PROTOCOL BOOK • APRIL 17, 2024

CHICAGO DERMATOLOGICAL SOCIETY 2024

Monthly Meeting

Co-hosted by Cook County Department of Dermatology

Chicago Dermatological Society

PROTOCOL BOOK
April 17, 2024

Co-hosted by
Cook County Department of Dermatology

Guest Speaker: **Susan Burgin, MD**
Director of Dermatology
Brigham and Women's Health Care Center at Westwood

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INVITED GUEST LECTURER

Susan Burgin, MD

Dr. Susan Burgin is an attending physician in the Department of Dermatology at Brigham and Women's Hospital in Boston and an associate professor of dermatology at Harvard Medical School. She trained as a dermatologist in South Africa before coming to the United States in 1996. She is a general and medical dermatologist and her clinical interests include dermatologic manifestations of systemic disease, diagnostic dilemmas, rare dermatoses, disease recognition in all skin colors, and drug eruptions. She has presented nationally and internationally on these topics. She is also a specialist in vulvar dermatoses and sees complex vulvar patients each week in her specialty clinic.

She is passionate about the art of clinical diagnosis and In 2020, after a decade of work, her book "Guidebook to Dermatologic Diagnosis" was published (McGraw-Hill). This book outlines a unique approach to differential diagnosis in dermatology complete with original algorithms and pathways, images in all skin tones, tables and diagrams. It is the culmination of a career spent teaching diagnosis and draws on her clinical experiences and teachers in South Africa, New York and Boston. It has received excellent reviews locally and abroad and is being used by residents and students across the country.

Dr Burgin is a dedicated teacher and is the recipient of numerous teaching awards during her time as an attending at NYU and at Harvard. She is the director of both the Fundamental Skin Exam and Advanced Skin Examination Courses at Harvard Medical School and a core teacher in the Immunity in Defense and Disease course at the Medical School.

In her role as the dermatology section editor for VisualDx, the renowned national and international clinical decision support website, she has mentored hundreds of students and residents in writing and editing and has expanded the rare disease and diagnostic pearls content, and dermatologic content as a whole. Additionally, she initiated the "Impact of Skin Color on Clinical Presentation" section, which describes variations in color presentation of dermatoses in different skin colors.

In terms of leadership, Dr Burgin currently serves as the Director of Educational Development and Scholarship for the Brigham Dermatology Department, Director of the Dermatology Grand Rounds and Visiting Professor Faculty Development Program, and Director of the Department's Education Committee. She is also Medical Director for the Westwood practice site. At the national level, she has held numerous service and leadership positions for the American Academy of Dermatology, American Board of Dermatology and Association of Professors of Dermatology, and she is also is a member of the American Dermatologic Association.

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PROGRAM

Co-Hosted by
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April 17, 2024
University of Chicago Gleacher Center

8:00 a.m.	**Registration & Continental Breakfast with Exhibitors**
8:30 a.m. - 10:15 a.m.	**Clinical Rounds** Slide viewing/posters – ongoing through the early morning
9:00 a.m.	**Welcome and Opening Comments** *Morayo Adisa, MD- CDS President*
9:00 a.m. - 10:00 a.m.	**Morning Lecture: What's New in Drug Eruptions** *Susan Burgin, MD*
10:00 a.m. - 10:30 a.m.	**Break and Visit with Exhibitors**
10:30 a.m. - 12:00 p.m.	**Resident Case Presentations & Discussion**
12:00 p.m. - 12:30 p.m.	**Box Lunches & Visit with Exhibitors**
12:30 p.m. - 1:00 p.m.	**CDS Business Meeting**
1:00 p.m. - 2:00 p.m.	**Afternoon Lecture: Diagnostic Dilemmas** *Susan Burgin, MD*
2:00 p.m.	*Program adjourns*

COOK COUNTY HEALTH

Cook County Department of Dermatology

Chicago Dermatological Society Meeting
April 17, 2024

Dermatology Residents

Second Year
Hiren Kolli
Jake Dudzinski
Subuhi Kaul

First Year
Amber Loren King
Shannon Younessi
Warren Perry
Adam Garibay

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Resident Case Presentations & Discussion

Key location: Full-Body Involvement **CASE 1**

HTLV-1 Associated Adult T cell lymphoma/leukemia

Presented by Amber Loren King MD, Elena Gonzalez MD, David Othman MD MHSA, Vesna Petronic-Rosic MD MSc MBA

History of Present Illness

A 65-year-old man from Chicago presented to John H. Stroger Hospital with a two-week history of a worsening diffuse, pruritic, and painful rash. The patient had no history of any prior underlying skin condition. Notably, he had recently been admitted to an outside hospital for the same rash, where he received intravenous antibiotics, fluconazole, and systemic steroids. Upon discharge, he was prescribed a prednisone taper and clindamycin. Despite this treatment, he presented to our hospital due to deterioration of his rash.

Past Medical History

Hypertension, deep vein thrombosis (DVT), pulmonary embolism

Medications

Apixaban

Review of Systems

Positive for unintentional weight loss, chills, weakness, dyspnea, nausea, and vomiting
Negative for fever, night sweats

Physical Exam

Non-skin:	No palpable lymphadenopathy
Skin:	Scalp, face, chest, abdomen, and extremities: erythroderma with thick, hyperkeratotic scale

Laboratory Data

The following labs were remarkable/abnormal:

WBC	50.4	[4.4-10.6k/uL]
Hemoglobin	12.7	[12.9-16.8 g/dL]
Platelets	151	[161-369k/uL]
Na	140	[135-145 mEq/L]
K	5.9	[3.5-5.0 mEq/L]
Creatinine	2.8	[0.6-1.4 mg/dL]
Ca	8.6	[8.5-10.5 mg/dL]
Bilirubin	1.3	[0.2-1.2 mg/dL]
ALP	234	[20-120 U/L]
GGT	84	[3-60 U/L]
AST	22	[0-40 U/L]
ALT	18	[5-15 U/L]
LDH	340	[85-210 U/L]
HIV 1 and 2 screen	Nonreactive	Nonreactive
HTLV 1/2 Antibody Screen	Reactive	Nonreactive
HTLV-1 PCR	Positive	Negative

Peripheral Blood Smear:
Atypical mature lymphocytes with flower-like cells.

Peripheral Blood Flow Cytometry:
Abnormal T-cell population expressing CD3, CD4, CD5, and CD2 with complete loss of CD7.

Another subset of dual CD4+/CD8+ T-cells was also identified with partial loss of CD7.

Bone Marrow Smear:
Albumin-prepared smear showed an increase in lymphocytes and monocytes, a subset of the lymphocytes showed marked nuclear lobulation (flower-like nuclei).

Bone Marrow Flow Cytometry:
Presence of an abnormal T-cell population comprising >90% of the Ly gate. A subset (29%) expressing CD3(dim), CD4, CD5 (bright) and CD2 with complete loss of CD7. Another subset (66%) expressing CD3 with dual CD4+/CD8+ expression, partial loss of CD7 and expression of the remaining T-cell markers.

Histopathology
LEFT LEG AND LEFT ARM, PUNCH BIOPSY:
Epidermal and superficial dermal involvement by transformed lymphoid cells in clusters. There were small-medium pleomorphic cells with prominent epidermotropism forming Darier nests and showing angiocentricity. Immunohistochemistry demonstrated an abnormal lymphoid population, positive for CD3, CD4 with a subset CD4+/ CD8+ and CD5 with significant loss of CD7. CD30 was expressed in a large proportion of the population in a strong membranous manner.

Radiology
CT Chest Abdomen and Pelvis Without Contrast: Prominent axillary lymph nodes, borderline enlarged spleen

Diagnosis
HTLV-1 Associated Adult T Cell Lymphoma/Leukemia

Treatment and Course
After the diagnosis was made, dexamethasone was administered for tumor debulking, and induction chemotherapy with cyclophosphamide and intrathecal methotrexate was initiated. Anti-viral therapy, combining zidovudine and weekly interferon, was also administered.

The hospital course was complicated by neutropenic fever with bacteremia, hospital-acquired pneumonia with respiratory failure, and seizures, necessitating transfer to the intensive care unit and intubation. Despite all interventions, the patient's clinical condition continued to deteriorate. Given the severity and lack of improvement, palliative extubation was elected, and the patient passed away approximately two months after the initial presentation.

Discussion
Human T-cell Lymphotropic Virus type 1 (HTLV-1), a retrovirus targeting CD4+ T lymphocytes, is associated with several diseases, including Adult T-cell Leukemia/lymphoma (ATLL), which develops in approximately 5% of infected individuals [2,4,5]. The virus is endemic in certain regions of the world, such as parts of Japan, the Caribbean, and Central Africa. HTLV-1 is primarily transmitted through breastfeeding, sexual contact, and contaminated blood products [2]. Chronic HTLV-1 infection is regarded as the necessary first step in a multi-step oncogenic process, with a median latency period of 50 years [6]. The virus encodes several regulatory proteins such as Tax and HTLV-1 basic leucine zipper factor (HBZ) that modulate the host immune response and promote T-cell survival [3,4,6].

ATLL is a rare entity with 4 distinct clinical subtypes: 1) acute, 2) lymphomatous, 3) chronic, and 4) smoldering which vary in disease course, prognosis, and response to treatment. Acute and lymphoma subtypes are typically more aggressive, while chronic and smoldering are relatively indolent. The diagnosis of ATLL involves a combination of clinical, immunohistochemical, flow cytometric, and molecular assessments. The recommended cell marker panel for diagnosis includes CD3, CD4, CD5, CD7, CD8, CD25, and CD30. Lymph node or extranodal tissue biopsy is often performed to identify flower-like cells with irregular polylobated nuclei, which are pathognomonic for ATLL. Additionally,

molecular techniques, including polymerase chain reaction (PCR), can be used to detect the presence of HTLV-1 proviral DNA [3].

The skin lesions of ATLL are polymorphous, and the prognosis of the disease can be predicted based on the type of skin eruption. Patients with nodulotumoral and erythrodermic presentations have poor prognoses. The acute subtype of ATLL is most common and is especially challenging to manage due to its aggressive nature and poor prognosis with a median overall survival of 6 months [1]. Treatment strategies often include combination chemotherapy (e.g. CHOP [cyclophosphamide, doxorubicin, vincristine, and prednisone]) and antiviral regimens (e.g. zidovudine and interferon). Allogeneic stem cell transplantation may be considered in eligible patients, but despite these treatment modalities, the overall survival remains low, emphasizing the need for early detection and innovative treatment approaches.

Clinical trials investigating immunomodulatory treatments with lenalidomide and monoclonal antibody therapy with brentuximab (anti-CD30), mogamulizumab (anti-CCR4), alemtuzumab (anti-CD52), and daclizumab (anti-CD25) are underway. An anti-Tax vaccine and IL-2 diphtheria toxin protein are among other modalities currently being explored [3,5].

HTLV-1 associated adult T-cell lymphoma represents a complex interplay between viral infection and T-cell transformation [7]. Understanding the epidemiology, pathogenesis, clinical features, and treatment options is crucial for improving outcomes in affected individuals. International collaborations can strengthen ongoing research efforts to identify novel therapeutic targets and enhance our understanding of this rare and challenging malignancy.

We present this case of HTLV-1 associated T-cell lymphoma for clinical interest.

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Key location(s): Mouth (tongue) **CASE 2**

Oral Plasma Cell Mucositis

Presented by Hiren Kolli MD and Vesna Petronic-Rosic MD, MSc, MBA

History of Present Illness

A 58-year-old woman presented with chronic tongue sensitivity and recurrent tongue lesions. For the past 10 years, she reported intermittent tongue burning and irritation she thought was related to salty or citrusy foods. She also endorsed recurrent lesions on both edges of the tongue. She had not tried any specific treatments for these symptoms. Dietary avoidance of citrus and salt seemed to help with the sensation disturbance but did not have any other effect on the lesions.

Past Medical History

Rheumatoid arthritis, hypertension, chronic kidney disease

Medications

Adalimumab, amlodipine, azathioprine, hydrochlorothiazide, leflunomide, losartan, prednisone (prn), spironolactone

Allergies

Codeine

Social History

Tobacco: Denies
Drugs: Denies
Alcohol: Denies

Review of Systems

Negative for fever, throat pain, trouble swallowing, hoarseness
Positive for mouth lesions, intermittent oral sensitivity

Physical Exam

Skin: The tongue had pink to erythematous, shiny papules coalescing into cobblestoned plaques localized to the lateral edges with a central smooth, depapillated, glistening red patch.

Laboratory Data

The following labs were remarkable/abnormal:

IgG	1,570 mg/dL	[694-1618 mg/dL]
IgA	476 mg/dL	[68-378 mg/dL]
IgM	105 mg/dL	[77-220 mg/dL]
Kappa/Lambda ratio	1.06 mg/dL (low)	[1.41-2.83 mg/dL]
SPE	Negative	
IFE	Negative	

Histopathology

ANTERIOR RIGHT TONGUE, SHAVE BIOPSY:
Sections are of mucosa with hyperplasia of the epithelium and exocytosis of lymphoid cells. The dermis has a dense, bandlike infiltrate with innumerable plasma cells. Collagen fibers appear thickened. Immunohistochemical stains show a mixture of background CD3 positive T cells and CD20 positive B cells with a brisk infiltrate of CD138/CD79a positive plasma cells that express polytypic kappa and lambda light chains by in situ hybridization. The plasma cells are negative for CD56, CD117 and Cyclin D1. Immunohistochemical stain for Treponema pallidum (performed on blocks A1 and A2) is negative. T cells are predominantly CD4 positive with co-expression of CD5

and CD7 and background CD8. CD30 highlights scattered single positive cells. The Congo red stain is equivocal.

Microbiology
TONGUE, FUNGAL CULTURE:
Candida albicans 1+ growth

Diagnosis
Oral Plasma Cell Mucositis

Treatment and Course
The patient reported clinical improvement with dietary changes, including avoidance of certain foods. For further symptomatic relief, she was instructed to apply clobetasol 0.05% topical gel to the affected areas as needed. The patient endorsed overall improvement of symptoms including regression of some lesions after the initial biopsy. An oral fungal swab was completed after her initial diagnosis and grew Candida albicans. She was then treated with a course of oral nystatin solution. Follow up from this treatment course is pending.

Discussion
Plasma cell mucositis (PCM) is a noncancerous condition characterized by the proliferation of polyclonal plasma cells in the mucous membranes. Its exact cause remains unknown. PCM was first reported by Zoon in 1952 as affecting the glans penis, and it was termed Zoon's balanitis.
Since then, similar pathologic changes have been noted at various mucosal sites including the oral mucosa. To date, fewer than 80 cases of oral PCM have been reported in the literature [7].

The clinical manifestations of PCM are diverse, typically showing a vividly erythematous oral mucosa with surface alterations such as cobblestone, nodular, papillomatous, granular, or velvety changes. The gingiva (65.82%) and lip (56.34%) are the most frequent sites involved, while tongue involvement was only seen in 20.89% of cases [3]. The condition exhibits a slight male predominance with a ratio of 1:2.1, and the average age of affected individuals is 56.6 years [4]. Plasma cell mucositis often coexists with concurrent or subsequent autoimmune or immunological dysfunctions, including seronegative rheumatoid arthritis (RA), Sjögren syndrome, autoimmune hepatitis, polymyositis, and diabetes mellitus [6]. Our patient had a history of advanced, deforming RA since the age of 24, but at the time of presentation was considered by Rheumatology to be inactive and controlled on multiple medications.

The diagnosis of PCM involves the triangulation of physical examination, serological tests, and histological examination. Histological findings show a dense plasma cell-rich infiltrate, and the plasma cells are not atypical or anaplastic and prominent nucleoli are not described [2]. Quantitative assays in PCMs should always be performed to confirm the polyclonality of the immunoglobulins and, thus, confirm that the lesion is a manifestation of a non-neoplastic polyclonal benign reactive process, as in our case. Finally, a potential etiology should be elucidated.

A systematic review found three potential etiologic hypotheses: an allergic process, inflammatory disease, and idiopathic [3]. Infections, including fungal (Candida albicans), viral (herpes virus), or bacterial (dental plaque), are implicated as potential triggers for plasma cell infiltrates. Candida albicans infection, in particular, is often linked to delayed hypersensitivity reactions, indirectly leading to the accumulation of a plasma cell infiltrate. A case report suggests that chronic exposure to fungal hyphae could cause subtle but persistent damage to mucosal integrity, inducing plasma cell lesions even in the absence of clinically apparent colonization [5]. This may have been the case in our patient, who tested positive for oral Candida infection after the diagnosis of PCM was made.

This idiopathic disorder has the potential to affect various anatomical regions, including the oral cavity, nasal mucosa, nasopharynx, larynx, oropharynx, hypopharynx, and esophagus [6]. Patients may manifest symptoms such as oral pain, dysphonia, chronic cough, persistent hoarseness, dyspnea, stridor, pharyngitis, and dysphagia. Management of PCM is challenging, and there is no consensus

on treatment. The use of topical and systemic steroids is beneficial, but adverse side effects limit prolonged use. Non-steroidal immunosuppressive agents have been used with varying success, but caution should be exercised when using potent immunosuppressive agents for this benign condition [8].
Of note, the patient mentioned that she had independently stopped using adalimumab a year prior to presentation at the dermatology clinic and observed slight improvement. However, Galvin et al. demonstrated resolution and lack of recurrence using adalimumab in one patient with PCM of the buccal mucosa, making it difficult to explain this aspect of the patient's history [4]. Surgical intervention becomes necessary in the presence of complications associated with PCM, such as tracheal strictures leading to airway obstruction symptoms. Additionally, debulking procedures on glottic and pharyngeal tissue may be required to address dysphonia or dysphagia resulting from a mass effect.

This case highlights a rare condition where the diagnosis depends on clinical and histopathological correlation. It is important to exclude or treat other pathologies with similar features such as autoimmune mucocutaneous bullous diseases, lichen planus, squamous cell carcinoma or fungal co-infection, to name a few [1]. We present this case to raise awareness of this disease among dermatologists, dentists, and oral surgeons, in the hope of obtaining a timely diagnosis and beginning appropriate therapy, if needed.

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Key location(s): Legs **CASE 3**

Anti-phosphatidylserine/prothrombin Complex Antibody (aPS/PT) Positive Antiphospholipid Syndrome

Presented by Jacob Dudzinski MD, Warren Piette MD, and Shilpa Mehta MD

History of Present Illness

A 33-year-old woman with a history of mixed connective tissue disease (MCTD), two episodes of pulmonary embolism (PE), and spontaneous abortion, presented to our dermatology clinic for slow-healing leg ulcers of five months duration. She was originally diagnosed with MCTD with predominant features of rheumatoid arthritis (RA) in 2019 but was lost to follow up. She suffered a spontaneous abortion that same year. She developed a PE in 2022 and had a hypercoagulability workup including Factor V Leiden, Prothrombin mutation, lupus anticoagulant (LAC), anticardiolipin antibodies (aCL), and anti-beta2 glycoprotein I antibodies (anti-β2GPI), all of which were negative. She was placed on rivaroxaban for unprovoked PE and self-discontinued before experiencing a repeat PE in 2023. Rivaroxaban was then resumed with poor compliance. Around July 2023, she developed multiple slow-healing ulcerations of the bilateral lower extremities which she attributed to a fall at work. She was being seen by outside hospital wound care and required multiple debridements for poor wound healing. She was eventually referred to our dermatology clinic for these ulcers.

Past Medical History

MCTD with predominant features of RA, PE (2022, 2023), 1st trimester spontaneous abortion (2019)

Medications

Hydroxychloroquine, rivaroxaban

Review of Systems

Negative for fever, chills, night sweats, weight loss, SOB, chest pain
Positive for arthralgias

Physical Exam

Skin: Bilateral Lower Extremities: Livedo reticularis and multiple stellate violaceous-brown-white atrophic scars
Left shin: 8x8cm superficial circular ulcer with pink granulation tissue, minimally undermined edge, and violaceous gray border
R shin: 2x2cm stellate ulcer with overlying eschar and violaceous gray border

Laboratory Data

The following labs were remarkable/abnormal:

ANA	Positive (Homogenous)	Negative
ANA Titer	>1:160	<1:160
DS-DNA Ab	113 IU/mL	0-3 IU/mL
Smith Ab	0.4 AI	0.0-0.9 AI
RNP/Smith	3.1 AI	0.0-0.9 AI
SSA-Ab	>8.0 AI	0.0-0.9 AI
SSB-Ab	<0.2 AI	0.0-0.9 AI
RF	182 IU/mL	<20 IU/mL
CCP Abs	>300 U/mL	0.0-2.9 U/mL
C3 compliment	80 mg/dL	88-201 mg/dL
C4 compliment	<6 mg/dL	16-47 mg/DL
PLT	355 k/uL	161-369 k/uL
PT	13.4 sec	11.7-14.5 sec
INR	1.03	NA
PTT	30.1 sec	23.5-35.1 sec
Factor V Leiden	Negative	Negative

Prothrombin Mutation	Negative	Negative
Lupus anticoagulant (LA)	Not detected	Not detected
Anticardiolipin antibodies (aCL)	Negative	Negative
Anti-beta2 glycoprotein I antibodies (anti-β2GPI)	Negative	Negative
Anti-phosphatidylserine/prothrombin Complex Antibody (aPS/PT) IgM	12 U	30 U
Anti-phosphatidylserine/prothrombin Complex Antibody (aPS/PT) IgG	107 U	30 U

Diagnosis

Anti-phosphatidylserine/prothrombin Complex Antibody (aPS/PT) Positive Antiphospholipid Syndrome

Treatment and Course

Repeat LAC, aCL, anti-β2GPI were negative, however given her cutaneous findings as well as her hematologic and rheumatologic history, there was a high index of suspicion for underlying seronegative antiphospholipid syndrome. A send out test for aPS/PT was performed which came back positive with high IgG titers. Patient refused biopsy. After discussion with hematology, it was decided to continue patient on rivaroxaban. Ulcers have since improved with diligent wound care.

Discussion

Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterized by arterial, venous, or microvascular thrombosis, with pregnancy morbidity in patients with persistent antiphospholipid antibodies (aPL) [1]. APS can be primary or associated with underlying SLE in which the risk of thrombotic events is much higher [2]. Cutaneous manifestations of APS vary and can include livedo reticularis, livedoid vasculopathy and atrophie blanche, anetoderma, and malignant atrophic papulosis, with livedo reticularis being the most common [3].

aPL are a heterogenous group of autoantibodies directed not just against phospholipids (a misnomer) but also phospholipid-binding proteins and other proteins of the coagulation pathway or cell surface, leading to thrombosis [4]. Although numerous aPL have been identified, the three most clinically relevant are anti-cardiolipin antibodies (aCL), anti–β2-glycoprotein I antibodies (anti-β2GPI), and lupus anticoagulant (LAC). It should be noted that LAC is a misnomer and that its presence confers an increased risk of thrombosis in APS [5]. To add to the confusion, LAC positivity is not related to detection of specific antibodies, but rather is determined through various coagulation assays [6]. Standardization of these assays has proven difficult and diagnostic yield can be impacted by changes in clotting factor levels and use of oral anticoagulants [6].

The 2023 ACR/EULAR APS classification criteria requires at least one of these three aPL to be positive as an entry criterion [1]. However, there exists a subset of patients with clinical manifestations of APS who test negative for these three aPL (so-called seronegative APS) [7]. Whether or not these seronegative APS cases are a result of true seronegativitity or due to serologic changes related to anticoagulant medications, consumption of clotting factors during APS flares, etc. are still up for debate [7,8]. Nonetheless, these challenging cases have spurred the search for other aPL that can aid in diagnosis. One such aPL that has been identified, anti-phosphatidylserine/prothrombin complex antibody (aPS/PT), has shown high specificity in the diagnosis of APS [9].

aPS/PT promote thrombin generation and thus confer an increased risk of thrombosis in APS [10.11]. Numerous studies have confirmed the utility of aPS/PT in supporting a diagnosis of APS in both seropositive and seronegative cases [8,9]. In addition, because detection of aPS/PT is based on

enzyme-linked immunosorbent assay (ELISA), its presence is not affected by variability in clotting factor levels or use of oral anticoagulants, unlike LAC. Its documented presence in multiple cases which fit APS has led to support for inclusion of aPS/PT in the APS classification criteria [9,11].

Our patient was subsequently diagnosed with aPS/PT positive APS. Given her history of poor compliance with rivaroxaban, it was unclear if patient was appropriately anticoagulated when she developed her leg ulcers. Nevertheless, after discussion with hematology the decision was made to continue rivaroxaban. It should be noted that preferred anticoagulation in APS is controversial [12,13], and studies looking specifically at aPS/PT positive APS are lacking. With diligent wound care our patients ulcers slowly improved and she has not since had any thrombotic events. We present this challenging case of a patient with negative serologies for classic APS markers (LAC, aCL, and anti-β2GPI) who was subsequently found to have positive aPS/PT. For cases in which there is a strong suspicion for underlying APS despite negative serologies, screening for aPS/PT should be considered and can help with earlier identification and treatment, decreasing the morbidity and mortality associated with a delayed diagnosis.

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Key location(s): Oral Mucosa **CASE 4**

Heck's Disease

Presented by Adam Garibay MD and Benjamin Falck MD

History of Present Illness

Four Siblings, 13-year-old female, 11-year-old female, 6-year-old male, and 4-year-old male presented to dermatology clinic with oral mucosa papules. Each patient started with oral mucosal papules at about 3 years of age and have been progressively growing in each sibling.

Past Medical History

None

Medications

None

Social History

Native Ecuadorian Heritage
No Sexual History

Review of Systems

Negative for fevers, fatigue, changes in bowel habits, abdominal pain, chest pain, difficulty breathing, or dysuria.

Physical Exam

Oral Mucosa: 13-year-old female: Upper and lower mucosal lip, bilateral buccal mucosa, and tongue with multiple papules coalescing into a cobblestone appearance. Posterior oropharynx with scattered mucosal papules.
11-year-old female: Upper and lower mucosal lip, buccal mucosa, and tongue with multiple scattered firm papules, minor evidence of papules coalescing
6-year-old male: A few non eroded papules on the tongue and buccal mucosa
4-year-old male: A few non eroded papules on the tongue

Histopathology

13-YEAR OLD FEMALE AND 11-YEAR-OLD FEMALE, LOWER MUCOSAL LIP PAPULE/SHAVE BIOPSY:
Suggestive of focal epithelial hyperplasia.
Comment: There is epithelial hyperplasia with parakeratosis occasional individual apoptotic cells and rare mitotic figures. Focally, hints of cytopathic change are noted. The PAS stain highlights large amounts of
glycogen throughout the epithelium, which are removed with the PAS-diastase process.
Immunohistochemical staining with p16 is mildly positive.

Diagnosis

Heck's Disease

Treatment and Course

In progress.

Discussion

Heck's disease, also known as Focal Epithelial Hyperplasia (FEH) or multifocal epithelial hyperplasia, is a rare viral infection primarily affecting the oral mucosa. It is caused by certain types of human papillomavirus (HPV), predominantly HPV types 13 and 32. Heck's disease is most commonly found in indigenous populations, particularly in Central and South America, but cases have been reported worldwide [1,2].

The hallmark of Heck's disease is the presence of multiple asymptomatic papules or nodules in the oral cavity, which may vary in size and color. These lesions typically occur on the buccal and labial mucosa, tongue, and soft palate. While the exact mode of transmission is not fully understood, it is believed to involve direct contact with infected saliva, often in childhood or adolescence [3,4] .

The diagnosis of Heck's disease is primarily clinical, based on the characteristic appearance of the lesions. However, biopsy and histopathological examination may be necessary to confirm the diagnosis, revealing focal epithelial hyperplasia with koilocytosis, a characteristic finding of HPV infection [5,6].

The histology protocol for working up Heck's disease begins with obtaining a shave biopsy and fixing it in 10% buffered formalin, embedding it in paraffin, and performing routine hematoxylin and eosin staining. Immunohistochemistry is conducted using p16 and consensus L1 capsid antibody to detect HPV L1 capsid protein. HPV DNA in situ hybridization is performed using probes for HPV types 6, 11, 16, 18, 31, 33, 35, 42, 43, 44, 45, 51, 56, 13, and 32. Positive results for HPV L1 capsid protein and HPV DNA in situ hybridization are interpreted as indicative of productive viral infection, particularly HPV 13. Viral DNA distribution in the biopsy specimen is noted, typically towards the surface. The intense signal on immunohistochemistry and in situ hybridization is considered indicative of high viral copy, typical of benign infections like verruca, condyloma, and FEH. Histological, cytological findings, and clinical presentation are combined to support a diagnosis of FEH, highlighting the potential utility of cytology in providing diagnostic information to dermatologists [7].

Management of Heck's disease focuses on symptom relief and prevention of complications. As the lesions are usually asymptomatic, treatment may not be necessary in many cases. However, for aesthetic reasons or if the lesions become symptomatic or interfere with mastication or speech, various treatment modalities may be considered. These include topical agents such as podophyllin, cryotherapy, laser therapy, or surgical excision Current HPV vaccinations do not currently include types 13 and 32. Although vaccination will not prevent Heck's disease, patients may still benefit from HPV vaccination for other pathologies [8,9].

While Heck's disease is considered benign and self-limiting, complications such as secondary infection or malignant transformation have been reported in rare cases. Therefore, long-term follow-up may be necessary, particularly in individuals with persistent or recurrent lesions [10,11] .

In conclusion, Heck's disease is a rare viral infection of the oral mucosa caused by HPV types 13 and 32. Although benign and usually asymptomatic, it can present diagnostic and therapeutic challenges. Increased awareness among clinicians, particularly in regions with a high prevalence of HPV-related diseases, is essential for early recognition and appropriate management of this condition.

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Key location(s): Left Ear and Extremities **CASE 5**

Borderline Lepromatous Leprosy with Type 1 Reaction

Presented by Subuhi Kaul MD and Shilpa Mehta MD

History of Present Illness

A 22-year-old man presented with a 1-month history of redness and mild itching of his left ear and right lower leg. One year before developing the erythematous skin lesions, he experienced dryness and pins-and-needles sensation in his right leg. He received a 10-day course of oral doxycycline for presumed cellulitis from the emergency room, with a transient improvement in redness, followed by recurrence after completion of the antibiotic course. Originally from Venezuela, he lived in Columbia for 5 years before arriving in Texas 2 months prior to presentation.

Past Medical History

None

Medications

None

Review of Systems

Negative for weakness of hands or feet, fever, and pain

Physical Exam

Skin:	Left Ear: diffuse erythema and infiltration sparing the helical crus and tragus. The right Lower Leg: large, ill-defined, hypoesthetic erythematous plaque extending from the mid lower leg to the foot with overlying diffuse fine scaling and a flattened medial plantar arch; the left foot instep had a dull red plaque; forearms showed scattered faint pink papules approximately 3 to 5 mm in diameter, with one edematous erythematous targetoid non-tender plaque, 2 cm in diameter, on the left wrist. Examination of the palms, soles, and oral mucosa were unremarkable.
Nerves:	Bilateral infraorbital, bilateral ulnar, left common peroneal were thickened, non-tender, and non-nodular.
Lymph nodes:	No palpable lymphadenopathy.

Laboratory Data

The following labs were remarkable/abnormal:

HIV 1 and 2 screen	Non-reactive	[Non-reactive]
Hepatitis B surface antigen	Non-reactive	[Non-reactive]
Hepatitis C antibody	Non-reactive	[Non-reactive]

Histopathology

RIGHT LEG AND LEFT POSTERIOR EAR LOBULE PUNCH BIOPSY:
A grenz zone with granulomatous dermatitis was present. The Fite stain revealed a moderate number of acid-fast bacilli within the granulomas and nerves in the dermis. The GMS, PAS, Giemsa, and Gram stains are negative for microorganisms.

Microbiology

Mycobacterial and fungal culture were negative.

Diagnosis

Borderline Lepromatous Leprosy with Type 1 Reaction

Treatment and Course

The patient was started on ibuprofen 600mg BID and referred to the National Hansen's Disease Program center in Chicago at the University of Illinois.

Discussion

Leprosy, also known as Hansen's disease, is caused by a slow growing acid-fast mycobacterium, belonging to the *M. leprae* complex, that includes *M. leprae* and *M. lepromatosis*. These obligate intracellular organisms cannot be cultured in artificial media [1,2]. Worldwide, humans are the predominant carriers of infection, apart from the Americas, where the nine-banded armadillo (*Dasypus novemcintus*) serves as a zoonotic reservoir [1]. Other reported animal hosts, albeit less common, include wild chimpanzees (*Pan troglodytes*), sooty mangabey monkeys (*Cercocebus atys*) in Africa, and red squirrels (*Sciurus vulgaris*) in the British Isles [3]. The chief method of transmission is via respiratory secretions.[1] Important risk factors for developing disease are prolonged close contact with a patient, genetic predisposition, and immunodeficiency [1,2]. Worldwide, 174,087 new cases of leprosy were recorded in 2022, with 21, 398 new cases in the Americas [4]. In contrast, there are less than 200 new cases reported every year in the United States [5].

The major organ systems involved are the skin, respiratory mucosa, eyes, peripheral nerves, and reticuloendothelial system. The clinical spectrum of disease varies widely depending on patient's immune status [1,2,5]. One of the most widely accepted classifications is the Ridley-Jopling classification system which integrates clinical features, histopathologic findings, and bacteriologic index. It categorizes leprosy along a spectrum, which includes polar tuberculoid leprosy (TT), borderline tuberculoid leprosy (BT), mid-borderline leprosy (BB), borderline lepromatous leprosy (BL), and lepromatous leprosy (LL) [1]. A simplified classification is utilized by the World Health Organization (WHO) to ensure adequate treatment in resource poor settings. The WHO classifies patients with slit skin smear positivity, nerve involvement, and more than 5 skin lesions into the multibacillary category, all other cases are considered paucibacillary [2].

The histopathology varies with patient immune status and is characterized by the presence of epithelioid cell granulomas with more macrophages and fewer lymphocytes towards the lepromatous pole. In addition, acid-fast bacilli are absent in the tuberculoid pole and abundant toward the lepromatous pole [1,2].

Reactions in leprosy are immunologically mediated episodes of acute or subacute inflammation and may punctuate the typically chronic course of leprosy. There are three major types of reactions: type 1, type 2, and Lucio phenomenon [1,2]. Type 1 reaction is a delayed hypersensitivity reaction that usually occurs in the borderline spectrum of leprosy. It is characterized by the sudden appearance of erythema and edema in existing skin lesions with or without associated neuritis, as seen in our patient. Neuritis is typified by nerve tenderness, new motor and/or sensory loss. Type 2 reaction, also called erythema nodosum leprosum, occurs due to immune complex deposition in lepromatous or borderline lepromatous leprosy and manifests as evanescent painful nodules with or without constitutional signs and symptoms. Lucio phenomenon is a vasculopathy that occurs in Lucio leprosy due to an overwhelming bacillary burden in arterioles and manifests as ulceration and necrosis [2].

In the US, leprosy is treated at special clinics run by the National Hansen's Disease Program [6]. Treatment of leprosy requires multidrug therapy with dapsone, rifampin and clofazimine for a period of 1-2 years based on the classification by bacillary load – paucibacillary or multibacillary [6,7]. Reactions are treated urgently due to the potential for lasting nerve damage and loss of vital function. Mild type 1 reactions are treated with NSAIDs, however, severe type reactions, with facial involvement or neuritis, are treated with oral corticosteroids while continuing multidrug therapy. Type 2 reactions may be treated with NSAIDs, corticosteroids, clofazimine, thalidomide, or other immunosuppressants [2,7].

We present this case to demonstrate type 1 reaction in multibacillary leprosy. Early recognition and treatment of reactions in leprosy is essential to prevent function threatening complications including permanent nerve or vision damage.

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Key location(s): Full-Body Involvement **CASE 6**

Pityriasis Rubra Pilaris

Presented by Warren M. Perry, MD, MBA and Benjamin Falck, MD

History of Present Illness
A 61-year-old woman presented with a 3-week history of a progressing, pruritic rash and associated skin pain. She previously received dexamethasone and cetirizine from her primary care provider with no improvement in her symptoms.

Past Medical History
Unspecified dementia

Medications
None

Social History
Spanish speaking
Lives with husband and sons
Husband is main caregiver without power of attorney

Review of Systems
Negative for joint pain/swelling; constitutional symptoms including fever, night sweats, or weight loss
Positive for pruritus and burning pain

Physical Exam

Skin:	Anterior and posterior torso: large, well demarcated, red-orange erythematous, scaly plaques with peripheral perifollicular papules Palms: waxy yellow-orange keratoderma concentrated in creases with associated subungual hyperkeratosis Scalp: thick, greasy yellow scale

Histopathology
RIGHT THIGH, PUNCH BIOPSY:
The epidermis is acanthotic. The stratum corneum has orthokeratosis alternating with parakeratosis, both horizontally and vertically. The dermis has a superficial perivascular infiltrate of lymphocytes. Overall, in the proper clinical context, the findings are favored to represent a lesion of pityriasis rubra pilaris or pityriasis rubra-like drug eruption.

Diagnosis
Pityriasis Rubra Pilaris

Treatment and Course
The patient was initially placed on clobetasol 0.05% for her palmoplantar keratoderma, clobetasol gel 0.05% for the scalp, triamcinolone 0.1% to be applied to the body, and hydrocortisone 1% to be applied to the intertriginous areas. The patient was scheduled for follow up in the dermatology clinic one month later.

At the one-month follow up, the patient had progressed to erythroderma with variable degrees of scaling. The patient and husband complained of pain with walking and difficulty completing daily activities. The husband noted that the patient had been more agitated, and her insomnia had worsened. The team decided to send the patient to the emergency department for inpatient admission and further management.

While in the hospital, the patient was started on cyclosporine 3mg/kg to expedite improvement of her signs and symptoms in addition to continuing her home topical steroids. Eucerin cream was applied as a daily moisturizer to improve scaling and help restore barrier function. The patient improved over 8 days and was discharged on cyclosporine, with topical steroids and Eucerin as adjuncts.

Between discharge and posthospital follow-up, the patient was started on adalimumab. While on adalimumab and cyclosporine, the patient showed continued significant reduction of erythroderma, keratoderma, scaling, and pruritus.

Discussion

Pityriasis rubra pilaris (PRP) is a rare inflammatory papulosquamous disorder first described as a variant of psoriasis [1]. This condition is reported to have an estimated average prevalence of 1 in 400,000 in the general population [2]. Based on the popular Griffith classification, our patient presented with Type I PRP with the classic presentation of reddish-orange, scaly plaques, waxy palmoplantar keratoderma, and follicular, keratotic papules. The etiology of pityriasis rubra pilaris remains unclear, making it a challenging condition to diagnose and treat effectively. Hypotheses about the pathogenesis include genetic factors, autoimmune dysfunction, abnormal vitamin A, and disordered keratinization, as well as immune triggers such as infections [1].

Treatment of Type I PRP is challenging and there remains no evidence-based standard therapeutic approach due to its rarity and often self-limited nature. Topical steroids, emollients, and topical keratolytics can be employed as initial treatment, but commonly, more aggressive management is necessary. A systemic review reported marked improvement with either acitretin or methotrexate [3]. In addition to these treatments, cyclosporine has been used as monotherapy and in combination with acitretin resulting in complete and partial clearance, respectively [3,4].

Currently, biologics are becoming a popular treatment of choice [3]. A systematic literature review on the treatment of Type I PRP with TNF-a inhibitors found them to be effective as monotherapy or in combination with methotrexate or acitretin [5]. One case series found elevated IL-17/23 in lesional and peri-lesional skin of a patient with PRP, which supports the role of IL-17/23 inhibitors in its management [6]. There have also been reports of improvement with PUVA, UVA1, and UVB [1]. Although these case reports and series show promise in the utility of these therapies, more research is needed to determine the efficacy and safety of these therapeutic approaches to PRP management.

In conclusion, PRP is a rare and perplexing papulosquamous condition with a challenging clinical course. For this reason, we present this case of classic adult type PRP to the Chicago Dermatology Society to highlight a classic presentation that responded well to adalimumab and cyclosporine and to review current management options for educational purposes and guidance in management.

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Key location(s): Various **CASE 7**

The Good, The Bad and The Ugly

Presented by Shannon Younessi, Vesna Petronic-Rosic MD, MSc, MBA, and Joerg Albrecht MD

NOTES

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