CASE # 1

PRESENTERS: Mandi Bietz, MD, Erin Vanness, MD, B. Jack Longley, MD

HISTORY: This is a 65 year old male who presented to the emergency department with a one week history of hand pain and rash. Two weeks prior to presentation he had started wearing an old wedding ring. The rash began under this ring on his left 4th finger, so he stopped wearing the ring and started applying various over the counter topicals, including triple antibiotic ointment. He also was soaking the hand in a hot tub nightly. When these measures worsened the rash he then presented to the emergency department and was admitted. He otherwise felt well without any fever, chills, night sweats. He did have residual fatigue and nausea from his recent chemotherapy infusion.

PMH: Locally advanced pancreatic cancer (currently undergoing chemotherapy as part of a clinical trial), hypertension, COPD, chronic rhinitis

MEDICATIONS: OUTPATIENT: triple antibiotic ointment (applied to rash on hand), alprazolam, bupropion, tamsulosin, trazodone, 5-FU/oxaliplatin/leucovorin/irinotecan (last combination chemotherapy treatment two weeks prior to admission). INPATIENT: vancomycin, cefepime

EXAM: On the left 4th proximal finger, there is an erythematous, purpuric, indurated plaque extending onto adjacent palm and adjacent fingers. Within this plaque are vesicles and bullae, especially at the peripheral, advancing edge.

LABS: Abnormal: Hemoglobin 11.7 (otherwise normal CBC) Normal: complete metabolic panel Cultures: blood cultures negative, surface culture and tissue culture positive for filamentous fungus

HISTOPATHOLOGY: Biopsy from finger shows acral skin with vesiculation and spongiosis. PASD stains show fungal elements in mid stratum corneum.

DIAGNOSIS: Bullous tinea

TREATMENT: Two-week course of oral fluconazole.

DISCUSSION: Bullous tinea is an uncommon presentation of a very common superficial skin infection. Tinea infection of the hands most often presents as diffuse hyperkeratosis of the palm that does not respond to emollients. When presenting in conjunction with tinea pedis, this is referred to as “two feet and one hand syndrome”. The organisms commonly responsible for tinea manuum are the same as for tinea pedis: *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum*. Bullous tinea is most often caused by *T. mentagrophytes* and usually occurs on the feet.

Superficial fungal infections of the skin are very common, and are typically easy to diagnose and treat. However, when the infection clinically mimics another cutaneous disorder or when the clinical presentation has been modified by use of inappropriate treatment, it can be more difficult to diagnose. Common mimickers of various forms of tinea include impetigo, cellulitis, eczematous dermatitis, lupus erythematosus, polymorphous light eruption, psoriasis, and rosacea. Patient specific factors that can alter clinical presentation include age, contact exposures, and immunosuppression. In our patient the bullous presentation and history of application of triple antibiotic ointment (containing bacitracin and neomycin) mimicked allergic contact dermatitis. His immunosuppressed status likely induced a more inflammatory form of tinea than would be typical in this location.

Treatment depends on the invasiveness and degree of inflammation. Typical tinea infections can often be successfully treated with topical antifungals. When the fungal infection is widespread, bullous, inflammatory, or involves deep components of hair follicles (Majocchi’s granuloma), oral antifungals are usually necessary to eradicate the infection.
KEY POINTS

- Superficial dermatophyte infections of the skin are common and their classic presentations are often easy to recognize and treat
- Atypical presentations can mimic a wide range of inflammatory and infectious cutaneous disorders
- Age, contact exposures, and immunosuppression can all alter the clinical presentation of superficial fungal infections and care should be taken to perform a more complete workup when the diagnosis is in question

REFERENCES:

CASE # 2

PRESENTERS: Mandi Bietz, MD, Daniel Bennett, MD

HISTORY: An otherwise healthy 18-month old girl presented with a 3 mm papule on her right upper arm. This was stable in size for the next 5 months when it was treated with cantharidin for presumed molluscum contagiosum. The lesion cleared but recurred 2 months later and was now enlarging. This was then biopsied when the child was 24 months old.

PMH: no significant PMH, on no medications

FAMILY HISTORY: no family history of melanoma, mother has a history of severely dysplastic nevi

EXAM: On the right tricep there was a 4 mm pink domed papule. No lymphadenopathy was present.

HISTOPATHOLOGY: Sections show an asymmetrical and deeply extending compound proliferation of enlarged fusiform and epitheliod melanocytes, many of which have amphophilic or finely granular cytoplasm. A small intraepidermal component is noted. In the dermis, coalescing and non-maturing nests and fascicles of melanocytes extend through an expanded reticular dermis, to a depth of 4.0 mm. Cells in mitosis are easily found, including in the deep melanocytes. Ki-67 cell proliferation index is elevated and there is significant loss of expression of p16. Array-based comparative genomic hybridization was performed and showed loss in chromosome 9 and gain in chromosome 20.

DIAGNOSIS: Childhood spitzoid melanoma, 4.0 mm in thickness

TREATMENT: Wide local excision with sentinel lymph node biopsy (negative for metastatic melanoma)

DISCUSSION: Childhood spitzoid melanoma is a very rare form of cutaneous melanoma. It lies on the end of a spectrum that begins with Spitz nevus. Spitz nevi were initially described as “benign juvenile melanoma” in 1948 by Sophie Spitz.1 Classic Spitz nevi present as reddish-pink domed papules, but there is also a pigmented variant. Classification has been controversial over the years, but typically Spitz nevi that present in childhood and follow the typical clinical and histologic criteria have been regarded as benign. Atypical Spitz nevi and atypical Spitz tumor are both terms that have been used for lesions showing some distinctly abnormal characteristic commonly absent in conventional Spitz nevi.1 Beyond that, however, these terms are not as yet clearly defined, but several papers have attempted to shed light on these categories of Spitz lesions.1,2

Characteristics of spitzoid melanoma differ based on whether it occurs in an adult or pediatric patient. Adult spitzoid melanoma is often clinically and dermoscopically indistinguishable from conventional melanoma. The genetic signature of adult spitzoid melanoma is also similar to conventional melanoma, often harboring BRAF or NRAS mutations. Childhood spitzoid melanoma (especially in patients under 10 years of age) is a peculiar entity, which differs clinically, histologically, and genetically from adult spitzoid melanoma and conventional melanoma.1,2 Childhood spitzoid melanoma often presents as a red nodule with an atypical vascular pattern. Histologically it is composed of pleomorphic epitheliod cells that can be seen in conjunction with monomorphic spindle cells typical of a Spitz nevus. Childhood spitzoid melanoma does not show BRAF or NRAS mutations.

Care must be taken to distinguish atypical spitzoid tumors from childhood spitzoid melanoma, even though there is considerable clinical and histologic overlap.3 Histologic features of childhood spitzoid melanoma include increased mitotic counts (especially deep in the specimen), increased Ki-67 index, and loss of P16 expression.2 Comparative genomic hybridization is performed in these lesions, and chromosomal copy number abnormalities are associated with melanoma. Expert review of these lesions is very important in the histopathological diagnosis.
Childhood spitzoid melanoma is rare, and these tumors seem to demonstrate biological behavior that is distinct from conventional melanoma. One small study compared childhood spitzoid melanoma with childhood non-spitzoid melanoma and found that even though spitzoid melanoma exhibited poorer prognostic factors (high Breslow thickness, high mitotic rate, positive sentinel lymph node) the mortality was lower than compared to non-spitzoid melanoma in children. Another retrospective study showed that decreased survival was related significantly to age >10 years, previous non-melanocytic malignancy, high Breslow thickness, high Clark level, and the presence of metastases at presentation. In their study, all patients who died were >11 years old at diagnosis. Another retrospective study showed that even in patients with metastatic spitzoid melanomas, age plays a significant role in survival. Their reported 5-year-survival rate in children with metastatic spitzoid melanoma between 0 and 10 years of age was 88%, compared with 49% in those between 11 and 17 years of age.

Treatment recommendations for childhood spitzoid melanoma are sparse. There is consensus that childhood spitzoid melanoma should undergo wide local excision and sentinel lymph node biopsy should be offered at similar Breslow depths to conventional melanoma. If either sentinel lymph node biopsy or imaging workup reveals metastatic melanoma, however, there are no evidence-based or consensus guidelines regarding adjuvant treatment.

**KEY POINTS**
- Childhood spitzoid melanoma is a rare form of cutaneous melanoma
- Histopathologic separation from Spitz nevi can be difficult, and relies on immunohistochemical markers and genomic, molecular, and cytogenetic studies
- Although prognostic data are limited, childhood spitzoid melanoma appears to have a less aggressive course as compared to childhood non-spitzoid melanoma, especially for children <10

**REFERENCES:**
CASE # 3

PRESENTERS: Katie Bonnichsen MD, Patrick Rush DO, Daniel Bennett MD

HISTORY: A 43 year-old male presented to clinic with a two-year history of an enlarging penile lesion. He reported a history of childhood trauma at the site of the penile mass and had noted rapid growth of the mass and development of an adjacent painful inguinal nodule over the last six months. Initial workup for sexually transmitted infections was negative.

PMH: Multiple toe amputations as a result of frostbite injury, otherwise negative

SOCIAL HISTORY: The patient reported heavy alcohol use in the past (sober at presentation), a 30+ pack-year smoking history, and intermittent marijuana use. He was employed in construction.

FAMILY HISTORY: Mother with a history of colon cancer

MEDICATIONS: Occasional over-the-counter Tylenol or ibuprofen for pain

EXAM: Significant for a 2.5cm erythematous exophytic verrucous nodule on the central ventral shaft of the penis with an adjacent 6cm erythematous ulcerated nodule in the left groin

HISTOPATHOLOGY: A punch biopsy performed of the penile lesion showed a dense proliferation of atypical basloid and epithelioid cells forming infiltrative cords and strands within a fibrotic stroma, individual cell keratinization, and focal areas of glandular cells forming lumina. Focal necrosis, nuclear pleomorphism, and mitotic figures were present. Immunoperoxidase staining showed the following profile: CEA(+), CK7(+), CK20(-), TTF-1(-), p63 focally (+), p16 focally “block type”(+), HMW-CK(+) with partial loss of expression, CK 5/6(+), PSA(-), PAX-8(-). In situ hybridization was positive for high-risk HPV (serotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68).

DIAGNOSIS: Metastatic HPV-positive primary cutaneous adenosquamous carcinoma of the penis

TREATMENT AND COURSE: The patient underwent excision of the left inguinal mass (which confirmed the diagnosis of metastatic primary cutaneous adenosquamous carcinoma) with a subsequent muscle flap and split thickness skin graft repair of the defect. He completed one of four cycles of TIP chemotherapy (paclitaxel, ifosfamide, cisplatin), but his course was complicated by a port infection and subsequent MRSA bacteremia. His providers felt that any subsequent chemotherapy or surgery would be too risky, so he instead completed treatment with definitive radiotherapy to the penis, bilateral inguinal regions, and pelvis.

DISCUSSION: Primary penile cancer is a relatively uncommon malignancy in the United States with an estimated incidence of less than 1% of all male cancers.¹ Risk factors include phimosis, poor hygiene, tobacco use, chronic inflammation, previous PUVA treatment, and HPV infection.²,³ Circumcision is thought to be protective.²

The majority (about 50%) of primary penile cancers are usual-type squamous cell carcinomas (SCC). The remainder of penile cancers are characterized as one of several subtypes of SCC recognized by the World Health Organization, each with its own distinct clinical and pathologic features and prognosis.²,³,⁴,⁵,⁶ One of these recognized subtypes is adenosquamous carcinoma (ASC), which is a rare variant comprising approximately 1-2% of penile cancers.² ASC is characterized by a combination of squamous tumor islands intermixed with areas of focal glandular differentiation. It most commonly occurs on the penile glans or in the perimeatal region. Although pathogenesis is unknown, it has been postulated that ASC may have a bimodal origin with cells originating from both periurethral mucin-producing cells and epithelial squamous cells on the surface of the glans.⁶,⁷ Nodal metastases at the time of presentation are common. Histological grade is typically high with specimens of ASC tending toward deep infiltration with a high rate of vascular and perineural invasion.⁷,⁸
As mentioned previously, HPV is a known risk factor for the development of penile carcinoma, and HPV-related tumors are thought to represent anywhere from 20-75% of penile cancers. In several reports in the literature, HPV-16 (high risk HPV) is noted to be most prevalent subtype of HPV identified. Higher HPV-positive rates have previously been recognized in the warty-basaloid, basaloid, and warty variants of squamous cell carcinoma. Given the rarity of adenosquamous carcinoma (the variant diagnosed in our patient), ASC has largely been excluded from the studies examining the relationship between SCC-subtype and HPV status. To our knowledge, this is the first case of HPV-positive ASC reported in the literature. Additionally, the location of this patient’s primary tumor (on the penile shaft) was unusual compared to the most common location for ASC (glans or perimeatal region) previously reported.

Given the rarity of adenosquamous carcinoma of the penis (and the subsequent lack of cases reported in the literature), we present this case of HPV-positive metastatic primary cutaneous adenosquamous carcinoma of the penis in an unusual location to highlight the possibility of HPV as an oncogenic factor in this subtype of SCC. Additional reporting of this rare variant of penile cancer is needed to confirm this relationship.

**KEY POINTS**

- Adenosquamous carcinoma is a rare variant of penile cancer, composed of both epithelial and glandular components, that represents 1-2% of all diagnosed penile cancers.
- HPV infection is a known risk factor for the development of established subsets of penile cancer, but to our knowledge, it has not previously been described in association with the adenosquamous variant of penile cancer.

**REFERENCES:**

CASE # 4

PRESENTERS: Lauren Brin, MD and Gary Wood, MD

HISTORY: A 56 year-old male presented with a three-month history of an eruption following cardiac catheterization in February 2015. Past dermatological history was significant for pseudo-Sezary syndrome secondary to hydrochlorothiazide versus lisinopril diagnosed in 2010. Pseudo-Sezary syndrome resolved following discontinuation of oral antihypertensives. During cardiac catheterization, the patient underwent placement of three drug-eluting Xience alpine stents. He was started on antiplatelet therapy with ticagrelor, which was later changed to prasugrel, and then to clopidogrel. Skin eruption began shortly following cardiac catheterization and progressively worsened. He was treated with IV corticosteroids, IV antihistamines, and several courses of oral prednisone without improvement.

MEDICATIONS: Xience alpine drug-eluting stents, clopidogrel, simvastatin, spironolactone, metoprolol succinate, cholecalciferol, coenzyme Q10, omega-3 fatty acids, aspirin, and fluticasone

ALLERGIES: Hydrochlorothiazide and lisinopril inducing pseudo-Sezary syndrome in 2010

EXAM: Significant for erythematous papules coalescing into plaques with light overlying scale involving the bilateral extremities, dorsal hands, and lateral trunk. There were also thick yellow hyperkeratotic plaques with underlying erythema involving the bilateral plantar feet. Involving the palmar hands were erythematous plaques with overlying white scale with overlying desquamation, hyperlinearity, and fissures.

HISTOLOGY: Spongiotic dermatitis with an atypical lymphoid infiltrate and epidermotropism. Immunohistochemical staining revealed CD3 and CD4 positivity with a decrease in the number of CD5 and CD8 expressing cells.

FLOW CYTOMETRY: Flow cytometry revealed a similar immunophenotype to previous specimens from 2010 with CD7 positive, CD4 positive, and CD26 negative T cells with a total absolute Sezary cell count of approximately 2400/μL.

DIAGNOSIS: Pseudo-Sezary syndrome (pseudolymphomatous reaction to a drug or other ingestant)

TREATMENT AND COURSE: The patient was initially treated with topical triamcinolone and clobetasol cream as well as discontinuation of oral spironolactone. Due to the time course of the patient’s presentation following cardiac catheterization and initiation of anti-platelet therapy, these agents were also possible etiologies of his presentation. However, the patient required antiplatelet therapy for 12 months following placement of drug-eluting stents and these medications were not practical to discontinue. Metoprolol was also a consideration as it has been described as an etiology of pseudo-lymphoma. After six months off of spironolactone therapy, the patient displayed considerable improvement in his skin eruption with at least 50% improvement at his most recent follow up.

DISCUSSION: Pseudolymphoma is defined by the presence of a lymphoproliferative process histologically, or in some cases clinically, which follows a benign course without presence of malignant lymphoma. Similarly, pseudo-Sezary syndrome (SS) also follows a benign course, yet clinically and histologically resembles SS. Pseudolymphoma is classically thought to be caused by various stimuli such as medications, including antihypertensives, anticonvulsants, antidepressants, and antipsychotics. Other etiologies include tattoo dyes, arthropod reactions, and infections such as Lyme disease, varicella-zoster virus, and HIV infection. It is theorized that chronic antigen stimulation of memory T cells leads to the development of mycosis fungoides (MF) and SS. A prospective analysis and case series of 1443 MF and SS patients found that 63.8% of patients started hydrochlorothiazide (HCTZ) prior to developing cutaneous T cell lymphoma. Within this study, 28.8% of patients experienced complete or partial remission after discontinuing HCTZ therapy. Three patients during this study were re-challenged to HCTZ and again developed MF lesions, which resolved or improved with cessation of therapy. The authors of this study propose that HCTZ can
act as an antigenic trigger for MF and patients diagnosed with pseudolymphoma could later progress onto overt MF or SS.  

SS is a rare disease accounting for less than 5% of all cutaneous T cell lymphoma. It has been classically defined by the presence of peripheral neoplastic T cells (Sezary cells) in addition to erythroderma and generalized lymphadenopathy. Diagnostic criteria for Sezary syndrome include presence of a T-cell clone in the peripheral blood, immunophenotypical abnormalities consistent with Sezary syndrome, and an absolute Sezary cell count of at least 1000 cells/μl.  

Histologic features of SS are typically similar to those found in MF. However, the infiltrate of SS is often more monotonous and epidermotropism can be absent. Immunophenotype by flow cytometry is classically CD3+, CD4+, and CD8- with loss of CD7 and CD26 expression. An immunophenotypic analysis of 97 cases of SS, demonstrated loss of CD7 (<50%) in 65% of cases. Although loss of CD7 is more typical of SS, our patient demonstrated CD7 positivity in both accounts of pseudo-SS.  

Interestingly, our patient has presented with two episodes of pseudo-SS with two unique etiologies. To our knowledge, there has not been another case of a patient developing two separate cases of pseudo-Sezary syndrome to two unique medications.  

**KEY POINTS**  
- Pseudo-Sezary syndrome is defined by a histologic lymphoproliferative process in addition to T cell clonality in the peripheral blood with benign clinical course.  
- Hydrochlorothiazide has been proposed as an antigenic trigger for mycosis fungoides.  
- Immunophenotype of Sezary syndrome by flow cytometry is classically CD3+, CD4+, and CD8- with loss of CD7 and CD26 expression.  
- Discontinuation of the offending medication in pseudolymphoma typically results in resolution.  
- Some authors believe that patients with pseudolymphoma are at risk of progression to overt mycosis fungoides or Sezary syndrome.  

**REFERENCES:**  
WISCONSIN DERMATOLOGICAL SOCIETY

CASE # 5

PRESENTERS: Lauren Craddock MD, George Reizner MD, Jack Longley MD

HISTORY: 45 year old male with history of alpha-1 antitrypsin deficiency status post bilateral lung transplant in 2005, on chronic immunosupression, with CKD, HTN, HLD, GERD, was seen as an inpatient consult after presenting with worsening diffuse pustular eruption and oligoarthritis over 5 days. The eruption started as a ‘red bump’ on his right shin, then progressed as he developed more red papules and pustules on his face, body, arms, legs, and soles. In addition to skin findings, he developed erythema with clear drainage in his right eye, as well as severe painful swelling in multiple joints. He denied any recent travel, camping, hunting, or extramarital sexual exposure. He did report repairing doors on a cattle farm about 2 weeks prior. Complete review of systems was negative except as above and positive for mild headache, fevers and chills, with dry non-productive cough for 1 week.

MEDICATIONS: Notable for immunosuppression with tacrolimus, mycophenylate mofetil, and prednisone prior to admission. Since admission, patient treated with doxycycline, ceftriaxone, and vancomycin.

EXAM: The patient was in marked pain and holding his right knee. Joint exam was notable for pre-patellar effusion of the right knee and synovitis of the right 4th finger DIP. Eye exam was notable for bilateral blepharitis with scleral injection. Skin exam was notable for multiple erythematous, infiltrated papules and clear pustules scattered over his left philtrum, neck, chest, abdomen, back, arms, legs, and bilateral plantar feet, with a hematoma on the left 3rd fingernail.

Labs including CBC with differential and complete metabolic panel were notable for WBC 13, CRP 8, ESR 62, Ferritin 560. Outside skin surface culture of fluid from one of the pustules two days prior was negative to date, and blood cultures from one day previous were negative.

Imaging was notable for MRI revealing scattered lesions within the brain parenchyma.

HISTOPATHOLOGY: Two biopsies were performed, one for histopathology, another for fungal, bacterial, and mycobacterial culture. On H&E, a suppurative dermatitis was present with large yeast forms, some with broad based budding highlighted on PASD staining. Present within the dermis were sheets of neutrophils with mononuclear cells and multinucleate giant cells containing yeasts. Gram stain was negative for bacteria, and Ziehl-Neelsen stain was negative as well.

DIAGNOSIS: Disseminated North American Blastomycosis with secondary CNS and pustular cutaneous involvement and reactive arthritis

TREATMENT AND COURSE: The patient was started on liposomal amphotericin B liposomal amphotericin B daily with 1L NS pre and post hydration after fungal smear revealed broad based buds consistent with blastomyces. Urine and serum antigen assays were positive for both blastomyces and histoplasmosis. After histopathology and fungal culture confirmed the diagnosis of disseminated blastomycosis, the patient was continued on a planned 4-6 week course of liposomal amphotericin B with rapid improvement of skin lesions, systemic symptoms, and reactive arthritis. One month later, the patient continued to do well with drops in his urine blasto antigen level, but he was unable to continue therapy with amphotericin due to worsening kidney functioning necessitating switch to voriconazole 300mg BID.

The following month, repeat MRI of the head showed resolution of previous intraparenchymal lesions. Infectious disease plans to continue voriconazole for a year and then consider lifelong itraconazole suppression. He continues on tacrolimus, mycophenylate mofetil and prednisone per Transplant Medicine.

DISCUSSION: Blastomycosis is caused by the endemic, dimorphic fungus, Blastomyces dermatitidis. This fungus is typically found in soil of the Mississippi and Ohio river valleys, as well as the Great Lakes region with cases appearing in Illinois and Wisconsin.¹ The majority of cases occur in the immunocompetent, but dissemination is more frequent in the immunocompromised.¹ Dogs may serve as
Blastomycosis may manifest as pulmonary, disseminated, or primary cutaneous disease. Pulmonary involvement after inhalation of spores may present as either an acute or chronic pneumonia with systemic symptoms of weight loss, fever, malaise and fatigue; patients may also be asymptomatic. Secondary cutaneous involvement is very common in disseminated blastomycosis, occurring in 40-80% of patients, with the skin being the most frequent extrapulmonary site of involvement. Furthermore, secondary cutaneous lesions via dissemination are more common than primary cutaneous disease via direct inoculation. Cutaneous lesions typically present as ulcerative and verrucous plaques, sometimes studded with pustules around the periphery. Only rarely does it present in a widespread pustular form, with only 7 previous cases being reported in the literature. Diagnosis of blastomycosis is most reliably made by direct visualization on tissue histopathology or cytology, and culture. Serological and urine antigen assays are less reliable. Treatment is typically directed by an Infectious Disease specialist, with initial therapy starting with amphotericin B for 1-2 weeks (4-6 weeks if CNS involvement) until improvement, followed by maintenance therapy with itraconazole. Non-life threatening infections may be treated with itraconazole alone.

**KEY POINTS**

- Blastomycosis is an endemic, dimorphic fungus found in the Mississippi and Ohio Valleys, as well as the Great Lakes area of Illinois and Wisconsin.
- Most commonly presents in immunocompetent as pulmonary disease.
- Pulmonary disease may be asymptomatic or present as acute or chronic pneumonia.
- In immunocompromised, dissemination from pulmonary source is most common.
- Skin is most common extrapulmonary site involved in disseminated disease.
- Cutaneous lesions typically appear as ulcerated, verrucous plaques but may also rarely occur as a diffuse pustular eruption.
- Diagnosis is most reliably made by histological or cytological examination. Culture is useful for confirmation. Urine and serological assays are less reliable.
- Treatment is best managed by an Infectious disease specialist but is initiated with amphotericin B until improved, then transitioned to itraconazole for completion of therapy.

**REFERENCES:**

CASE # 6

PRESENTERS: Katherine Garrity MD, Robert Glinert MD

HISTORY: 29 year old male with past medical history of seasonal allergic rhinoconjunctivitis and Tetralogy of Fallot status repair in infancy presenting with three week history of yellow, malodorous drainage from umbilicus. The onset of umbilical drainage was approximately one week after acute onset, worsening, sharp epigastric pain, associated with subjective fever and diarrhea. He was evaluated in the emergency department (ED) and underwent CT scan, which showed terminal ilium thickening, concerning for inflammatory bowel disease (IBD). Laboratory evaluation in emergency department showed neutrophilia (81.3%), lymphopenia (8.7%), and ALT of 83 U/L. He was discharged from emergency department and told to establish care with gastroenterology for IBD workup.

He treated the umbilical drainage at home with topical hydrogen peroxide and Neosporin. Given persistence of drainage, his primary care physician prescribed topical mupirocin ointment and erythromycin lotion for one week. Bacterial culture grew normal skin flora. He did not improve with antibacterial medications, so his primary care physician prescribed oral fluconazole and topical nystatin cream for one week. Again, he had no improvement; thus, he was referred to dermatology.

Upon evaluation in dermatology clinic he complained of continued sanguineous discharge, intermittent cramping lower abdominal pain, and lethargy; his diarrhea had resolved. He adamantly denied any manipulation or foreign body instrumentation to umbilicus.

MEDICATIONS: cetirizine, ibuprofen and fluticasone nasal spray

EXAM: The internal skin of umbilicus demonstrated serosanguineous crust circumferentially. Deeper to this was macerated skin with thin yellow slightly cloudy fluid. Approximately one centimeter into the umbilicus at 2-3 o’clock was a 2x2x3mm bright red, pedunculated smooth papule. Adjacent and deeper to this papule was a sinus tract filled with yellow fibrinous material. This sinus tract was easily probed to two centimeters without resistance. We did not probe further than two centimeters due to patient discomfort.

HISTOPATHOLOGY: Keratin filled cyst lined by cuboidal epithelium without granular layer. Tubular segment of modified transitional epithelium with attached portion of adipose tissue. Surrounding dermis consists of granulation tissue with reactive changes.

IMAGING: Colonoscopy with CT of abdomen demonstrated a small tubular structure in the right lower quadrant adjacent to a small bowel loop may questionably represent the appendix without findings of acute appendicitis. Ultrasound demonstrated possibly a sinus tract extending posteriorly and to the left from the umbilicus; the mass seen on CT was thought to be draining and collapsed based on clinical history. Sinogram demonstrated a left sided lateral curvilinear sinus tract from the base of the umbilicus.

DIAGNOSIS: Urachal remnant including cyst and sinus tract, with connection to bladder.

TREATMENT AND COURSE: After dermatologic evaluation, we coordinated for next day gastroenterology consult for further workup to rule out cutaneous fistula in setting of recent CT demonstrating terminal ileal thickening. Further imaging studies, including ultrasound and sonogram, were suggestive of either vitelline duct remnant or urachal cyst. A referral was made to general surgery for definitive treatment. This was achieved with open excision of umbilicus and urachal cyst followed by laparoscopic excision of urachal remnant. His postoperative course was complicated by urinary tract infection which was treated successfully with antibiotics. His subjective fever and diarrhea were attributed to a concomitant, unrelated gastroenteritis per gastroenterology.

DISCUSSION: The urachus is an embryologic structure that serves as a channel between the bladder and umbilicus during the first trimester of pregnancy with the function of draining urine. This channel
typically seals off and obliterates around the 12th week of gestation. However, if an abnormality occurs during this process of obliteration then a disorder of the urachus can occur. These include patent urachus, urachal sinus, urachal cyst and diverticulum. All of these disorders are typically asymptomatic and only detected on imaging studies incidentally. Common complications of urachal abnormalities include infection, drainage of fluid, pain/tenderness, erythema, mass, and, rarely, malignant degeneration. Abdominal pain alone has been report as the sole complaint and can mimic an acute abdomen due to appendicitis, as was initially suspected in our patient in the ED. Remnants found in adults require management because of a greater risk for infection, and in older patients, due to an increased risk of neoplastic differentiation. In case series, 51-67% of adults with urachal mass had urachal carcinoma, most commonly adenocarcinoma, at time of presentation. Hematuria, especially without dysuria, should be screened for in patients with any of the aforementioned complaints, as it is a strong predictor of urachal carcinoma. Patients’ age should also be taken into account as the highest incidence of urachal carcinoma is in fifty to sixty year old individuals. The differential diagnosis of an umbilical mass should include vitelline duct anomalies, appendicitis, granulomatous inflammatory conditions, granulation tissue from the umbilical stump, hematoma, abscess, umbilical hernia, urachal carcinoma and tumors of the abdominal wall. In women, endometriosis should also be considered. CT is the most important in the diagnostic work-up. Ultrasound can be helpful, but is not sufficient, as shown by our case as continuous drainage led to collapse of the cyst. Discerning between benign and malignant pathology may be difficult with CT due to unclear contrast enhancement; however, a supravesicular mass with calcification is highly suggestive of urachal carcinoma because 50%–70% of urachal carcinomas contain calcification. Histologically, the urachus, and its remnants, are composed of 3 layers; an innermost layer of modified transitional epithelium similar to urothelium, a middle fibroconnective tissue layer and an outer layer of smooth muscle continuous with the detrusor. The surrounding dermis or soft tissue often shows fibrosis, calcification and reactive changes. Surgical excision of benign urachal remnants is generally curative. Traditional surgical approach to the excision of persistent urachal remnants is a lower midline laparotomy or semicircular infraumbilical incision. Laparoscopic approaches are now favored given high success rates, minimally invasive nature and optimal cosmetic outcomes.

KEY POINTS
- Umbilical masses associated with drainage and pain in a young person are likely benign.
- Although rare, disorder of the urachus should be consider in the differential of umbilical masses.
- In adults, urachal abnormalities should be treated given high rates of infection and increased risk for malignant degeneration, most commonly to adenocarcinoma in those aged over 50 years.
- Surgical excision with pathologic confirmation of diagnosis is the standard of care for treating urachal remnants.

REFERENCES:
HISTORY: Patient is a 67 year old man with a history notable for a recent diagnosis of stage IV squamous cell carcinoma of the lung involving the right lower lobe and T12 vertebral body, on palliation who presented with a 2 month history of large plaques on his torso and proximal extremities, which subsequently developed large flaccid pustules and erosions. Despite clinical appearance lesions were minimally symptomatic and he otherwise felt well. He denied facial, ocular, oral, or anogenital involvement. He has no history of eczematous dermatitis, psoriasis, Darier disease, or known oral, genital, or cutaneous herpes simplex.

PMH: Stage IV squamous cell carcinoma of the lung, chronic obstructive pulmonary disease

MEDICATIONS: albuterol MDI, albuterol-ipratropium MDI, Budesonide-formoterol inhaler,

FAMILY HISTORY: No psoriasis, atopy

EXAM: Well-appearing elderly man in no distress. There was no palpable lymphadenopathy involving the lower neck, chest, axilla, abdomen, back, buttocks, upper arms, thighs, proximal forearms and shins, there are numerous annular to serpiginous, erythematous, edematous papules and plaques, in multiple areas coalescing into broad sheets. Many plaques have central shallow erosions or partial central clearing with keratolytic scale. There are few intact large flaccid pustules ranging from 5-15 mm in diameter. Eruption spares the scalp, face, hands and feet, and there is no ocular, oral, genital, or perianal inflammation, erosion, or ulceration.

HISTOPATHOLOGY: Hematoxylin-Eosin staining shows subcorneal blisters containing dense collections of acantholytic squamous cells admixed with neutrophils as well as eosinophils. Acantholytic squamous cells demonstrate chromatin margination, no definitive giant cells identified. There is a brisk superficial perivascular and diffuse mixed infiltrate with lymphocytes, neutrophils, and eosinophils with focally eosinophilic spongiosis. Away from blisters there is a multifocal acantholysis with neutrophil exocytosis. Special staining for PASD and Gram stain are negative. Immunoperoxidase staining for HSV highlights acantholytic squamous cells, but staining is less intense than in controls. Later HSV 1/2 PCR was negative.

Direct immunofluorescence was negative. Indirect immunofluorescence for paraneoplastic pemphigus panel was negative.

DIAGNOSIS: Subcorneal pustular dermatosis (SCPD, Sneddon Wilkinson) with secondary HSV infection

TREATMENT: Patient was initially provided high potency topical steroid but declined to use it. He declined systemic therapy. At last follow up lesions were clinically improving.

DISCUSSION: Subcorneal pustular dermatosis (Sneddon Wilkinson) is a rare, benign, chronic and relapsing cutaneous condition. Cutaneous findings are notable for annular and serpiginous plaques with development of flaccid pustules of varying size, often no longer intact at time of exam. Also occasionally noted are “half and half” blisters in which neutrophils layer to the inferior portion of the blister. Pustules are typically sterile, although secondary bacterial infection is often noted. It typically involves the trunk, proximal extremities, and flexural areas including axilla and groin, with usual sparing of face, distal extremities, and mucous membranes. Lesions are usually asymptomatic although mild pruritus or irritation can occur.
Etiology of this disease is unclear. A subset will stain positive for IgA against desmocollin in the epidermis on DIF and so are felt to be a variant of IgA pemphigus. Another subset will progress to more classic pustular or plaque psoriasis. Associated diseases include plasma cell dyscrasias, other lymphoproliferative disorders, with anecdotal reports for multiple autoimmune and inflammatory disorders. To date there is no published association with solid tumors including non-small cell lung cancer. Lymph node exam, complete review of system, and serum electrophoresis is recommended.

Given benign course and minimal symptoms treatment can be deferred. Dapsone is the treatment of choice, but effect is often delayed and symptoms typically recur on cessation. Topical steroids can ease symptoms but usually do not lead to clearance. Acitretin, colchicine, anti-TNF antibodies and a myriad of antibiotics have also been reported to be successful.

Given cytopathic effects on H&E and weak positive immunoperoxidase staining for HSV, we cannot definitively rule out that his eruption represents disseminated cutaneous HSV. The eruption in these cases typically involves grouped tense vesicles and pustules rather than his large flaccid pustules and erosions. It is atypical for disseminated HSV to present without primary oral or genital lesions, lesions are typically painful or pruritic, and disseminated involvement is associated with constitutional symptoms including fever, regional lymphadenopathy, or internal organ involvement, which he lacked. At follow-up HSV PCR swab from persistent lesion was negative. Given this and his typical clinical appearance we favor the diagnosis of SCPD with superimposed focal mild Kaposi varicelliform eruption-like HSV infection over primary disseminated HSV. We were unable to find a published association with SCPD and HSV infection, and it bears further investigation whether there is a pathogenic role for HSV in a subset of patients affected with SCPD

KEY POINTS

- Subcorneal pustular dermatosis (Sneddon Wilkinson) is a rare chronic relapsing sterile pustular eruption.
- Given association with IgA pemphigus and monoclonal gammopathy DIF and SPEP should be considered.
- Dapsone is first-line therapy
- This case uniquely presents SCPD in association with pulmonary squamous cell carcinoma and secondary HSV infection

REFERENCES:
Vlada Groysman, MD; Chief Editor: Dirk M Elston, MD. Subcorneal Pustular Dermatosis. Medscape medicine


CASE # 8

PRESENTERS: Lydia Kim, MD; Daniel Bennett, MD; Ladan Mostaghimi, MD

HISTORY: H.O. is a 22 year old Hispanic male with a PMH of metastatic nonseminomatous germ cell tumor, Stage IIIC, of the left testicle who was transferred from an outside hospital for a gastrointestinal bleed requiring multiple transfusions. During his admission, he was noted to have several lesions on his right upper chest that had appeared 1 month prior. These lesions were non-tender, non-pruritic, and easily bled. One of the larger lesions had opened, bled, seemed to resolve, but then reappeared.

PMH: Nonseminomatous germ cell tumor, Stage IIIC, of the left testicle with metastasis to the right lung and several foci in the brain, s/p left testicle resection (12/21/2015) and partial right cerebellum resection (12/30/2015). Radiation treatment and chemotherapy were planned to start following recovery of cerebellar resection.

MEDICATIONS: ferrous sulfate, omeprazole, levetiracetam

FAMILY HISTORY: Negative for testicular cancer

EXAM: On the right upper chest are several grouped, exophytic, vascular papules some of which coalesce into a plaque measuring approximately 2-3 cm. Hemorrhagic crust and bleeding of the larger plaque are noted. There is one solitary 7 mm vascular papule inferior to the larger plaque.

HISTOPATHOLOGY:
12/31/2015 Cerebellar tumor: Metastatic choriocarcinoma
1/19/2016 Right upper chest: Metastatic choriocarcinoma with lymphovascular invasion.

LABS/IMAGING:
Labs: WBC 7.4 Hgb 6.8 Hct 21 Plt 338; CMP within normal limits; Beta-HCG >225000 mlU/mL (Non-pregnant women: ≤ 5 mlU/mL); AFP 3.3 (nl 0-8.8); LDH 274 (nl 125-220)

12/29/2015 MRI Head with and without contrast: 18x18x16 irregular and peripherally enhancing mass centered in the right cerebellar hemisphere, compatible with an intracranial metastatic deposit. Presence of associated curvilinear enhancement extending anterolaterally from the mass is concerning for presence of superimposed leptomeningeal disease. 3 areas of punctate nodular enhancement in the left middle frontal gyrus concerning for new metastatic disease since prior exam on 12/21/2015.

1/21/2016 CT Chest Abdomen Pelvis with IV contrast: Marked interval increase in metastatic disease from CT studies of 12/19/2015. Increased size and number of pulmonary nodules. New nodules in the right lateral chest wall. New extensive hepatic metastases. New bilateral renal metastases. New retroperitoneal mass in the right lower quadrant.

DIAGNOSIS: Metastatic choriocarcinoma to skin.

CLINICAL COURSE: New onset seizure-like activity prompted a repeat MRI head (1/21/2016) showing several new, rapidly growing foci of metastatic disease. Within two weeks of skin biopsy, patient passed away from complications of an intestinal perforation and hemorrhage which revealed metastatic choriocarcinoma.

DISCUSSION: Testicular cell tumors are the most common malignancy in young men, peaking between the ages of 20 and 34, with an incidence of new testicular cancer diagnoses reaching 8820 in the U.S. in 2014. Most cases are diagnosed at an early stage and are highly curable with radical orchiectomy with 5-year overall survival greater than 95%.
More than 95% of testicular cancers are germ cell tumors of which two types exist: seminomatous and nonseminomatous. For seminomatous tumors, chance of cure is high even in advanced disease. Patients affected with seminomatous tumors present at an older age with a median at diagnosis of 40 years. Nonseminomatous tumors are comprised of embryonal cell carcinoma, yolk sac tumor, choriocarcinoma, and teratoma. Patients affected with nonseminomatous tumors present at a younger age, with median at diagnosis of 30 years.3

Choriocarcinoma is a highly malignant tumor with a far worse prognosis, with 5-year survival being less than 80%.2 Choriocarcinoma presents with elevated human chorionic gonadotropin, often widespread disease, and rapid progression of disease in a young male with a testicular mass. Choriocarcinoma syndrome is characterized by rapid hematologic spread to multiple organs with intra-tumoral bleeding. This can be a medical emergency with high morbidity and mortality. The most validated indicator of poor prognosis is lymphovascular invasion.3 Appropriate work up includes staging with CT chest, abdomen, and pelvis and MRI of the brain while initiating treatment. Early aggressive treatment with chemotherapy improves prognosis and should not be delayed for orchiectomy, biopsy, or sperm banking. Goals should be to normalize tumor markers. Advanced targeted therapies and clinical trials should be considered for refractory disease.

Cutaneous metastasis of choriocarcinoma is very rare, with only 15 cases having been reported in English literature. Of these, only 9 reported cases are of cutaneous metastasis of testicular choriocarcinoma.4 Cutaneous metastasis is a poor prognostic sign and is associated with advanced disease.5

KEY POINTS
- Choriocarcinoma is an aggressive malignant tumor often presenting with widespread disease.
- Early aggressive treatment is imperative as delay due to orchiectomy, biopsy, or sperm banking can lead to a fatal outcome.
- Cutaneous metastasis of testicular choriocarcinoma is exceedingly rare and is associated with advanced disease.

REFERENCES:
CASE 9

PRESENTERS: Klint Peebles MD, Gloria Xu MD PhD, Daniel Bennett, MD

HISTORY: 40 yo Caucasian man with history of well-controlled HIV, PTSD, and depression who was referred to dermatology with 6-8 months of asymptomatic perianal lesions, presumed to be condyoma acuminata. Lesions had increased in number since their initial appearance with occasional scant blood on wiping. He reported that a prior course of oral clindamycin was of no benefit. Additional findings included “itchy spots” on his palms, soles, chest, and back for at least 4-5 months prior to presentation. Presumptive treatment for both psoriasis and dermatophytosis had been ineffective.

He denied any recent fevers, chills, night sweats, arthralgias, myalgias, fatigue, abdominal pain, diarrhea, oral mucosal lesions, dysphagia, dysuria, or penile discharge.

FAMILY AND SOCIAL HISTORY: No family history of psoriasis, hidradenitis, or inflammatory bowel disease.

Patient identifies as gay with a history of both penetrative and receptive anal intercourse. He has been married to his male partner for several years. They are in a monogamous relationship. His husband is HIV negative, and they use condoms during intercourse but had notably not been sexually active in at least 9 months prior to his presentation due to the patient’s perianal lesions.

MEDICATIONS: Atripla (tenofovir/efavirenz/emtricitabine), Sertraline, Quetiapine, Carbidopa/Levodopa, Sildenafil as needed

EXAM: General: Alert and oriented, interactive, in no acute distress. Mild resting tremor noted.
Skin exam: At the perianal area extending from the anal verge to the medial gluteal folds were numerous confluent shiny, waxy, vegetative and verrucous papules and plaques. There were no fistulas, sinus tracts, or pustules. At the suprapubic area, scrotum, and penis, including the glans, there were scattered discrete erythematous and reddish-pink papules and thin plaques. Central chest and upper back showed well-defined hyperkeratotic pink and salmon-colored papules coalescing into thin scaly, psoriasiform plaques. There were well-defined, scattered, circinate, some more annular and some more targetoid, thin scaly reddish-pink plaques with preserved skin lines at the bilateral palms and soles.

There was no conjunctival injection. Oral cavity exam significant only for bite lines and no ulcerations or erosions.

LABS AND DATA:
HIV viral load undetectable, CD4 count 526 cells/uL.
Annual screening RPR negative each of 4 years prior to presentation and most recently 5 months prior to presentation.
RPR reactive at time of presentation, titer 1:128. TP-PA reactive. FTA-ABS reactive. VDRL reactive.
CSF studies, including VDRL, unremarkable.
Negative HBV and HCV serologies; immune to HBV.

HISTOPATHOLOGY: Biopsy of the chest revealed a mixed perivascular and lichenoid infiltrate with lymphocytes, histiocytes, and clusters of plasma cells. There was irregular epidermal hyperplasia with interface changes and occasional necrotic keratinocytes. PASD was negative.

DIAGNOSIS: Secondary Syphilis
**TREATMENT AND COURSE:** Patient was treated with 2.4 million units intramuscular benzathine penicillin x1 dose with marked improvement in cutaneous findings at follow-up. RPR titer downtrended to 1:16 four months after treatment. Curiously, patient had been diagnosed with an atypical presentation of Parkinson’s Disease by neurology 3 months prior to presentation given an unclear history of chronic dizziness, occasional falls, and prior diagnosis of essential tremors. CSF studies were negative for evidence of neurosyphilis. It is unclear when he was infected with syphilis as he was adamant about his monogamous relationship and denial of sexual activity through 9 months prior to presentation. Interestingly, his annual screening RPR had been negative 5 months prior to his presentation (3-4 months after his last reported episode of sexual intercourse). His husband did not show any signs or symptoms of infection although a record of definitive testing is unclear.

**DISCUSSION:** Syphilis is a sexually acquired, chronic infection caused by *Treponema pallidum* and is characterized by a variety of clinical manifestations. The secondary stage typically begins 4-10 weeks after the primary infection and invariably occurs in almost every patient in the absence of inappropriate treatment for primary disease. During 2005-2013, the annual incidence of syphilis doubled nationwide, disproportionately affecting men. The largest increases are occurring among MSM (men who have sex with men), where the disease is considered an epidemic. Overall rates are highest among African-American men although the more recent increases have been greatest among Hispanic and Caucasian men.

Syphilis increases the likelihood of acquiring and transmitting HIV with rates of coinfection as high as 50-70% among MSM infected with primary or secondary disease. Additionally, there are high rates of HIV seroconversion following infection with syphilis. The possibility of neurosyphilis should always be considered as it can occur in any stage of the disease. In patients with HIV, a careful comprehensive neurologic exam should be performed in all patients. CSF examination should be completed in the setting of unusual neurologic signs or symptoms as well as in cases of unknown duration of infection in those patients with HIV.

Finally, the prozone phenomenon may cause a false-negative nontreponemal test result, typically during secondary syphilis, when a high concentration of treponemal antigen does not permit detectable antigen-antibody complex formation. Limited reports suggest this may occur more often in HIV-infected patients, but definitive evidence is lacking. This phenomenon can be overcome by diluting the specimen and should be specifically requested if clinically appropriate.

**KEY POINTS**

- As the “great masquerader,” syphilis in all of its stages should be ruled out in the setting of consistent signs and symptoms regardless of reported sexual history.
- Infection rates are rising rapidly, with the largest increases occurring among MSM.
- Evaluation of the CSF to rule out neurosyphilis is indicated in any patient with HIV diagnosed with syphilis of unknown duration independent of viral load or CD4 T-cell count.
- Consider the prozone dilution phenomenon if clinical suspicion is high in the absence of positive serologic testing.

**REFERENCES:**

CASE # 10

PRESENTERS: Abigail Taub, MD; William Aughenbaugh, MD; Daniel Bennett, MD.

HISTORY: A 39 year old HIV negative female returned to dermatology clinic for follow up of nodulocystic acne. She had completed three months of oral isotretinoin with minimal improvement. Acne lesions were pruritic, but not painful.

PMH: none

MEDICATIONS: isotretinoin 60 mg by mouth daily

FAMILY HISTORY: unknown

EXAM: On the face and chest, there were scattered excoriated erythematous papules. No open or closed comedones.

HISTOPATHOLOGY: none

LABS: rapid HIV testing was positive

DIAGNOSIS: Eosinophilic folliculitis

TREATMENT: ketoconazole cream bid, isotretinoin 60 mg daily, and referral to Infectious Diseases for initiation of anti-retroviral therapy

DISCUSSION: Multiple cutaneous disorders have been recognized as important clues to the diagnosis of HIV infection.

Eosinophilic folliculitis is one of the most characteristic and common pruritic dermatoses associated with HIV. It generally occurs in patients with CD4 counts less than 200 cells/mm³ and may represent an exaggerated reaction *Malassezia* yeast. Patients present with excoriated follicular papules on the face and upper trunk. Multiple treatments have been tried including topical corticosteroids, topical tacrolimus, topical permethrin, topical antifungals, UVB phototherapy, itraconazole, dapsone, and oral retinoids. Controlling pruritus is difficult. Another non-infectious pruritic eruption associated with HIV is papular pruritic eruption of AIDS. It is a pruritic skin eruption characterized by greater involvement of the extremities than the face or trunk. It is more prevalent in Africa than North America or Europe. Clinically, lesions are symmetrically distributed, non-follicular papules. PPE of AIDS occurs with CD4 counts less than 50 cells/mm³.

There are also multiple cutaneous infections associated with HIV. The earliest cutaneous manifestation of HIV may be an exanthem occurring during primary infection. This is referred to as acute retroviral syndrome and consists of fever, lymphadenopathy, pharyngitis, and a morbilliform exanthem occurring 2-4 weeks after HIV exposure. Patients with CD4 counts less than 100 cells/mm³ may have more frequent recurrences of herpes simplex virus (HSV) typical in appearance as well as chronic, non-healing, deep ulcerations. HIV-infected patients have a 7-15 times greater risk of developing herpes zoster. HIV-associated zoster may be multidermatomal, ulcerative, chronic, verrucous, or widely disseminated. Patients with CD4 counts less than 250 cells/mm³ can have extensive and large molluscum lesions. Any part of the body can be affected, but lesions favor the face, neck, and intertriginous areas. The clinical differential diagnosis includes cutaneous involvement of disseminated fungal infections including *Cryptococcus*, *Histoplasma*, *Pneumocystis jiroveci*, *Coccidioides Paracoccidioides*, and *Penicillium*. Oral hairy leukoplakia due to EBV may be an early sign of HIV infection, affecting up to 25% of HIV-infected individuals. Lesions are usually asymptomatic and appear as white plaques with hair like projections along
the lateral aspect of the tongue. HIV-infected patients are also predisposed to recurrent and severe cutaneous bacterial infections, most commonly *Staphylococcus aureus*.

Patients with HIV are at higher risk of cutaneous neoplasms. HIV positive patients have a three- to five times higher risk of non-melanoma skin cancers. In patients with CD4 counts less than 200 cells/mm$^3$, cutaneous lymphomas of B- or T-cell lineage may develop. Kaposi sarcoma, due to human herpesvirus type 8, is the neoplasm most closely associated with HIV infection. Eruptive atypical nevi have also described in HIV-positive patients.

### KEY POINTS
- Pruritic non-infectious dermatoses include eosinophilic folliculitis and papular pruritic eruption of AIDS.
- Eosinophil folliculitis occurs in patients whose CD4+ counts are less than 200 cells/mm$^3$.
- Papular pruritic eruption of AIDS occurs in patients whose CD4+ counts are less than 50 cells/mm$^3$.
- Acute retroviral syndrome consists of fever, lymphadenopathy, pharyngitis, and a morbilliform exanthema occurring 2-4 weeks after HIV exposure.
- Cutaneous infections include atypical presentations of viral, bacterial, and fungal infections.
- Patients with HIV are at higher risk of cutaneous neoplasms including eruptive atypical nevi, NMSC, cutaneous lymphomas, and Kaposi sarcoma.

### REFERENCES:

HISTORY: A 46 year old HIV positive male with past medical history significant for recent initiation of anti-tuberculosis therapy was admitted to the hospital for a pruritic rash and skin sloughing for 12 days.

PMH: HIV positive (CD4 count: 454), pulmonary tuberculosis

MEDICATIONS: rifampin, isoniazid, pyrazinamide, and ethambutol

FAMILY HISTORY: unknown

EXAM: Thin African male. Diffusely on the trunk and extremities, there was superficial desquamation with a flaky paint appearance. On the bilateral plantar feet, there was hyperkeratosis with scattered hyperpigmented macules and patches. Atrophic tongue with irregular denudation of papillae.

HISTOLOGY: none

LABS: none

DIAGNOSIS: Nutritional deficiency

TREATMENT:
- High protein diet
- Riboflavin 20 mg by mouth daily
- Nicotinamide 100 mg by mouth three times daily
- Pyridoxine 100 mg by mouth daily
- Folic acid 1 mg by mouth daily
- IM B12 1 mg/week for one month, then monthly

DISCUSSION: Within days of vitamin and protein supplementation, the patient had resolution of desquamation followed by hyperpigmentation. This patient demonstrated features of protein calorie malnutrition (kwashiorkor) and multiple vitamin deficiencies (niacin, pyridoxine and cyanocobalamin). Kwashiorkor is characterized by peripheral edema and superficial desquamation described as “enamel paint spots” or “flaky paint.” Niacin (Vitamin B3) deficiency results in pellagra, classically dermatitis, diarrhea, and dementia. The dermatitis is characterized by a photodistributed hyperpigmented scaly eruption. Other findings include cheilitis, peri-anal and peri-oral erosions, and peripheral neuropathy. Isoniazid, for which the patient was taking for tuberculosis, can result in pyridoxine (Vitamin B6) deficiency. Signs and symptoms of pyridoxine deficiency include periorificial seborrheic dermatitis-like lesions, angular cheilitis, glossitis, conjunctivitis, anorexia, and peripheral neuropathy. Cutaneous findings of cyanocobalamin (Vitamin B12) deficiency include hyperpigmentation of flexural surfaces, palms, and soles. Patients also have glossitis, megaloblastic anemia, and peripheral anemia.
KEY POINTS

- Kwashiorkor is protein energy malnutrition characterized by edema and “flaky paint” desquamation
- Vitamin A deficiency can lead to phrynoderma ("toadskin"), night blindness, xerophthalmia, and Bitot spots (gray-white patches on the conjunctivae)
- Vitamin C deficiency can lead to bleeding gingivae, petechiae, follicular hyperkeratosis, corkscrew hairs, impaired wound healing, loose teeth, and subperiosteal hemorrhage
- Vitamin B1 deficiency can lead to skin glossitis, glossodynia, fatigue, peripheral neuropathy, and encephalopathy
- Vitamin B2 deficiency can lead to angular cheilitis, conjunctivitis, and scaly papules or ulcers in the head, neck, and anogenital region
- Vitamin B3 deficiency can lead to photodistributed hyperpigmented and scaly dermatitis, cheilitis, diarrhea, and dementia
- Vitamin B6 deficiency can lead to a periorificial seborrheic dermatitis-like eruption, angular cheilitis, glossitis, nausea, and peripheral neuropathy
- Vitamin B9 deficiency can lead to cheilitis, glossitis, diffuse hyperpigmentation, and megaloblastic anemia
- Vitamin B12 deficiency can lead to diffuse hyperpigmentation especially of palms and soles, glossitis, megaloblastic anemia, and peripheral neuropathy

REFERENCES:

WISCONSIN DERMATOLOGICAL SOCIETY

CASE # 12

PRESENTERS: Abigail Taub, MD; William Aughenbaugh, MD, Daniel Bennett, MD.

HISTORY: A 3 day old HIV unexposed female neonate was brought to dermatology clinic for evaluation of a vascular tumor present since birth.

PMH: normal vaginal delivery

MEDICATIONS: none

FAMILY HISTORY: noncontributory

EXAM: Violaceous plaque on the left neck extending onto the temporal and occipital scalp. Black hemorrhagic crusts within the posterior portion of the plaque.

HISTOPATHOLOGY: none

LABS: regular monitoring of CBCs

IMAGING: ultrasound attempted but unable to obtain due to bleeding

DIAGNOSIS: Rapidly involuting congenital hemangioma

TREATMENT: wound care. Patient required suture ligation of bleeding vessels on two separate occasions as well as red blood cell transfusion after the second episode of bleeding.

DISCUSSION: This infant was born with a fully developed vascular tumor. The differential diagnosis considered included a congenital hemangioma and kaposiform hemangioendothelioma.

Congenital hemangiomas can be further characterized as rapidly involuting congenital hemangiomas (RICHs) and non-involuting congenital hemangiomas (NICHs). Over one month, the tumor became flatter and duller purple, making RICH the most likely diagnosis. RICHs rapidly involute within the first year of life. RICHs represent less than 3% of all hemangiomas. They are fully developed at birth and do not proliferate. They tend to be violaceous tumors that are hard or firm on palpation with telangiectasias on the surface and surrounded by rim of pallor. In the United States, they are generally diagnosed via ultrasound in utero. They occur most commonly on the head or limbs near a joint. Most involute by 8-14 months, but can stop involuting at any point and become a NICH. The associated vessels are large and superficial which can lead to life-threatening hemorrhage. Doppler or MRI is recommended for ulcerated RICH to evaluate the size and depth of the vessels involved. Recommended treatment of exposed vessels is embolization. NICHs do not spontaneously involute. They occur slightly more often in male infants. Congenital hemangiomas, unlike infantile hemangiomas, are GLUT-1 negative and are not associated with PHACES Syndrome (posterior fossa and other structural brain malformations, cardiac defects, eye anomalies, sternal defects and supraumbilical raphe).

Kaposiform hemangioendothelioma (KHE) is a rare vascular tumor of childhood that presents as an ill-defined violaceous plaque. It can be associated with a life-threatening platelet trapping syndrome known as Kasabach-Merritt phenomenon. KHE can be locally aggressive and occasionally multifocal along lymphatic pathways. Treatment consists of complete surgical excision where feasible.

Infantile hemangiomas are the most common soft tissue tumor of infancy. They are not present at birth, but instead develop in the first weeks to months of life. The majority of growth occurs from 2-5 months of age with almost all hemangiomas fully developed by 8 months of age. For most children, infantile hemangiomas involute by 3.5 years of age. Indications for treatment include location on the nose, lip,
pinna, periocular, or genital skin, and ulceration. Active intervention consists of topical timolol or systemic propranolol.

**KEY POINTS**

- Rapidly involuting congenital hemangiomas (RICHs) are fully formed congenital vascular tumors that involute spontaneously
- Non-involuting congenital hemangiomas (NICHs) are fully formed congenital vascular tumors that do not involute spontaneously
- RICHs and NICHs are Glut-1 negative
- RICHs and NICHs are not associated with PHACES syndrome
- Kaposiform hemangioendothelioma is a vascular tumor that can be associated with a life threatening platelet trapping syndrome known as Kasabach Merritt phenomenon
- Infantile hemangiomas are the most common soft tissue tumor of infancy
- Treatment of infantile hemangiomas consists of expectant management, topical timolol, and oral propranolol

**REFERENCES:**

CASE # 13

PRESENTERS: Noor Tazudeen MD; Anne Rosin MD

HISTORY: S.F. is an 81-year-old male who presented to dermatology for a pruritic, urticarial eruption of his trunk that started 4 weeks prior to his clinic visit. He initially attributed the eruption to new synthetic T-shirts he wore but noticed no improvement after discarding these. He was treated by urgent care providers with three separate prednisone tapers, each starting at 40mg. Each time his dose was reduced to 10mg he would flare. At his initial dermatology visit, he was started on topical clobetasol and minocycline; however, he soon noticed vesicles developing within his urticarial plaques as well as on his buccal mucosa and required higher doses of prednisone in addition to mycophenolate mofetil for control.

PMH: Unremarkable; no history of malignancy or systemic conditions.

MEDICATIONS: Fish oil, multivitamins, Vitamin D supplement

FAMILY HISTORY: No history of blistering skin eruptions in his relatives.

EXAM: The chest, abdomen, and back show multiple erythematous, urticarial papules and plaques, extending inferiorly to the proximal thighs and involving the inguinal folds. Three intact vesicles are noted on the left dorsal wrist. No pustules. No oral, genital, or ocular lesions noted.

HISTOLOGY: Initial shave biopsy revealed focal eosinophilic spongiosis. Subsequent punch biopsy for DIF showed strong linear immunofluorescence for both IgG and C3 at the BMZ. Salt-split skin analysis showed positive immunofluorescence for IgG and C3 on dermal side.

OTHER DATA:
ELISA negative for IgG antibodies against BP 180 and BP 230.
ELISA negative for IgG antibodies against Collagen VII and laminin-332; leaving anti laminin gamma-1 as the pathogenic protein.
Age appropriate cancer screening negative.

DIAGNOSIS: Anti-laminin gamma1 pemphigoid/anti-p200 pemphigoid

DISCUSSION: Anti-laminin gamma1 pemphigoid is a rare autoimmune subepidermal blistering disorder with approximately 50 cases being published since its original description in 1996. The disease results from pathogenic autoantibodies that target a component of the dermoepidermal junction, the extracellular matrix protein Laminin gamma1. Originally termed anti-p200 pemphigoid, the 200-kd antigen target was identified as laminin gamma1 in 2009 by Dainichi et al. Clinically, anti-laminin gamma1 pemphigoid is non-specific bullous disease and can mimic many other blistering dermatoses, including bullous pemphigoid, linear IgA bullous dermatosis, dermatitis herpetiformis, and inflammatory epidermolysis bullosa acquisita. Typical patients are between 50-70 years old and patients of Japanese descent frequently have concurrent pustular psoriasis. Twenty percent of patients have involvement of oral and/or genital mucosa.

Anti-laminin gamma1 pemphigoid lesions demonstrate a subepidermal split histologically, with neutrophils and occasionally eosinophils in the papillary dermis. Direct immunofluorescence microscopy or perilesional skin reveals linear deposits of IgG and C3 along the dermoepidermal junction. Indirect immunofluorescence shows serum antibodies that bind to the dermal side of salt-split skin, differentiating this disorder from bullous pemphigoid. ELISA can be used to identify anti-laminin332 antibodies or antibodies to collagen VII, representing the other two disorders which can show similar DIF and IIF findings. Non-reactivity to these antigens leaves laminin gamma1 as the target antigen.
No standard therapeutic management of anti-laminin gamma1 pemphigoid has been established. Superpotent topical steroids, systemic corticosteroids, dapsone, doxycycline, azathioprine, and cyclosporine have all been described as having efficacy in controlling symptoms. There is scarce but increasing evidence for colchicine, IVIg, and ustekinumab for management\(^1\). The clinical course is variable, with unpredictable remission and relapse, requiring maintenance therapy for months to years in most cases\(^1\).

**KEY POINTS**

- Anti-laminin gamma1 pemphigoid is a blistering dermatoses which can mimic BP, inflammatory EBA, DH, or LABD.
- DIF will show linear IgG and/or C3 along the basement membrane zone, with IIF showing serum antibodies binding to dermal side of salt split skin.
- There is no standard therapy, but superpotent topical corticosteroids, systemic steroids, and dapsone have shown efficacy in inducing and maintaining remission.
- Consider anti-laminin gamma1 pemphigoid in patients with blistering diseases with conflicting laboratory studies.

**REFERENCES:**

CASE #: 14

PRESENTERS: David Wright, MD, Rita Lloyd, MD, Daniel D. Bennett

HISTORY: A 48 yo male presented to our clinic with a 3 month history of a rash that occurred after a R rotator cuff repair using a titanium suture anchor. About 1.5 weeks after surgery, the patient noted pain and redness over the R shoulder. At that time, the pain from his surgery was improving and this was a new pain. The rash was not located directly over the incision site. He noted that blisters soon arose in the erythematous areas and his pain became debilitating. He underwent treatment with multiple courses of antibiotics prior to seeing us, including PICC line placement and 6 weeks of IV daptomycin. He also underwent washout and joint aspiration x 2 with negative blood cultures and joint aspirate cultures. None of the treatments seem to help significantly and the rash continued to expand and cause significant pain.

PMH: Chronic Sinusitis, Obstructive Sleep apnea, HTN

MEDICATIONS: Acetaminophen, albuterol, azelastine, fentanyl, fluticasone-salmeterol, gabapentin, lisinopril, meloxicam, montelukast, morphine, omeprazole, trazadone, hydrocodone

LABS: Mild anemia (Hg 13.9), Normal ESR and CRP when we saw him, but had been elevated in the past. Negative lyme titer, normal ANA, borderline positive RF.

EXAM: Erythematous, edematous plaques over the R back, shoulder and upper arm, with erythema extending onto the back and chest. Superficial erosions were noted in some areas.

HISTOPATHOLOGY: Vacuolar interface dermatitis with superficial and deep periadnexal and perivascular infiltrate with lymphocytes, histiocytes, neutrophils, and occasional eosinophils. Numerous necrotic keratinocytes were noted at all levels of the epidermis.

DIAGNOSIS: Hypersensitivity reaction to the suture anchor

TREATMENT AND COURSE: The patient initially improved on a 3 week taper of prednisone, but the rash and pain recurred upon discontinuation. Patch testing showed no reactions to titanium, cobalt, chromium, nickel, glues or plastics. Lymphocyte transformation testing (MELISA©) was performed showing a positive reaction to nickel at the time, although using current cutoffs, his test would be considered negative. We recommended removal of the suture anchor, and after some discussion with his orthopedic surgeons and a consult at the Mayo Clinic, the suture anchor was removed. Pathology from tissue taken at the time of removal showed giant cell reaction and fibrosis around the anchor. The patient's rash and symptoms resolved within a week of suture anchor removal.

DISCUSSION: Hypersensitivity to metal implants, although relatively uncommon, should be on the differential when an eruption is noted soon after an implant. Dental, orthopedic, cardiologic, and gynecologic implants have all been implicated in hypersensitivity reactions. The reaction can often be confused with infection or a reaction to perioperative medications. It can manifest in various ways including poor healing, implant failure, joint pain, rash, or other systemic symptoms. Up to 5% of joint arthroplasty failures can be attributed to delayed-type hypersensitivity. The majority of cutaneous eruptions are eczematous in nature, but there are reports of bullous, urticarial and vasculitic eruptions. Rashes are usually localized over the area of the implant but can become more generalized.

Patch testing is generally considered the gold standard for identification of metal hypersensitivity to implants. Various patch series have been recommended in the literature depending on the type of implant. Nickel, Cobalt and Chromium are the metals most commonly implicated in implant hypersensitivity. Generally, unless a person has a previous history of metal allergy, testing prior to implantation is not recommended. The downsides to patch testing are subjectivity of interpretation, cost,
time, and potential for sensitization in a previously non-allergic patient. Some have suggested that patch testing may not be ideal for evaluating implant hypersensitivity as the cutaneous environment is different than the internal environment.

Lymphocyte transformation testing is another modality sometimes employed in the diagnosis of metal hypersensitivity. It is an in vitro test that measures lymphocyte response to an antigen. Lymphocytes are incubated with a specific antigen and proliferation is measured vs. controls. A stimulation index (SI) is reported. Standardization across labs is lacking however, and testing can be costly. High false positive rates have been reported in the literature. Several labs offer this test, but until further studies are done to establish standard procedures and SI values, it should be used cautiously.

Treatment usually requires removal of the implanted device, which requires a high level of suspicion. It can at times be a difficult task to convince patients and surgeons to pursue removal, especially if the cutaneous reaction is atypical.

**KEY POINTS:**

- Hypersensitivity reactions should be on the differential diagnosis when a rash develops shortly after implant surgery
- Rash presentation can be variable, and is not always a classic eczematous eruption
- Patch testing is the gold standard for diagnosis currently
- Pre-surgical patch testing is not generally recommended

**REFERENCES:**