Etanercept in the treatment of Stevens-Johnson syndrome and toxic epidermal necrolysis; UCLA and USC experience
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Background: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are amongst the few true dermatologic emergencies, with mortality rates approaching 25-35% in untreated patients. Although the pathogenesis is not well understood, a hypersensitivity reaction to certain inciting agents such as medications or infections is thought to play a role. Recent evidence that TNF-may be implicated in the pathogenesis of SJS/TEN prompted investigation into the utility of TNF antagonists in the management of SJS/TEN. A recent study by Paradisi et al described 10 TEN patients treated with etanercept. Their average SCORTEN was 3.6, carrying a predicted mortality rate of 35-58%, which was significantly higher compared to the observed mortality rate of 0%. This prompted the use of etanercept at UCLA and USC for the management of SJS/TEN.

Methods: A total of 31 patients with SJS/TEN were recruited for this case series at UCLA and USC between 2015-2016. An inpatient dermatologist made the diagnosis based on physical examination and pathological findings. Medications were reviewed, and the suspected agent discontinued at the time of diagnosis. Of the 31 patients, 18 received treatment with etanercept alone, four with both etanercept and IVIG, five with IVIG, and four with supportive care alone. Those who qualified received a single subcutaneous injection of etanercept 50mg. Patients were followed closely during the course of their hospitalization and post-discharge. The following data was collected for each patient: SCORTEN, %BSA, and mortality.

Results: Out of 31 total patients identified at USC/UCLA with SJS/TEN, 11 patients at UCLA and 11 patients at USC received etanercept. The mortality rate was 0% in the etanercept group at UCLA (SCORTEN 1.8) compared to a predicted mortality rate of 17.3%. The mortality rate in the non-etanercept group at UCLA (SCORTEN 2.4) was 33%, compared to a predicted mortality rate of 28%. Preliminary data from USC show similar findings, however final analysis is still in process.

Conclusion: To our knowledge, this is the largest case series to date looking at the use of etanercept for treatment of SJS/TEN. Our data are in agreement with findings in the literature demonstrating that etanercept may be beneficial in patients with acute onset of SJS/TEN. Given the limited number of cases reported in the literature, further multi-institutional studies are needed to further elucidate the role of etanercept in the management of SJS/TEN.

Successful treatment of refractory pityriasis rubra pilaris with ustekinumab in a pediatric patient
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Pityriasis rubra pilaris (PRP) is an uncommon inflammatory dermatosis characterized by erythematous salmon-colored plaques with islands of sparing and palmoplantar hyperkeratosis. Both adult and juvenile forms of PRP exist, with variable natural history in both populations. Some cases undergo spontaneous resolution, while others prove extremely difficult to treat. We present the case of a 7-year-old Asian female with refractory PRP first diagnosed at 7 months of age. Previous treatment included phototherapy, oral and topical steroids, topical retinoids, and cyclosporine. The patient’s family was hesitant to continue the current regimen or to add systemic retinoids due to concern for toxicity. Recent data show that ustekinumab, an IL-12 and IL-23 antagonist, can be safely used in pediatric patients with psoriasis. After explaining the benefits and risk, both parents consented to the addition of ustekinumab 45 mg subcutaneous injection, initially administered at 0 and 4 weeks. At week 4, her erythema had already diminished significantly from BSA 80% to BSA 20%. She also noted experiencing less pruritis and feeling more comfortable at school. At week 8, she was clear of generalized erythema and only continued to have mild hyperkeratosis of the hands. She is currently on week 20 of treatment and remains clear of erythema with no adverse events experienced. There is currently only one reported case of pediatric PRP treated with an FDA-approved biologic medication (adalimumab). The successful use of ustekinumab presents another option for children with refractory PRP. This is particularly encouraging for young patients, as ustekinumab is not associated with the same degree of toxicity as cyclosporine and methotrexate. Indeed, it has a favorable side effect profile even when compared to other biologic drugs such as the TNF-inhibitors etanercept and adalimumab. Its maintenance dose schedule of 4 injections per year (compared to weekly or biweekly injections for other biologics) is also valuable in the pediatric population, where each shot may prove emotionally difficult for the patient. Our report suggests the need for future prospective studies in this patient population.
Accidental hydroxychloroquine overdose resulting in neurotoxic vestibulopathy

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Background: Hydroxychloroquine (HCQ) is an oral antimalarial medication commonly used off-label for a variety of rheumatologic and dermatologic conditions. The main long-term risk is retinopathy. Despite a good safety profile and few side effects, HCQ can be toxic and even fatal when taken in excess due to its cardiotoxic effects. Its parent compound, chloroquine, is associated with the development of seizures, visual disturbance, dizziness, and other neurologic abnormalities when taken in excess. No documentation of such findings exists for HCQ overdose. 

Case Summary: We present a case of a 64-year-old woman who complained of acute onset headache, bilateral tinnitus, and left-sided facial numbness and tingling in the setting of accidentally overdosing on HCQ. She unknowingly drank water contaminated by 10 full and 10 half-dissolved HCQ tablets. By the next morning, the patient began to experience worsening in the tingling sensation and it spread to her left arm, thigh, and distal extremities. She also complained of new onset blurring of her peripheral vision and feeling “off balance.” Despite a complete neurologic and ophthalmologic work-up with unremarkable imaging and blood work, the patient has had no improvement in her tinnitus, left-sided paresthesias, visual disturbance, or ataxia. This is a unique case of HCQ overdose resulting in permanent neurotoxic vestibulopathy. 

Discussion: The phenomenon of neurotoxic vestibulopathy is well-documented in the literature with another quinoline antimalarial drug—mefloquine. Mefloquine is known to induce a chronic toxicity syndrome in the central nervous system due to injury of the neuronal cells of the vestibular system and brainstem. This finding has yet to be reported in the literature with HCQ overdose. Learning Points: HCQ has the potential to produce permanent symptoms of neurotoxic vestibulopathy including tinnitus, headache, dizziness, vertigo, disequilibrium, paresthesias, ocular disturbance, and neuropathy; The mechanism of HCQ induced neurotoxicity is thought to be similar to that of mefloquine, involving the toxic accumulation in the neuronal cells of the vestibular nuclei and brainstem; First-line treatment for HCQ overdose involves an immediate visit to the nearest emergency department followed by early gastric decontamination, hemodynamic support, cardiac monitoring, arrhythmia evaluation, electrolyte repletion, and potentially intravenous lipid emulsion to avoid fatal cardiovascular complications.

Multiple adult-onset squamous cell carcinomas arising in generalized scleroderma scars

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Morphea, or localized scleroderma, is an inflammatory disorder of unknown etiology characterized by cutaneous sclerotic change, with potential for deeper soft tissue involvement. Malignant transformation is rare and more typically seen in active morpheic lesions of the generalized or panniculotropic variants. We describe a case of an adult male who developed large squamous cell carcinomas (SCC) within clinically inactive morphea scars. A 35-year-old Caucasian male with a history of generalized morphea of childhood presented with a 10.6 x 8.5 cm ill-defined, bleeding ulcer with surrounding erythematous papules and nodules on his right lower leg. The lesion was located within a skin graft, set within a larger morphea scar that had been quiescent for years. The patient had been treated for chronic wounds with multiple debridements and skin grafts over the course of eight years, without resolution or a diagnosis. A biopsy ultimately revealed SCC. Three excisions were performed, but margins remained positive. Given the extent of the lesion, the patient underwent below-knee amputation for definitive tumor removal. Several months later, the patient presented with two additional rapidly enlarging lesions: a 4.2 x 5.9 cm ulcerated verrucous plaque of the left thanar eminence and a 2.2 x 3.0 cm erythematous hyperkeratotic plaque of the left upper chest. Both lesions were superimposed upon larger areas of morpheic scarring without clinical evidence of active morphea. Histopathologic examination showed moderately to poorly differentiated, anaplastic SCC in both cases. Of note, an initial biopsy of the left thanar lesion was read as verruca vulgaris, likely due to inadequate sampling. The patient underwent Mohs surgery for each lesion followed by skin grafting without complication. While several cases in the literature suggest an increased risk of developing cutaneous SCC in active morphea, this is the first described case of a Marjolin’s ulcer-like effect in multiple quiescent morphea scars. This case highlights the need for careful monitoring of the scars of morphea patients, even after long-term inactivity. Furthermore, the initial misdiagnosis in two of the three lesions, one of which led to severe morbidity, suggests that a high index of suspicion must be maintained for the development of SCC in these patients. This is especially important given the aggressive nature of tumors reported to arise within lesions of morphea.

Effective use of ustekinumab in a patient with concomitant psoriasis, vitiligo, and alopecia areata

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Psoriasis is a relatively common immune-mediated disease characterized clinically by formation of well-demarcated plaques with silver scale. Two somewhat less common autoimmune diseases of the skin are vitiligo, characterized by depigmented macules and patches, and alopecia areata (AA), characterized by patches of non-scarring hair loss. We present the case of a 39-year-old South Asian woman with all three of these conditions. The patient initially presented to our clinic in February 2016 with a several-year history of moderate generalized plaque psoriasis. In addition to psoriasis, the patient also had a one-year history of non-segmental vitiligo of the face, scalp, and neck and a two-year history of patchy alopecia of the scalp. In the past, the patient had been treated with etanercept for her psoriasis with no improvement noted. She had also received intra-lesional triamcinolone injections for vitiligo with only minimal improvement. After explaining the benefits and risk, the patient consented to try treatment with ustekinumab 90 mg subcutaneous injection, initially administered at 0 and 4 weeks. Subsequent doses were administered every 8 weeks. The patient showed significant improvement in erythema and scaling of psoriatic lesions by week 8 and complete resolution by week 16. In addition to the excellent response seen with her psoriasis, the patient showed impressive improvement in vitiligo and AA lesions. At week 16, hair density had visibly increased and repigmented macules were noted around the hair follicles in previously depigmented patches. As ustekinumab is an FDA-approved therapy for plaque psoriasis, the patient was not surprised that this patient’s psoriatic lesions improved dramatically. However, marked improvement in patches of vitiligo and AA were also noted. It is the striking increase in hair density and perifollicular repigmentation that suggest IL-12/23 blockade may be a promising therapeutic strategy for patients with these autoimmune conditions as well as psoriasis. Prospective studies of IL-12/23 antagonists such as ustekinumab could provide an effective option for these difficult-to-treat conditions and add to our understanding of their pathophysiology.
Eruptive keratoacanthomas in the setting of pembrolizumab therapy

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Case history: A 92-year-old man with stage IV squamous cell carcinoma of the left frontoparietal scalp failed initial surgery and chemoradiation, prompting initiation of treatment with pembrolizumab, a monoclonal antibody that binds to the programmed cell death–1 (PD-1) receptor thereby blocking its interaction with its immune suppressing ligands and allowing restoration of host immune anti-tumor response. Four months into treatment, the patient demonstrated numerous violaceous macules and hypertrophic scaling papules of his forearms and lower extremities, thought to represent a hypertrophic variant of the well-characterized drug-induced lichenoid dermatitis observed in patients on PD-1 inhibitor therapy. In addition, the patient developed painful skin-colored and violaceous smooth papulonodules of his dorsal hands and wrists. Diagnostic testing: Multiple punch biopsies were performed of lesions on the bilateral dorsal hands, demonstrating features suggestive of a lichenoid dermatitis. Focal larger nodules however demonstrated cup-shaped atypical squamoproliferative lesions with glassy cytoplasm compatible with keratoacanthomas. Therapy and course: For one symptomatic lesion, the patient underwent debulking by shave excision. The majority of lesions otherwise reduced in size and/or resolved with intralesional triamcinolone injections and topical clobetasol 0.05% ointment. Overall, the patient reported significant improvement in the size of lesions and associated pain with conservative measures. Advanced teaching points: To date, eruptive keratoacanthomas have not yet been reported in the setting of pembrolizumab or other PD-1 inhibitor therapy. Mechanistically, this may represent a de novo phenomenon; however, it is possible that exuberant lichenoid dermatitis may histologically mimic eruptive keratoacanthomas. Lastly, this presentation could represent an ‘abscopal’ effect of pembrolizumab on pre-existing photodamaged skin. In this case, close follow-up with repeat biopsies was critical for diagnostic clarification. The eruptive keratoacanthomas resulted from violaceous smooth papulonodules rather than classic lichen planus-like lesions. Our patient’s course suggests that conservative symptom-driven treatment may suffice rather than aggressive surgical intervention. Ultimately, further characterization will help elucidate the underlying mechanism of this entity, and guide optimal treatment for this challenging condition.

Painful Cyanosis, Ulcers, and Necrosis of the Left Leg

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A 66-year-old woman presented with a two-week history of unilateral progressive edema, pain, cyanosis and enlarging ulcers of the left lower extremity. On exam of the left leg, there was diffuse, weeping edema distally with cyanosis extending proximally to the mid-tibia. The left plantar foot was necrotic and sloughing, and the dorsal foot had one large hemorrhagic, tense bulla. Two fibrinous ulcers were visualized on the left lower leg. Laboratory findings were significant for a leukocytosis of 26 x 10^9/L, lactic acid 2.5 mmol/L, and CRP 130.0 mg/L. Given concern for sepsis, she was placed on broad spectrum antibiotics. However, blister fluid and successive blood cultures were negative. Culture of an ulcer did reveal Serratia marcescens, Escherica coli, and Enterococcus. Doppler ultrasound revealed occlusive thrombosis starting at the level of the left external iliac vein and extending to the posterior tibial vein. Hypercoagulability work-up was delayed in the setting of an acute clot. Phlegmasia cerulean dolens, characterized by extensive iliofemoral vein thrombosis leading to impaired arterial flow, was diagnosed. The patient was started on heparin transfusion, but ultimately developed progressive cyanosis and succumbed to circulatory collapse during thrombectomy. Phlegmasia cerulea dolens (“painful blue inflammation”) is a serious sequela of extensive iliofemoral vein thrombosis. Clots occlude and inhibit the venous system of the affected extremity, leading to elevated venous hydrostatic pressure and increased tissue pressure. Arterial flow is diminished, despite patent arterial lumens. Superficial venules engorged with desaturated blood result in cyanosis. Patients may develop hemorrhagic bullae, paresthesias, and motor paralysis. Venous gangrene develops in 40% to 60% of cases. Massive fluid sequestration can lead to circulatory collapse and shock. Mortality is estimated at 25% to 40%. Doppler ultrasonography remains the most reliable and fastest non-invasive diagnostic tool, although CT or magnetic resonance venography may further characterize the process. Predisposing factors include underlying malignancy, pregnancy, and other pro-thrombotic states. Initial management typically includes intravenous heparin and fluid resuscitation with elevation of the limb. With progression to critical limb ischemia, catheter-directed thrombolysis, surgical thrombectomy, or percutaneous transluminal angioplasty can be performed.
A complex case of secondary syphilis in the inpatient setting

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Case Presentation: 54 year-old man with remote history of Hodgkin’s Lymphoma presented to ophthalmology clinic for two month history of decreased visual acuity of bilateral eyes (left > right). Incidentally, patient was noted to have atrial fibrillation with rapid ventricular rate and was sent to Emergency Department for further work-up. Upon admission, incidental aortic vegetation was discovered and patient was started on Vancomycin and Ceftriaxone for presumed subacute endocarditis. History was also notable for unintentional weight loss, joint pains, visual hallucinations, and widespread psoriasiform rash involving trunk and extremities. Dermatology was consulted for rash. Further history revealed patient had 2 month history of asymptomatic rash which began on abdomen, back, and anterior legs. As an outpatient, patient was started on prednisone due to concern for temporal arteritis given elevated ESR and CRP and vision change, however, temporal artery biopsy was negative. Patient’s rash subsequently flared with prednisone and became pruritic and widespread extending to upper arms, and palms and soles. Patient also had history of high-risk sexual behaviors about 6 months prior. Labs were negative for HIV, but positive for RPR with titers at >1:1024. Confirmatory labs revealed reactive TP-PA and VDRL in CSF (1:4). Ophthalmology work-up revealed bilateral chorioretinitis involving the optic nerves supporting diagnosis of ocular syphilis. Patient was transitioned to Penicillin G 4 million units every 4 hours for 14 days for treatment of neurosyphilis. Patient’s rash and vision rapidly improved with antibiotics and repeat RPR titer decreased to 1:512. Teaching Point: We present a rare case of secondary syphilis with ocular syphilis and neurosyphilis. Both neurosyphilis and ocular syphilis can occur at any stage of syphilis and treatment of choice is penicillin G. Ocular syphilis can involve almost any eye structure with posterior uveitis and panuveitis most common. Lumbar puncture is recommended for all patients with neurologic, auditory, or ophthalmologic symptoms. Test patients for HIV given possible co-infection; patients with both syphilis and HIV are more likely to develop neurosyphilis and may progress to tertiary syphilis more rapidly. As incidence of syphilis is on the rise, it is important for us to continue to consider this diagnosis in our patients.

Cytotoxic lymphoma initially presenting with widespread noncaseating granulomas

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A 42-year-old male presented with a six-month history of a worsening eruption consisting of scaly erythematous plaques and nodules on the upper and lower extremities associated with fatigue, weight loss, fevers, night sweats, and lower extremity edema. A cutaneous biopsy demonstrated granulomatous lobular panniculitis with negative infectious stains. He was found to have pancytopenia on laboratory evaluation, and a bone marrow biopsy revealed small non-caseating granulomas without evidence of malignancy. Flow cytometry of the peripheral blood revealed a phenotypically normal T-cell population. Further laboratory evaluation was notable for a markedly elevated angiotensin converting enzyme level without evidence of an underlying autoimmune disease or infection. The patient was diagnosed with systemic sarcoidosis with subcutaneous involvement and treated with systemic corticosteroids. The patient’s cutaneous findings and lower extremity edema initially stabilized but then progressively worsened. A repeat skin biopsy was performed, which revealed extensive subcutaneous necrosis rimmed by atypical, pleomorphic lymphocytes that stained positive for CD2, CD3, CD56, and TIA-1, and negative for CD4, CD5, CD7, CD8, CD20, BF1, and EBER-1. Gamma M1 was weakly positive. T-cell receptor gene rearrangement detected a clonal T-cell population in the tissue, peripheral blood, and bone marrow. Taken together, a diagnosis of primary cutaneous gamma/delta T-cell lymphoma (PCGD-TCL) was made. The patient also endorsed new onset episcleritis along with persistent fatigue. Laboratory evaluation was significant for worsening pancytopenia, markedly elevated ferritin, hypertyglycemia, hyperfibrinogenemia, and elevated soluble CD25. Given concern for hemophagocytic lymphohistiocytosis (HLH), the patient was admitted to the hospital and is currently undergoing treatment with dexamethasone and etoposide with plans for allogeneic stem cell transplantation upon stabilization. This case highlights an unusual presentation of an aggressive cytotoxic lymphoma initially presenting with features consistent with sarcoidosis. Review of the initial skin biopsy confirmed lack of cellular atypia. PCGD-TCL is a rapidly progressing malignancy with an immunophenotype similar to that seen in our patient. Clinically, plaques and ulceronecrotic nodules develop, frequently on the extremities. It is sometimes associated with HLH, particularly in those with panniculitis-like tumors. A high degree of suspicion must be employed to re-evaluate the diagnosis when the disease course is inconsistent with the expected treatment outcome.

Novel use of apremilast for treatment of recalcitrant vegetative pyoderma gangrenosum

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We describe a patient with a 3-year history of recalcitrant vegetative pyoderma gangrenosum (PG) who responded to apremilast. A 73-year-old man presented with nonhealing superficial erosions for several months at sites of prior surgical procedures on the back and posterior thigh. Multiple biopsies demonstrated a diffuse mixed-cell infiltrate of neutrophils and histiocytes with scattered multinucleated giant cells with more peripherally located lymphocytes, plasma cells and eosinophils, consistent with vegetative PG. Work-up of systemic associations revealed an IgA kappa monoclonal gammapathy of unknown significance. Over the subsequent 2.5 years, he failed conservative therapy with intrallesional corticosteroids, high-potency topical corticosteroids, topical tacrolimus and doxycycline; other immune-modulating agents such as dapsone, colchicine, methotrexate, and a two-year course of oral prednisone also failed to improve his lesions. The addition of oral apremilast at 30 mg twice daily rapidly led to complete resolution of the back erosion and near complete resolution of the thigh erosion within 4 months, and the patient was able to discontinue methotrexate and taper his prednisone. This patient’s rapid response to the off-label, novel use of apremilast for vegetative PG recalcitrant to multiple topical and systemic therapies is remarkable and may suggest a new option for patients with recalcitrant PG. Objectives: Present a case of the novel use of apremilast for vegetative pyoderma gangrenosum; Review the presentation of the rare disorder vegetative pyoderma gangrenosum; Review the treatment options for pyoderma gangrenosum.
MAGIC syndrome with gastrointestinal involvement masquerading as Crohn’s disease

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**Background:** Behcet’s syndrome is a rare autoimmune disease characterized by recurrent aphthous ulcers with two or more of the following features – genital ulcers, eye findings (posterior uveitis or retinal vasculitis), skin findings (papulopustular lesions), or perianal disease. A subgroup of those affected will also develop inflammation of cartilage, which is referred to as MAGIC (Mouth and Genital Ulcers with Inflamed Cartilage) syndrome, which describes patients with overlapping features of Behcet’s and relapsing polychondritis. Gastrointestinal involvement can also rarely be seen and the following case describes a patient with Behcet’s presenting with inflammation of the colon masquerading as Crohn’s disease. **Case Presentation:** A 38-year-old female with a nine-year diagnosis of Crohn’s Disease was admitted to the hospital for a Crohn’s flare in October 2016. The patient presented with a 3-week history of worsening abdominal pain, periumbilical crusting, mouth ulcers, and hemorrhagic crusting of the bilateral naris further complicated by a 1-week history of bilateral ear pain, erythema and tenderness with sparing of the lobules, and purulent drainage. Ear cultures of the purulent drainage were negative for bacteria. The patient’s labs were unremarkable except for an elevated ESR (54 mm/hr; n=25) and CRP (11.89 mg/L; n=8). Skin biopsy of the periumbilical crusting showed spongiform and psoriasiform dermatitis with impetiginization. An anti-collagen II antibody test was sent because of the bilateral ear inflammation and was strongly positive (37.6 EU/mL; n=20).

Upon further review of the patient’s medical records, it was discovered that prior colon biopsies had shown evidence of acute and chronic inflammation, but were negative for granulomas, which is pathognomonic for Crohn’s disease. Given the patient’s history of uveitis, bilateral auricular chondritis, and recurrent oral and genital ulcers, as well as the positive anti-collagen II antibody test, the patient’s diagnosis was revised to MAGIC syndrome with gastrointestinal Behcet’s. **Discussion and Conclusion:** Gastrointestinal involvement in Behcet’s is uncommon, affecting only 7-15% of patients, and may be the earliest manifestation of disease. In patients with Behcet’s, screening for gastrointestinal symptoms is important to recognize because of the potential complications such as perforation or fistula formation.

Subacute cutaneous lupus erythematous associated with anti-programmed cell death (PD) – 1 therapy

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Programmed cell death 1 (PD1) inhibitors are a rapidly emerging therapy used for a variety of metastatic malignancies. These therapies have been linked with multiple adverse effects, including dermatitis and autoimmune disease. We describe two patients presenting to our institution on PD1 inhibitor therapy for metastatic non-small-cell lung cancer who developed clinical and histologic findings consistent with subacute cutaneous lupus erythematosus (SCLE). In the first case, the patient developed a photo-distributed dermatitis after 2 doses of nivolumab 3 mg/kg intravenously every 2 weeks. Initial laboratory evaluation showed a low positive anti-nuclear antibody (ANA) titer (1:40), and a positive anti-Ro-SSa (anti-Ro) antibody. PD1 inhibitor therapy was successfully reinitiated while the patient was treated with prednisone (doses 10-120 mg daily), triamcinolone 0.1% ointment twice daily, and hydroxychloroquine 200 mg twice daily. His original rash recurred with resumption of nivolumab. However, he developed myalgia, elevated CK and small, tender ulcerations on his distal interphalangeal joints and proximal interphalangeal joints, nasal bridge and ears, and a high titer ANA (1:2560). Nivolumab was discontinued. He is currently being monitored off of chemotherapy without progression of his tumor. The second patient developed a photo-distributed dermatitis starting shortly after her 3rd dose of pembrolizumab 2 mg/kg intravenously every 3 weeks. She presented to clinic 5 months after discontinuation of pembrolizumab for a persistent rash in spite of treatment with prednisone and infliximab. Laboratory evaluation revealed a high titer ANA (1:2560), positive anti-Ro and anti-La-SSb antibodies, and positive anti-histone antibodies with no clinical evidence of systemic disease. She was treated with prednisone (doses 20-60 mg daily) and triamcinolone 0.1% ointment twice daily. She switched to an alternative chemotherapy. When related to use of PD1 therapies, the risk of progression of SCLE to systemic lupus erythematosus is unknown. This observation challenges the current protocol in which many patients with dermatitis on PD1 inhibitor therapy are treated with infliximab, which may exacerbate systemic and cutaneous lupus erythematosus manifestations. The connection between oncologic response and development of SCLE and other connective tissue disease is unknown and warrants further investigation.

Early congenital syphilis: recognizing symptoms of an increasingly prevalent disease

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**Background:** Congenital syphilis (CS) is an infectious disease resulting from transplacental transmission of Treponema pallidum spirochetes from an infected mother to fetus during pregnancy. While uncommon, CS has shown an increased incidence in the United States (US) since 2012. **Case Report:** We present the case of a 5-week old female infant with blistering rash on the palms and soles. Initial testing was positive for Herpes Simplex Virus IgM with indeterminate Rapid Plasma Reagin (RPR). Patient was initially treated with acyclovir and IV benzathine penicillin and developed an urticarial rash, prompting transfer. The infant displayed decreased movement of the left upper extremity, clinically consistent with pseudoparalysis of Parrot. Osseous survey revealed lucency of the proximal medial and lateral left tibial metaphyses, consistent with periostitis. Cutaneous involvement was limited to few tan crusted papules on the palms and soles. The patient’s mother then reported a history of false positive RPR at 31 weeks gestation. Cerebrospinal fluid (CSF) studies of the infant resulted with positive VDRL and positive MHA-TP. Histopathology of a crusted papule revealed a lichenoid infiltrate composed of lymphocytes, histiocytes and plasma cells. Immunohistochemical staining for T. pallidum was negative, thought to be due to prior penicillin administration. The initial rash was felt to be a Jarisch-Herxheimer reaction, and patient completed treatment with a 10-day course of IV penicillin. **Advanced teaching points:** While CS is largely considered a historic entity, it has been increasing in incidence in the US since 2012. Diagnosis of CS can be difficult as infants may be asymptomatic or present with nonspecific signs. This case highlights the presentation of minimal cutaneous involvement as well as skeletal involvement after birth, observed as pseudoparalysis of Parrot with radiological findings of periostitis. The classic clinical signs of early CS include snuffles, lymphadenopathy, mucocutaneous lesions, pneumonia, rash, and hemolytic anemia or thrombocytopenia. Prolonged untreated CS can lead to permanent deformities, including Hutchinson’s triad of interstitial keratitis, Hutchinson’s teeth, and neural deafness. RPR testing may result in false negatives or indeterminate results, further complicating diagnosis. Given these difficulties in screening and the increasing incidence of CS, clinicians may need to refamiliarize themselves with its clinical findings.
Bullous pemphigoid coupled with lichenoid drug eruptions arising in cancer patients receiving anti-PD-1 immunotherapy

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Background: Immune checkpoint inhibitors targeting programmed death 1 (PD-1) receptors have increasingly been shown to achieve durable responses in several cancers. Anti-PD-1 therapies may cause cutaneous adverse events, such as generalized maculopapular and lichenoid eruptions, which typically respond to topical steroids and do not require interruption of cancer treatment. Autoimmune blistering disorders have rarely been associated with anti-PD-1 agents. Cases: We present 2 cases of bullous pemphigoid (BP) coupled with lichenoid drug eruptions secondary to anti-PD-1 therapy. An 83 year old male with recurrent tongue SCC on pembrolizumab and an 84 year old male with metastatic SCC of the lung on nivolumab, both presented with several months of innumerable pruritic erythematous papules and annular plaques with rare bullae on the scalp, trunk and extremities. These eruptions were recalcitrant to high potency topical steroids. Anti-PD-1 therapy was held in both cases, but the eruptions persisted. Systemic steroids led to improvement, with flaring upon withdrawal. Biopsies from bullous and perilesional skin showed a moderate lichenoid infiltrate with focal subepidermal split. Direct immunofluorescence showed linear IgG and C3 along the dermoepidermal junction, confirming BP. Both patients were treated with doxycycline 100 mg twice per day, nicotinamide 500 mg three times per day, and clobetasol 0.05% ointment twice per day, with significant improvement. Systemic immunosuppression was avoided and anti-PD-1 therapy was resumed in both patients. Advanced teaching points: These cases illustrate the diagnosis and treatment in 2 patients who developed BP while receiving anti-PD-1 therapy. Their clinical courses were distinct from traditional drug-induced BP in that their skin eruptions did not rapidly resolve upon withdrawal of the causative agent. Recognizing anti-PD-1 induced BP is important, for it enables treatment without systemic immunosuppressives (i.e., doxycycline and nicotinamide) and allows for resumption of anti-PD-1 therapy.

Demodex folliculitis mimicking recalcitrant graft-versus-host disease

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Background: Cutaneous graft-versus-host disease (GVHD) typically presents as a morbilliform eruption and occurs within a few weeks of allogeneic stem cell transplantation. When isolated to the skin and involving less than 25% of the body surface area (grade 1), it is treated with topical steroids. Case: A 38 year old female with a history of acute myeloid leukemia, who underwent allogeneic stem cell transplantation, presented 60 days post-transplant with itchy erythematous perifollicular papules and patches on the face, neck, chest, and dorsal hands. The rash was exacerbated by tapering of systemic immunosuppression and donor lymphocyte infusions, and transiently improved with topical steroids. Skin biopsy demonstrated suppurrative folliculitis with eosinophils, and subsequent KOH preparation showed numerous demodex mites. The patient was started on topical permethrin 5% cream repeated 1 week apart, metronidazole 0.75% cream twice per day, and discontinuation of topical steroids, with near resolution. Advanced teaching points: Demodex folliculorum is a common inhabitant of normal pilosebaceous glands, but immunosuppression increases its risk for a pathogenic role, whereby it causes suppurative folliculitis and manifests as pruritic papules and pustules. Since the morphology of demodex folliculitis can resemble GVHD and both conditions initially flare with tapering of systemic immunosuppression, differentiating the two can be difficult. A key distinguishing feature is that grade 1 GVHD typically responds well to topical steroids, whereas demodex folliculitis initially responds but becomes refractory. This case illustrates the importance of considering demodex folliculitis in immunosuppressed, post-transplant patients whose clinical picture mimics recalcitrant GVHD, as the appropriate treatments are vastly different.

Recalcitrant EGFR inhibitor papulopustular eruptions: the importance of screening for secondary infection

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Background: Papulopustular eruptions occur in more than 80% of patients receiving cancer treatment with EGFR inhibitors. Typically, within 2 weeks of starting therapy erythematous papules and pustules develop on the scalp, face and upper trunk, which evolve to crusted lesions that resolved over 8 weeks. Pustules are usually sterile, but superinfection can occur. Treatment involves a combination of topical steroids and antibiotics, most commonly topical clindamycin +/- oral tetracyclines. Cases: We present 3 cases of recalcitrant EGFR inhibitor papulopustular eruptions. Case 1 is a 59 year old male with metastatic lung adenocarcinoma on cetuximab and afatinib, who presented with a 4 week history of painful, crusted papules and pustules on a background of confluent erythema involving the scalp. Case 2 is a 58 year old male with tonsillar squamous cell carcinoma on cetuximab, who presented with a 6 week history of heavily crusted, painful papules and furuncles on the upper chest. Case 3 is a 54 year old female with metastatic lung adenocarcinoma on erlotinib, who presented with a 3 week history of heavily crusted, painful papules and pustules on her face. All 3 patients experienced worsening rash despite treatment with topical steroids, clindamycin solution, and oral doxycycline. Cultures from pustules revealed clindamycin and tetracycline resistant MSSA (case 1), clindamycin and tetracycline resistant MRSA (case 2), and klebsiella pneumoniae (case 3). Upon switching to appropriate antibiotic therapy, all 3 patients experienced rapid improvement in their skin eruptions. Advanced teaching points: The diagnosis of EGFR inhibitor papulopustular eruptions is usually straightforward, based on morphology, distribution and time course. While about one third of patients with EGFR inhibitor eruptions become secondarily infected, the causative organism is most commonly staphylococcus aureus, which is covered by conventional treatments. These cases illustrate atypical features of EGFR inhibitor eruptions, such as heavy crusting, severe pain, larger lesions, and no improvement on standard therapy. Recognizing these features is important, as it will prompt further evaluation for infection with uncommon organisms, lead to appropriate, targeted antimicrobial therapy, and prevent unnecessary dose reduction of EGFR inhibitors.
**Toxic epidermal necrolysis (TEN) associated with anti-PD-1 antibody therapy**

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Anti-programmed cell death receptor-1 (PD-1) immunotherapies, such as nivolumab, are increasingly being used in the treatment of metastatic or unresectable melanoma and other cancer types. Cutaneous reactions are the most frequent side effects reported with these immune checkpoint inhibitors, and they are usually mild and treated with topical corticosteroids. We present a case report of a patient on nivolumab who developed toxic epidermal necrolysis (TEN), which was fatal despite multiple systemic therapies. A 50-year-old woman with metastatic melanoma developed an initially morbilliform eruption following her first cycle of combined checkpoint inhibition with ipilimumab and nivolumab. Over three months and two additional doses of nivolumab monotherapy, the eruption evolved into a diffuse, tender, exfoliative dermatosis. Histology demonstrated interface dermatitis with full thickness epidermal necrosis. The patient was diagnosed with TEN, and her severity of illness score for TEN was 5. The patient was started on high-dose steroids and infliximab, as treatments for both immune-related adverse effects from anti-PD-1 inhibitors and TEN. With no improvement within 48 hours, intravenous immunoglobulin was given for three doses. The patient developed septic shock and passed away on hospital day six. Programmed cell death ligand (PD-L1) immunostaining was performed in both the initial biopsy of the initial morbilliform eruption and the biopsy at time of TEN presentation. PD-L1 staining revealed notable increased PD-L1 expression in the epidermis, primarily the keratinocytes, over the progression of the eruption. **Conclusions and learning points:** To our knowledge, this is the second case of TEN associated with nivolumab; the mechanism for drug eruptions secondary to immune checkpoint inhibitors is not yet known. However, increased expression of PD-L1 by immunohistochemistry, as the eruption progressed to TEN, may suggest that nivolumab and other immune checkpoint inhibitors may activate T-cells non-specifically, allowing the T-cells not only to target tumor cells, but also to target keratinocytes, subsequently leading to keratinocyte apoptosis. With the growing use of anti-PD-1 therapies, we recommend that dermatologists take an early and active role in management of cutaneous adverse effects, given that some can become severe and potentially fatal.

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**Toxic erythema of chemotherapy presenting with hemorrhagic mucositis**

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Toxic erythema of chemotherapy (TEC) is a group of overlapping toxic skin reactions secondary to cytotoxic chemotherapy (including high-dose conditioning regimens for stem cell transplants [SCT]) administered 2-3 weeks prior to presentation with bullae, intertrigo, and/or palmpoplantar erythema. TEC can be misdiagnosed as an allergic drug reaction, graft versus host disease, or Stevens-Johnson syndrome (SJS). Correct diagnosis of TEC can avoid interruptions in chemotherapy, harmful systemic interventions, and false establishment of drug allergies. We highlight an atypical presentation of TEC with concomitant oral/anal mucositis secondary to SCT conditioning that may be misdiagnosed as SJS. **Case presentation:** A 52-year-old woman on day 7 status post allogeneic SCT for angioimmunoblastic T-cell lymphoma was evaluated by the inpatient dermatology team for hemorrhagic oral mucositis and esophagitis. This was initially attributed to her melphalan/fludarabine conditioning completed 1-day prior to receiving an unrelated, unmodified, 10/10 match peripheral blood SCT. Three days after initial consultation, the patient developed a superficially desquamative, intertriginous eruption with persistent oral mucositis and new anal erosions. The patient subsequently developed palmpoplantar erythema and painful, superficial, moist dusky and erythematous intertriginous desquamation, demonstrating a positive Nikolsky sign. She did not have urethral or ocular mucosal involvement. Her course was complicated by ongoing candidal sepsis, multi-organ dysfunction and delayed engraftment. Medications started in the 3 weeks prior to onset of mucositis included micafungin, meropenem, pantoprazole, and vancomycin. SCT donor had no history of drug rashes. Punch biopsies revealed pauci-cellular interface dermatitis with focal apoptosis and dyskeratosis of adnexal epithelium without significant inflammation or full thickness necrosis. While involvement of two mucosal sites and positive Nikolsky sign were initially concerning for SJS, the self-limited clinical course and the pauci-inflammatory infiltrate coupled with only focal apoptosis best supported a diagnosis of TEC with mucositis attributed to melphalan/fludarabine. Cutaneous desquamation and mucositis were resolving with supportive wound care 2 weeks after presentation. The primary team was advised to restart any medications discontinued for this rash; however, she died shortly after due to diffuse alveolar hemorrhage.

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**Coxsackie virus: A Rare Cause of Papular Purpuric Gloves and Socks Syndrome**

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Papular purpuric gloves and socks syndrome is a distinct rash involving the hands and feet or the so-called “stocking glove distribution.” The exanthem is characterized by erythema, petechiae, purpura, edema, and worsening neuropathy. The most commonly reported cause is parvovirus B19, a single-stranded DNA virus. We present a case of coxsackie virus, a single-stranded RNA virus, presenting as papular purpuric gloves and socks syndrome in an eighty-three year old male. Our patient was hospitalized for concerns of vasculitis. Past medical history significant for coronary artery disease with stenting, hypertension, and diabetes mellitus complicated by peripheral neuropathy. The rash began as a tender spot on the left medial foot that evolved to affect both feet and hands. The rash was non-pruritic, however was accompanied by a new neuropathy along the right hand. Along both dorsal and planter hands and feet, physical examination revealed several petechiae, some coalescing into non-blanchable plaques and few purpuric papules on edematous skin. Our patient was slightly febrile with a temperature of 100.5°F. Laboratory findings were positive for coxsackie A9 antibody, all others including parvovirus B19 IgM, hepatitis C, hepatitis B, HHV-6, and EBV were negative. Histopathologic examination revealed a superficial perivascular lymphocytic infiltrate with extravasated erythrocytes and hemorrhage consistent with a viral exanthem. During his hospitalization, the patient reported his five year old granddaughter subsequently developed a rash involving her hands, feet, and mouth. The patient was treated symptomatically for his fever and his rash resolved after two days. One week phone follow-up revealed that our patient developed onychomadesis of a few digits consistent with coxsackie virus. In summary, papular purpuric gloves and socks syndrome is a unique exanthem with parvovirus B19 reported in two-thirds of cases. Clinicians, however, must remain astute to the other, more rare causes.