difficulty making a fist, and difficulty walking. Approximately three months after the onset of myalgias, she developed lightening of the skin surrounding the nailbeds as well as progressive darkening and hardening of her arms, legs, upper back, and chest. She also reported swelling and “burn-like lesions” of her hands.

Past medical history: No significant past medical history
Family history: No family history of autoimmune disease
Review of systems: Positive for cold extremities. Negative for difficulty swallowing, tightening of skin of the face, or shortness of breath
Medications: Multivitamin, melatonin

Physical Examination
Lichenification and hyperpigmentation was present on the bilateral arms. There was moderate skin tightening and hyperpigmentation of the bilateral calves. Most fingers demonstrated depigmented macules of the eponychium with telangiectasias appreciated on dermoscopy.
Poorly demarcated salt-and-pepper discoloration of the forehead, temples along the hairline, and bilateral cheeks was observed. Mottled hypopigmentation was seen on the right upper back and on the face which spared the eyelids. There were also multiple, well-demarcated, circular tan and brown macules along the soles of the feet and longitudinal melanonychia involving multiple digits.

Labs and Imaging
Labs: Elevated CRP 1.00 (reference range 0.10-0.80 mg/d) and ANA > 1:2560, nucleolar pattern
Imaging: No imaging

Histopathology
A punch biopsy from the right upper back showed thickened and sclerotic collagen bundles extending into and widening the subcutaneous septae consistent with systemic sclerosis. Alcian blue stain highlighted normal dermal mucin. PASD stain was negative for yeast or hyphal elements.

Clinical Images
Case B: History
A 23-year-old female presented with a history of mixed connective tissue disease. At age 15, she developed Raynaud’s phenomenon, joint stiffness, and muscle weakness. The patient was initially managed on meloxicam, prednisone plus hydroxychloroquine, and mycophenolate mofetil but self-discontinued all three medications in 2018 because she found them ineffective. Since then, she reported progressive skin thickening of the forehead and forearms, swelling of the hands, dry eyes and mouth, diffuse itching, and morning joint stiffness.

Past medical history: Anxiety and depression
Family history: No past family history of autoimmune disease
Review of systems: Positive for persistent diarrhea
Medications: Escitalopram daily, combined oral contraceptive, nifedipine as needed

Physical Examination
Skin thickening and tightening of the face and distal upper extremities was noted. Oral aperture was decreased, and the patient was unable to make a fist.

Labs and Imaging
Labs: Labs were remarkable for elevated rheumatoid factor (RF), ESR 46 mm/h (ref range: 0-20 mm/h), CRP 8.5 (ref range: <5.0 mg/L) and ANA >1:160 (non-reactive <1:40), anti-RNP antibodies >8.0 (ref range: 0.00-0.90 AI), and anti-Smith antibodies >8.0 (ref range: 0.00-0.90 AI). Anti-cyclic citrullinated peptide (anti-CCP) antibodies, Jo-1, SPEP, and anti-centromere antibodies were negative.

Imaging: Pulmonary function tests (PFTs) showed normal pulmonary function and an echocardiogram showed no abnormalities.
Case C: History
A 45-year-old female with cognitive delay presented with skin thickening and tightening of the hands, upper back, and groin for one year. The patient also reported lower extremity muscle weakness and pruritus of the forearms. Her symptoms worsened with cold exposure.

Past medical history: Cognitive delay

Family history: No family history of autoimmune disease

Medications: Methotrexate 20mg weekly and prednisone 15 MG daily

Physical Examination
Tight and thickened skin was noted, primarily affecting the hands, arms distal to the elbows, and face. She was unable to make a fist and had limited oral aperture. During treatment course with tocilizumab, patient developed ulcerations over the bilateral proximal and distal interphalangeal joints.

Labs and Imaging
Labs: Labs were remarkable for a strongly positive anti-RNA polymerase III antibody (>80) and a mildly elevated ESR 21 mm/h (reference range 0-20 mm/h). Creatinine kinase was normal. RF, anti-CCP antibody, as well as antibodies to dsDNA, SSA, SSB, RNP, Smith, Scl-70 and centromere were negative.

Imaging: Chest CT scan showed no evidence of interstitial lung disease. An echocardiogram showed mild left atrial enlargement. She was not able to perform PFTs appropriately.
Tocilizumab for Systemic Sclerosis

Treatment

- Patient A was initially recommended intravenous tocilizumab infusions but was unable to obtain insurance coverage. She was subsequently started on subcutaneous tocilizumab 162 mg administered once weekly. Within three months, patient A noticed improvement in morning stiffness, tightness of the skin of her hands, and range of motion of her fingers and arms.
- Patient B was started on hydroxychloroquine 200 mg twice daily and tocilizumab 162 mg administered subcutaneously once weekly. Within four months, patient B noted improvements in joint pain, skin thickening, and hand swelling.
- Patient C was started on tocilizumab 80 mg/4 mL intravenous infusion. After two months, she experienced significant dizziness and was switched to subcutaneous tocilizumab 162 mg once weekly. Within three months, patient C reported decreased pain and swelling in the hands. However, she soon after developed ulcers over the bilateral proximal and distal interphalangeal joints with subsequent superinfection. After one year on tocilizumab, it was discontinued by her rheumatologist due to lack of efficacy.

Discussion

- Systemic sclerosis (SSc), also known as scleroderma, is an immune-mediated disease characterized by fibrosis of the skin and internal organs that has a higher mortality rate than any other rheumatologic disease.\(^1\) Annual incidence is an estimated 0.6 to 5.6 per 100,000 adults, with a high female predominance.\(^2\) Despite the high mortality rate, survival has improved with earlier detection and management.\(^2\)
- Common clinical features include inflammation of the fingers causing early edema with subsequent progressive sclerodactyly, which is pathognomonic of SSc. Reduced oral aperture, decreased facial expression, xerostomia, and sicca syndrome are signs of orofacial fibrosis.
- In current practice, mycophenolate mofetil is often the first-line treatment for skin manifestations of SSc, primarily due to its efficacy in treating associated interstitial lung disease. Methotrexate is also commonly used as an alternative.\(^3\) Cyclophosphamide, rituximab, and tocilizumab may be considered for cases refractory to first- and second-line therapies.\(^3\)
- The cellular mechanism driving SSc remains poorly understood. However, increased IL-6 levels have been associated with higher mortality, more severe skin involvement, and increased incidence of progressive pulmonary decline in patients with SSc.\(^4\)
- Granted an FDA Breakthrough Therapy designation in 2015 for treatment of SSc, tocilizumab is an anti-IL-6 receptor antibody. A phase 2 clinical trial evaluating tocilizumab for SSc found that it did not elicit a significant reduction in skin thickening, although a meaningful trend was observed.\(^5\) The subsequent phase 3 clinical trial found no significant effect on skin sclerosis over 48 weeks but determined that tocilizumab may preserve lung function in some patients with early SSc-associated ILD.\(^6\)
- An unpublished case series of 7 patients with SSc treated with tocilizumab found that patients who initiated treatment within a year of diagnosis showed improved response.\(^7\) Intravenous appeared to be more effective than subcutaneous administration, and improvement in SSc hand symptoms varied depending on the specific digits that were involved.\(^7\)

Teaching Points

- Tocilizumab may be beneficial to some patients in the treatment of SSc. Common side effects include hypertension, injection site reaction, rash, constipation, elevated liver enzymes, and elevated lipids. Liver function testing and lipid monitoring are recommended.\(^8\)

CASE 18
A 54-year-old female with skin hardening

Presenters
Sara D. Ragi, MS
Rachel K. Lim, BS
Esther Henebeng, MD
Gladys H. Telang, MD

History
A 54-year-old female with an approximately 20-year history of type 2 diabetes mellitus (T2DM) presented with hardening of the skin on the trunk and all extremities. The patient described general skin tightening and thickening developing over the course of five years. These symptoms were not present in childhood.

Past medical history: Anemia and hypothyroidism

Family history: Notable for diabetes mellitus type I in her sister and father. No family history of cutaneous disorders

Medications: Insulin, tirzepatide, amlodipine, aspirin, atorvastatin, losartan, levothyroxine, escitalopram, ferrous sulfate, calcium, vitamin D3, and omega-3 fish oil

Physical Examination
There were firm, indurated pink plaques on the back, chest, legs and arms with subtle peau d’orange features and woody induration. The upper and mid back was affected to a greater degree than the legs and arms.

Pertinent negatives: No nail, oral, mucosal, or scalp findings.

Labs and Imaging
Labs: HgA1c range: 7.5 to 10.0. BMP: glucose range 116 to 198, otherwise unremarkable. Lipid panel: elevated cholesterol 202. TSH normal. PTH 84.7 (ref range 10-65 pg/mL). Calcium 1.13 (ref range 1.20-1.38 mmol/L). PTH 66 after intake of po calcium, felt to be secondary hyperparathyroidism due to hypocalcemia. Vit D 36 (ref range 20-100ng/ml). SS-A/Ro, SS-B/La, and RF were within normal limits.

Protein electrophoresis: notable for an elevated PEP A2-Glob 1.17 (ref range 0.66-0.91 g/dL), Beta-Glob 1.24 (ref range 0.66-0.99 g/dL), and Gamma-globulin 1.55 (ref range 0.56-0.91 g/dL). Final interpretation stated the M component was not seen.

Immunoglobulin: IgA elevated 338 (RR 61-303 mg/dL), IgG and IgM normal

HIV: Non-reactive

Imaging: Cardiac ECHO showed no signs of restrictive cardiomyopathy

Histopathology
Punch biopsy of the upper back revealed a normal epidermis with scant superficial perivascular inflammation. There was marked dermal thickening composed of enlarged, thick collagen bundles with increased stromal mucin deposition. The increased dermal mucin was overtly present on H&E stain and contributed to increased separation between individual collagen bundles.

Clinical Image
Generalized Scleredema of Buschke

**Treatment**
- An initial 3-month trial of high potency topical steroids provided no benefit.
- Currently, the patient is receiving whole body phototherapy (UVA1) 2-3 times a week for 18 months.
- The patient was presented for further treatment options. Treatment with teprotumumab infusions, an IGF-1R blocker which inhibits ocular fibroblast mucin production in thyroid eye disease, was considered. This medication is costly ($16,330/month) and not currently FDA approved for scleredema.

**Discussion**
- Scleredema of Buschke is a rare connective tissue disease of unknown etiology that may be associated with infections, hematological abnormalities, T2DM, and autoimmune disorders (see table below).
- It is characterized by painless induration and thickening of the skin typically affecting the face, back, shoulders, and neck and defined by the deposition of collagen in the dermis with excessive mucopolysaccharide production which causes skin thickening, stiffness, and impaired joint mobility and flexibility.\(^1\)
- The pathogenesis of type III scleredema of Buschke (scleredema diabeticorum), has been hypothesized to involve glycosylation of collagen fibers causing impaired degradation resulting in reduced skin elasticity.\(^1\) Hyperglycemia of diabetes may stimulate fibroblast production and synthesis of extracellular matrix components.\(^2\)
- Scleredema diabeticorum (SD) prevalence in diabetics is from 2.5-14.0%.\(^3\)
- Early complications include reduced joint flexibility (primarily of the fingers or shoulders) and later complications include visceral disease which may require management by subspecialists.\(^1\)
- Histopathological features of SD include thickened collagen bundles throughout the dermis separated by mucopolysaccharides (mainly mucin).\(^4\) There is variable mucin and fibrosis depending on the stage of disease. Excess mucin production in early disease may be due to hyperglycemia and resultant advanced glycation end-products (AGEs) making collagen fibers resistant to degradation.\(^4\)
- Although SD is a highly treatment-resistant disease, treatments include phototherapy (UVA1, PUVA), immunomodulators, radiotherapy, systemic antibiotics, and topical or intralesional corticosteroids. In addition, patients with diabetes should be encouraged to optimize glucose control and weight.\(^5\)

*| Scleredema of Buschke Subtypes |
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<td><strong>Type I</strong></td>
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<td><strong>Type II</strong></td>
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<td><strong>Type III</strong></td>
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**Teaching Points**
- Scleredema presents with woody induration and skin thickening of the face, back, shoulders, and neck.
- Generalized scleredema is a rare dermatologic disorder that may be underrecognized in type II diabetes mellitus patients. A full workup should be performed to assess for paraproteinemia, infection, hyperparathyroidism or other underlying complications of the disease including lung or cardiac disease.

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CASE 19
A 65-year-old male with sclerodermatous skin changes

Presenters
Tatiana Abrantes, MD
Fatima N. Mirza, MD, MPH
Leila Shayegan, MD
Leslie Robinson-Bostom, MD
Jennie Muglia, MD

History
A 65-year-old male presented with firm and taut skin changes involving his torso and bilateral upper and lower extremities that had been present for approximately 6 years. He denied any pruritus but noted increased stiffness in all extremities which had improved throughout the years with physical therapy. The patient also reported restrictive breathing due to being unable to fully expand his chest as well as dysphagia, peripheral neuropathy, and ocular dryness.

Past medical history: Acute myeloid leukemia s/p allogeneic stem cell transplantation (SCT) (2016) complicated by DVT/PE, peripheral neuropathy, chronic sinusitis, dysphagia, restrictive lung disease; SCC right temple s/p Mohs 2023
Family history: No reported family history of malignancy or blood disorder
Medications: triamcinolone 0.1% ointment, prednisone, trimethoprim-sulfamethoxazole, penicillin, acyclovir, isavuconazonium, fluconazole

Physical Examination
On the bilateral upper extremities, lower extremities, and trunk, affecting approximately 60% BSA, the skin is taut, hardened, and hyperpigmented. The bilateral lower legs have a shiny, hidebound appearance. There is decreased range of motion of the upper and lower extremities.

Labs and Imaging
Labs:
2019: Hypogammaglobulinemia (IgG 257 (ref range 700-1600 mg/dL), IgA 54 (ref range 70-400 mg/dL)) and lymphopenia (0.12, ref range 0.21-2.74 K/uL)
2023: Transaminases and bilirubin within normal limits
Genetics: FLT3+ acute myeloid leukemia

Histopathology
2016 - punch biopsy performed at an outside facility showed rare necrotic keratinocytes with minimal perivascular lymphohistiocytic inflammation.

Clinical Images
Sclerodermatous Graft-Versus-Host Disease

Treatment

- Since 2016, the patient has trialed numerous therapies for his sclerodermatous skin changes including tacrolimus, sorafenib, sirolimus, ibrutinib, colchicine, and ruxolitinib.
- Additionally, he has participated in clinical trials, including a belumosudil (KD025) trial in 2019 that he discontinued one year later due to worsening of his symptoms and a baricitinib trial at the NIH in 2021.
- From 2018-2021, patient underwent extracorporeal photopheresis as frequently as twice weekly.
- Since August 2017, the patient has been on and off prednisone. He is presently weaning off at 7mg/day.
- In June 2023, the patient elected to begin triamcinolone 0.1% ointment twice daily to the affected areas.
- The patient has been followed by hematology/oncology, gastroenterology, pulmonology, ENT, ophthalmology, infectious disease, and dentistry.

Discussion

- Chronic graft versus host disease (cGVHD) is the most common long-term complication after allogeneic SCT.\(^1\)\(^2\)
- The most frequently involved organs in patients with cGVHD are the skin, mouth, and liver, with less frequent involvement of the eye, lung, gastrointestinal tract, joint/fascia, and genital tract.\(^1\)
- Sclerodermatous cGVHD (ScGVHD) of the skin is characterized by inflammation and progressive fibrosis of the dermis and subcutaneous tissues resembling morphea, systemic sclerosis, or eosinophilic fasciitis.\(^2\)
  - ScGVHD is generally a late manifestation of cGVHD with a mean onset > 1 year after transplantation.\(^2\)
  - Sclerotic lesions can lead to extremity contractures, limited range of motion, ulceration, and fasciitis.\(^3\)
- First line treatments of localized ScGVHD include topical corticosteroids and topical calcineurin inhibitors. First line systemic therapies include oral corticosteroids.\(^4\)
- Second line therapies include extracorporeal photopheresis, mycophenolate mofetil, mTOR inhibitors such as sirolimus and everolimus, JAK inhibitors such as ruxolitinib, phototherapy, methotrexate, imatinib, and rituximab. Emerging treatments include spleen tyrosine kinase (Syk) inhibitors, Rho kinase inhibitors, abatacept, ibrutinib, IL-2, and T-regs.\(^4\)
- To capture skin severity, the NIH has developed the following scoring system, with higher scores associated with worse survival.\(^5\)

<table>
<thead>
<tr>
<th>Score % BSA</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>No BSA involved</td>
<td>1-18% BSA</td>
<td>19-50% BSA</td>
<td>&gt;50% BSA</td>
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</tbody>
</table>

GVHD features to be scored by BSA:
Check all that apply:

- Maculopapular rash/erythema
- Lichen planus-like features
- Sclerotic features
- Papulosquamous lesions or ichthyosis
- Keratosis pilaris-like

No sclerotic features
Superficial sclerotic features “not hidebound” (able to pinch)

Check all that apply:

- Deep sclerotic features
- “Hidebound” (unable to pinch)
- Impaired mobility
- Ulceration

Abnormally present but explained entirely by non-GVHD documented cause (specify) ___

Teaching Point

- ScGVHD is often recalcitrant to treatment and requires multidisciplinary care as complications such as infections and secondary malignancies are common.

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**CASE 20**
A 71-year-old female with hyperpigmented papules on the auricular conchae

**Presenters**
Samer Wahood, AB  
Fatima N. Mirza, MD, MPH  
Fadwa Ahmed, MD  
Asha Gowda, MD  
Gladys Telang, MD

**History**
A 71-year-old female with type IV skin presented with a few year history of multiple small asymptomatic hyperpigmented papules on both ears. Similar lesions were not present on other body sites.

Past medical history: Chronic cough, bilateral cataracts, hypothyroidism, longitudinal melanonychia, guttate hypomelanosis, seborrheic dermatitis, seborrheic keratosis, xerosis of the skin, and sun-damaged skin

Family history: Diabetes, cardiovascular disease, and hypertension

Medications: Conjugated estrogen 0.3 mg once daily, levothyroxine 75 mcg once daily, aspirin 80mg once daily, ketoconazole 1% shampoo, and biotin

**Physical Examination**
Localized to the bilateral auricular conchae cavum and cymbae, antihelix, and scapha were multiple 2-3 mm, dull, brown to tan, waxy papules.

Pertinent negatives: There were no nail, oral, mucosal, or scalp findings.

**Labs and Imaging**
Labs: A myositis antibody panel was negative.

Imaging: Chest CT revealed “bilateral mostly bibasilar subpleural interstitial densities, likely chronic in nature”. CXR was within normal limits.

**Histopathology**
Shave biopsy from the left auricular concha showed variably sized aggregates of amorphous, eosinophilic material in the papillary dermis with admixed dendritic melanophages, embraced by gently elongated rete. The overlying epidermis demonstrated acanthosis, focal vacuolar basal degeneration, orthohyperkeratosis, and follicular plugging. There was CK5/6 positive and Congo red focal brick red positive staining in the papillary dermal deposits.

**Clinical Image**
Primary Cutaneous Localized Amyloidosis of the Auricular Concha

Treatment
- The benign nature of the lesions was discussed with the patient. No treatment was necessary; however, the patient was counseled on the option of shave removal as needed.

Discussion
- Primary cutaneous localized amyloidosis (PCLA), also known as primary cutaneous amyloidosis (PCA), is characterized by amyloid deposition in the superficial dermis without involvement of other tissues and organs.
- PCLA of the auricular concha typically presents as asymptomatic 2-3mm papules in women between the ages of 40 and 70 with Fitzpatrick skin phototypes III or IV.
- Rare cases of PCLA localized to the external ear—concha cavum, cymba, antihelix, and scapha—have been described.
- As in other subtypes of PCLA, amyloid deposits in PCLA of the auricular concha are cytokeratin positive. While CK5/6 positivity is characteristic of lichen and macular PCLA,\(^1\) to our knowledge, there is no description of CK5/6-positive PCLA of the auricular concha.\(^2,3\) Our finding of CK5/6 positivity in PCLA of the auricular concha supports the hypothesis that PCLA of the auricular concha exists on a continuum with other PCLA subtypes rather than representing an entirely distinct entity.
- While previously reported cases typically describe PCLA as skin-colored papules,\(^2,3\) our case demonstrates that PCLA of the auricular concha may present as hyperpigmented papules that clinically resemble small seborrheic keratoses or melanocytic proliferations.

<table>
<thead>
<tr>
<th>Types of Primary Cutaneous Localized Amyloidosis(^4)</th>
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<tr>
<td><strong>Type</strong></td>
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<tr>
<td>Lichen Amyloidosis (LA)—most common</td>
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<tr>
<td>Macular Amyloidosis (MA)</td>
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<tr>
<td>Nodular Amyloidosis (NA)—rarest</td>
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<tr>
<td>Biphasic Amyloidosis (BA)</td>
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<tr>
<td>PCLA of the Auricular Concha</td>
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Teaching Points
- The presence of CK5/6 positivity in PCLA of the auricular concha support the hypothesis that this entity exists on a continuum with the other forms of primary cutaneous localized amyloidosis.

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Case 20: Primary Cutaneous Localized Amyloidosis of the Auricular Concha
The photographs of Rhode Island landscapes and cityscapes included in this casebook are courtesy of:

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