San Diego Dermatological Society Annual Meeting at UCSD

September 29, 2016

Hosted by
UC San Diego
Department of Dermatology
Dedicated to the memory
and enduring legacy

of

Dr. Terry O’Grady


Oceans

by Edward Louis Severson III

hold on to the thread
the currents will shift
guide me towards you
know something's left
and we're all allowed to dream
of the next time we touch...

you don't have to stray
two oceans away
waves roll in my thoughts
hold tight the ring...
the sea will rise...
please stand by the shore...
I will be...
I will be...
there once more.
ORDER OF EVENTS

5:45 – 6:30 PM  Patient Viewing

3rd Floor Medical Offices South (Ambulatory Care Center)
UCSD Hillcrest Hospital

6:30 – 7:00 PM  Buffet Dinner followed by San Diego Dermatological Society Business Meeting

1st Floor Main Auditorium
UCSD Hillcrest Hospital

7:00 – 8:00 PM  Speaker Introduction: Taraneh Paravar, MD

Annual Dr. Terry O’Grady Lectureship in Dermatopathology

“Many Faces of Lupus”
Jean L. Bologna, MD
Professor, Department of Dermatology,
Yale School of Medicine

8:00 – 9:00 PM  Patient Case Presentations: led by Taraneh Paravar, MD and Brian Hinds, MD
CASE LIST

Case 1: CVID-associated granulomatous dermatitis

Case 2: Localized xanthomas arising in the setting of Noonan syndrome and lymphedema praecox

Case 3: Severe end-stage lichen planopilaris

Case 4: Systemic sclerosis

Case 5: Severe Darier disease

Case 6: Atrichia with papular lesions

Case 7: Lichen planus (inverse variant)

Case 8: Pseudoporphyria secondary to naproxen

Case 9: Cutaneous follicle center [B-cell] lymphoma

Case 10: Cutaneous sarcoidosis

Case 11: X-linked ichthyosis (poster presentation)

Case 12: Cutaneous post-transplant lymphoproliferative disease (PTLD), polymorphic B-cell variant with kappa light restriction (poster presentation)
HISTORY: SB is a 24-year-old female with a history of combined immunodeficiency who presented for evaluation of several lesions on her right lower extremity. The first group of these lesions appeared on her right ankle 16 years ago after she broke her ankle. The lesions were neither pruritic nor painful, and they did not respond to treatment with topical or intra-lesional steroids. Excisional biopsies were performed on 5 of the lesions, all with pathology suggestive of granuloma annulare. The lesions recurred within months of the biopsies, and the right ankle lesion overall remained stable over the next several years. Eight years ago she noticed a similar lesion on her right thigh. The lesion was excised, and pathology was again suggestive of granuloma annulare. She was treated with infliximab, with no new lesion development during this time, however the medication was discontinued after 8 months due to long-term risks of further immunosuppression.

On presentation to our clinic about 4 years after discontinuing the infliximab, the patient reported that the lesion on her right thigh had grown over the past 3 months, and occasionally ulcerates and drains yellow fluid. She denied fevers or other constitutional symptoms.

PAST MEDICAL HISTORY: Combined immunodeficiency (originally diagnosed as common variable immunodeficiency, or CVID, at age 3, however more recently a deficiency in her cellular immune function has also been detected), aspergillus pneumonia in 2010, asthma, allergic rhinitis

MEDICATIONS: Beclomethasone 80 mcg/ACT inhaler 2 puffs daily, human immune globulin 60 mg subcutaneous q 7 days, levonorgestrel 13.5 mg IUD, sulfamethoxazole-trimethoprim 800-160 mg PO 3 times per week

ALLERGIES: Voriconazole – hives; Amoxicillin-clavulanate – nausea/vomiting

FAMILY HISTORY: None

PHYSICAL EXAMINATION:
- Violaceous firm papules coalescing into an ovoid 5.5 x 2.5 cm plaque on the right inner thigh with one adjacent 1.2 cm violaceous papule laterally
- Violaceous patch with no palpable dermal nodularity on the right medial ankle, with overlying xerosis and some lichenification

LABORATORY DATA: CBC with differential and CMP are WNL. Tissue cultures showed no growth of acid fast bacilli, anaerobic organisms, or fungal organisms. Scant growth of methicillin resistant Staphylococcus aureus was seen.
PATHOLOGY: Punch biopsy of the right thigh: sections demonstrate a nodular to diffuse infiltrate of macrophages, some multinucleated, arranged interstitially and in a palisaded array in the dermis. Central necrosis and debris are apparent. There is flanking fibrosis with a plasmacyte-rich infiltrate. Stains for bacteria, mycobacteria and fungi with Brown-Brenn, acid fast bacilli, and Periodic Acid Schiff-diastase respectively revealed no organisms. Overall these findings are most consistent with palisaded granulomatous dermatitis.

DIAGNOSIS: CVID-associated granulomatous dermatitis

Presented for interest

DISCUSSION: Granulomatous disease has been reported in 8-22% of patients with CVID. The most common sites of involvement include the lungs, spleen and lymph nodes, however granulomas have been reported in several other organs including the skin, bone marrow and liver. Granulomatous disease can precede the diagnosis of CVID by up to 18 years, but it can also be diagnosed concurrently or after a diagnosis of CVID has been established.

The diagnosis of granulomas in a patient with CVID is especially important to note since granulomatous changes in these patient are associated with an increased risk of autoimmune conditions, namely idiopathic thrombocytopenic purpura and autoimmune hemolytic anemia.

Treatment of CVID-associated granulomas is challenging, as it typically requires immunosuppressive agents that would otherwise not be recommended in a patient with a baseline immunodeficiency. Steroids have traditionally been the first-line treatment, with hydroxychloroquine being an alternative. More recent case reports have also suggested the efficacy of tumor necrosis factor-alpha inhibitors in resolving these lesions (Lin et al, Thatayatikom et al).

REFERENCES:
CASE # 2

NOTE: Face, legs

PATIENT INITIALS: JG   AGE: 24   SEX: M   RACE: Hispanic

PRESENTED BY: Megan Brown, MD, Stella Chen, BS, Wynnis Tom, MD, Tissa Hata, MD

HISTORY: JG is a 24-year-old Hispanic male who presented for evaluation of numerous yellow papules on his left dorsal toes. These papules were largely asymptomatic and had erupted spontaneously two-months prior to evaluation. The patient denied any previous trauma. He reported swelling in the left leg that had developed abruptly 15-months prior to the onset of the papules. While not particularly painful, the swelling seemed to worsen after his work shifts or with prolonged standing.

PAST MEDICAL HISTORY: Noonan syndrome, abnormal rotation of the small bowel, renal asymmetry, and seminal vesicle asymmetry

MEDICATIONS: None

ALLERGIES: No known drug allergies

FAMILY HISTORY: No relatives with similar skin findings

PHYSICAL EXAMINATION:
• The left lower extremity exhibited prominent firm edema extending from the mid-thigh to the foot, with multiple coalescing pink-yellow small firm papules on the left second and third toes. The patient was also noted to have short stature, triangular facies, low-set hairline, webbed neck, and widely spaced nipples.

IMAGING:
• Venous Doppler ultrasound negative for deep vein thrombosis and reflux
• CT pelvis with patent bilateral common iliac, internal and external iliac, and common femoral veins
• MRI at level of the knee with moderate diffuse soft tissue swelling

PATHOLOGY: Biopsy of a lesion on the left second toe revealed a nodular proliferation of mononuclear cells situated wholly in the dermis with vacuolated, foamy cytoplasm. Extracellular lipid was also evident.

DIAGNOSIS: Localized xanthomas arising in the setting of Noonan syndrome and lymphedema praecox

Presented for interest and any treatment suggestions.

TREATMENT: The patient was evaluated by vascular surgery and discussed at the Multidisciplinary Vascular Lesion and Birthmark Center (VLC) at Rady Children’s Hospital for the rapid onset of left lower extremity swelling. Both teams agreed that the patient’s
clinical exam and workup are consistent with a diagnosis of primary lymphedema (i.e. lymphedema praecox). Symptomatic management and physical therapy for the lymphedema was recommended. The patient has recently started wearing a lymphedema boot. He uses a stationary bike and wears compression hose daily. A low-salt and decreased long-chain triglyceride diet was also recommended. After 10 weeks, he still has marked circumferential enlargement of the left lower extremity despite adherence to these interventions. He has several more xanthomas extending to the fifth toe, which are easily traumatized despite wider shoes. The benefits and risks of octreotide are being weighed versus oral retinoids for the lymphedema. Laser treatment may be an option for the xanthomata.

**DISCUSSION:** Lymphedema praecox is a form of primary lymphedema which develops between the age of 2 and 25 years (Cheville et al). It accounts for 80% of all cases of primary lymphedema. Moreover, it is observed in some patients with Noonan syndrome (Cheville et al, Romano et al). Noonan syndrome results from a mutation in the RAS/MAPK cell signaling pathway, mostly commonly in PTPN11 (protein tyrosine phosphatase, non-receptor type 11) gene (Bertola et al). Noonan syndrome can be associated with dysplasia of lymphatic vessels, and an estimated 20% develop lymphedema (Romano et al, Bertola et al). The most common manifestation is dorsal limb lymphedema, which tends to resolve in childhood (Burgt v der et al). The development of localized or eruptive xanthomas in the setting of lymphedema is very rare, with only 20 case reports reported worldwide to date (Dana et al, Wooling et al). Only one other case report outlines xanthomata in a 14-year-old boy with Noonan’s syndrome (Wang et al). In all of these reported cases, the xanthomas either improved or resolved as the lymphedema improved (Dana et al, Wooling et al). The etiology of the xanthomas in the setting of lymphedema remains largely unknown.

There are few effective measures for lymphedema management after physical measures (supportive care, surgical etc) have been tried. We are considering a trial of, octreotide, a somatostatin analog, which has been used for pulmonary and intestinal lymphangectasia and in a few cases of lymphedema with yellow nail syndrome (Makrilakis et al). Another treatment option may be an oral retinoid as this as been shown helpful in two reported cases of elephantiasis, perhaps by enhancing lymphatic vessel regeneration (Polat et al).

**REFERENCES:**

NOTE: Scalp

PATIENT INITIALS: MA  AGE: 50  SEX: F  RACE: Hispanic

PRESENTED BY: Wiggin Wu Lee, MD, Wynnis Tom, MD

HISTORY: MA is a 50-year-old female who presented in 2014 for evaluation of hair loss. She initially started having hair loss on the vertex of her scalp in the 1990s; it has since spread centrifugally. She reports associated pustules, pain, pruritus, and scaling. She had previously tried antifungal shampoos, topical steroids, vitamins A and C supplements, essential oils, and possibly intramuscular steroids, all which did not help much. She was currently taking doxycycline 100mg BID which she felt helped with her symptoms.

Punch biopsies were consistent with lichen planopilaris (LPP). In balancing risks and benefits given active peripheral disease yet the majority being unsalvageable, the patient was started on lidex solution daily, intralesional kenalog (ILK) 10mg/ml injections at each clinic visit, doxycycline 100mg PO BID, and hydroxychloroquine 200mg BID. She felt significant improvement with less itching and less hair loss. In September 2015, she was noted to have increased sun sensitivity with doxycycline so she was switched to minocycline 100mg BID and all other treatments were continued with no progression of disease.

Unfortunately, she was lost to follow up for 6 months and in March 2016, she returned with increased hair loss and symptoms again. She had not been on any treatments for the last 3 months. She was restarted on minocycline, clobetasol cream BID on weekdays, hydroxychloroquine, and ILK injections/visit. She has had no progression of disease since.

PAST MEDICAL HISTORY: None

MEDICATIONS: Minocycline 100mg BID PO, hydroxychloroquine 200mg BID PO, clobetasol cream BID Monday-Friday

ALLERGIES: No known drug allergies

FAMILY HISTORY: Noncontributory

PHYSICAL EXAMINATION:
- Vertex of scalp with a large over 10cm patch of scarring alopecia with loss of follicular ostia.
- Mild to moderate perifollicular erythema on the border of the scarring and alopecic scalp
- No other areas of skin involvement or hair loss. No oral lesions.

LABORATORY DATA: CBC, CMP, LFTs all within normal limits. ANA negative
PATHOLOGY: 2 punch biopsies from the A) left medial parietal scalp and B) left lateral parietal scalp both showed an inflammatory lymphocytic scarring alopecia, most consistent with lichen planopilaris.

DIAGNOSIS: Severe end-stage lichen planopilaris

Presented for interest and any treatment suggestions

DISCUSSION: Lichen planopilaris (LPP) is the most common cause of immune-mediated inflammatory cicatricial alopecia (James et al). If not diagnosed and treated early, it can lead to devastating, irreversible hair loss. Unfortunately, therapies can often be ineffective and compliance can be challenging as treatments are mainly aimed towards prevention of disease progression.

In 2003, Mirmirani et al. suggested that after a clinical and pathology diagnosis of LPP is established, the severity of disease activity should be documented at least every 3 months. In 2010, the LPP activity index, a scoring system that allows quantification of symptoms and signs, was introduced and can be a useful tool in quantitatively comparing disease activity (Chiang et al).

In terms of treatment, hydroxychloroquine 200 mg BID PO is recommended if the patient is symptomatic or has signs of active disease. Intralesional and topical corticosteroids may be used concurrently. After 2-4 months, hydroxychloroquine may be changed to cyclosporine (3-5mg/kg/d) if disease activity has not improved.

Recent studies have shown that LPP scalp biopsies, when compared to normal scalp biopsies, exhibit a decreased expression of the peroxisome proliferator-activated receptor (PPAR)-γ, leading to an increase in proinflammatory nuclear transcription factors, interleukins, and proteolytic enzymes (Karnik et al). Based on this theory, since 2009, there have been several studies and reports of pioglitazone, a synthetic PPAR-γ ligand, as a treatment option for LPP. However, its efficacy has varied from 14–70% (Spring et al, Mesinkovska et al). One retrospective analysis of 22 patients treated with pioglitazone 15mg daily, for a median of 10.5 months, showed its efficacy in controlling the symptoms, inflammation, and disease progression in 72.7% of patients. Further studies are still needed to confirm beneficial effects for LPP. More importantly, increased incidences of heart failure have been associated with pioglitazone when used to treat diabetes; therefore, its use in LPP remains controversial.

Lastly, in severe end-stage disease, hairpieces and strategic hair styling are beneficial, including in the case of our patient.

REFERENCES:

CASE # 4
NOTE: Whole Body

PATIENT INITIALS: LR  AGE: 63  SEX: F  RACE: Caucasian

PRESENTED BY: Natasha Carter, MD PhD, Taraneh Paravar, MD

HISTORY: LR is a 63-year-old female with a 5 year history of systemic sclerosis with ulcerations of the PIPs and elbows. She has renal, lung, skin and cardiac involvement. She has end stage renal disease and is on hemodialysis. She has NYHA class 4 congestive heart failure. She has interstitial lung disease. Her most recent PFTs from March of 2015 show FVC of 1.58L which is 50% of her predicted value. She was previously treated with methotrexate and mycophenolate mofetil. She has been on prednisone for many years and is currently on 7.5mg daily. She uses petrolatum daily and collagenase ointment on ulcers. She is also followed by cardiology, pulmonology, nephrology and rheumatology.

PAST MEDICAL HISTORY: End stage renal disease, myocardial infarction 2011, stroke 2014, heart failure, melanoma, chronic pain

MEDICATIONS: Petrolatum daily, collagenase 250unit/gm ointment to ulcers daily, prednisone 7.5mg PO daily, aspirin 81mg PO daily, carvedilol 15mg PO daily, multivitamin, folic acid, calcium 667mg TID, hydromorphone PO PRN, losartan 50mg daily, nitrolycerin PRN, omeprazole 20mg PO daily, ticagrelor 90mg PO BID, paroxetine 20mg PO daily.

ALLERGIES: No known drug allergies

FAMILY HISTORY: None

PHYSICAL EXAMINATION:
• Skin: type II
• Mat telangiectasias on bilateral cheeks
• Minimally decreased oral aperture
• Indurated and firm bound down skin of upper and lower extremities including hands and feet; firm induration and tapering of fingers
• Flexion contractures of fingers
• Healing ulcers at the bilateral elbows, left 4th PIP and MCP joints
• Indurated and firm bound down skin on the upper chest and shoulders
• Small white subcutaneous nodules on extensor extremities

LABORATORY DATA: ANA positive with speckled and diffuse patterns, >1:640. SCL-70 Ab Negative. CBC and CMP were notable for Hgb 11.1, HCT 34.7, BUN 61, and CR 6.9 but were otherwise within normal limits

PATHOLOGY: N/A
**DIAGNOSIS: Systemic sclerosis**

**Presented for interest**

**DISCUSSION:** Systemic sclerosis is an autoimmune connective tissue disease of unknown etiology. Patients make antibodies to a limited group of autoantigens including anti-centromere and anti-topoisomerase. These autoantibodies have prognostic implications for the patients and can help guide their care.

Scleroderma is characterized by symmetric hardening of the skin of the fingers, hands and face that may generalize. The generalized form is called systemic sclerosis. Internal organ involvement is frequent and affects the lungs, gastrointestinal tract, heart and kidneys; lung involvement is the leading cause of death. Limited scleroderma was formerly known as CREST syndrome. Many patients present on a spectrum between limited and systemic presentations.

Treatment focuses on internal organ involvement; effective therapy for cutaneous fibrosis remains inadequate. A randomized controlled, double-blind study looking at drug effects on interstitial lung disease published in the Lancet Respiratory Medicine 2016 showed similar efficacy between mycophenolate mofetil for 2 years vs cyclophosphamide for 1 year. However, it did show better tolerability and toxicity profile in the group treated with mycophenolate mofetil. The skin effects were not evaluated in the study (Tashkin et al).

Looking to the future there may be promising novel treatment options in the pipeline. Gerber et al showed an integrin-modulating therapy that could prevent fibrosis and autoimmunity in mouse models of scleroderma. Translation of such therapies could be life changing for patients with systemic sclerosis (Gerber et al).

**REFERENCES:**

HISTORY: EM is a 58-year-old male with a 50-year history of Darier disease presents for management of severe symptoms. Since diagnosis at the age of 8, his condition has progressed and now causes tremendous irritation and involves large body surface areas including thick plaques. Many such lesions on the eyelids, nose, and ears have led to disfiguration. He was previously treated with various topical steroids and later isotretinoin for 31 years with no good effect. On the contrary, the symptoms continued to worsen, now causing severe pruritus, pain with movement and recalcitrant yeast infectious of the intertriginous skin. He also developed depression and social isolation because of his disfiguring skin condition, body odor, and failure despite multiple treatments.

The isotretinoin was recently discontinued and acitretin 25 mg qday was started, which was later titrated to 50 mg qday. The patient was able to tolerate this dosage despite side effects including mild xerosis and palmar/plantar skin peeling managed with emollient use as well as hyperlipidemia controlled with gemfibrozil. However, the patient reported little improvement at the 2-month follow up. We, therefore, started calcipotriene 0.05% cream BID as an adjunct treatment. At the following two visits, the patient reported excellent effect with nearly complete clearing on the chest and upper back, as well as great improvement of the scalp and face. He denied any skin irritation caused by calcipotriene. Of note, his blood test showed hypocalcemia. He was prescribed a calcium/vitamin D3 supplement. Secondary yeast infections were well controlled with an increased dose of fluconazole.

PAST MEDICAL HISTORY: Hyperlipidemia, depression.

MEDICATIONS: Acitretin 50 mg daily, fluconazole 400 mg daily, gemfibrozil 600 mg daily, calcium-vitamin D 600-400 mg-U BID, bacitracin 500 U/gm ointment daily, econazole 1% cream daily, fluocinonide 0.05% solution daily, ketoconazole 2% shampoo daily, nystatin-triamcinolone ointment daily, hydroxyzine 50 mg q6h PRN, tamsulosin 0.4 mg daily, omeprazole 20 mg daily

ALLERGIES: Cortisone - swelling

FAMILY HISTORY: None

PHYSICAL EXAMINATION:
- Numerous yellow, thick and verrucous keratotic papules and plaques covering most of the skin on face, ears, scalp, neck, chest, upper back, abdomen, and groin.
- Areas of denuded skin are noted in groin and lower back, weeping with serosanguinous fluid.
- Conjunctivae are mildly injected.
• Palmar aspects of hands have small pits.
• All fingernails and toenails have alternating longitudinal red and white bands, as well as dystrophy and distal V-shaped nicking.

LABORATORY DATA: Triglycerides 251 (normal range 10-170), cholesterol 190 (normal range <200), HDL 29 (normal range >40), LDL 111 (normal range <160), Ca 10.2 (normal range 8.5-10.6)

PATHOLOGY: N/A

DIAGNOSIS: Severe Darier disease

Presented for interest

DISCUSSION: Darier disease is a skin condition caused by an autosomal dominant mutation in the ATP2A2 gene which encodes the SERCA2 protein which regulates cellular calcium homeostasis. The primary lesions are keratotic and crusted papules in a “seborrheic” distribution involving the scalp, face, neck, chest and back. Intertriginous areas such as abdominal fold and groin can also be involved with secondary infections. The typical findings on nails show alternating longitudinal red and white streaks and notching of the distal edge of the nail plate.

Common treatment for Darier disease include topical corticosteroids and retinoids, systemic isotretinoin and acitretin, and surgical removals for recalcitrant lesions. Calcipotriene is a synthetic derivative of vitamin D3. It has been used in treating many skin conditions such as plaque psoriasis, ichthyosis, morphea, Grover’s disease, and Hailey-Hailey disease. The effectiveness in treating Darier disease, however, is under-investigated. The mechanism of action of calcipotriene in achieving clinical effectiveness in our case is unclear. Whether or not calcipotriene facilitates re-balancing of calcium homeostasis will be an interesting future research question.

REFERENCES:
• Abe M, Inoue C, Yokoyama Y, Ishikawa O Successful treatment of Darier’s disease with adapalene gel 2010 28(2):197-8
CASE # 6

PATIENT INITIALS: XL  AGE: 22  SEX: M  RACE: Asian

PRESENTED BY: Keith Roby, MD, Megan Brown, MD, Brian Hinds, MD

HISTORY: XL is a 22-year-old Asian man who presented for extensive and refractory alopecia that started when he was a child. He has never had a haircut in his lifetime. Over the last several years, in addition to the alopecia universalis-like phenotype, he has noticed many asymptomatic papules arise on the face, scalp, and chest.

PAST MEDICAL HISTORY: Congenital cataracts status post corrective surgery at six-months of age, and congenital glaucoma. He reported no difficulty with hearing, sweating, dentition, and had no thickening of his palms or soles.

MEDICATIONS: Bimatoprost gtt, dorzolamide gtt daily

ALLERGIES: No known drug allergies

FAMILY HISTORY: No relatives with similar skin findings or problems with hair growth. No known consanguinity.

PHYSICAL EXAMINATION:
- Minute vellus hairs of the scalp, eyebrows, cutaneous lip, and extremities with preserved follicular ostia
- Atrichia of eyelashes, inside nasal vault, and of intertriginous skin
- Scattered small cystic papules on the scalp, face, and chest
- Hyperlinear palms without palmoplantar keratoderma
- Nystagmus
- Normal nails, oral mucosa, and teeth
- Normal stature, no bony abnormalities

LABORATORY DATA: CBC and CMP are WNL. Calcium, alkaline phosphatase, Parathyroid hormone and thyroid-stimulating hormone also within normal range. Serum 25-hydroxyvitamin D [25(OH)D] levels were mildly low at 21 ng/mL [range 30-100ng/mL]. Exom sequencing has been submitted and remains pending.

PATHOLOGY: Sections show a diminution in the number of hairs with scattered miniaturized hairs that show normal infundibulum, but exhibit cyst formation at the bases, within the mid-dermis along with a sparse perifollicular lymphocytic infiltrate. Terminal hairs and sebaceous glands were lacking.

DIAGNOSIS: Atrichia with papular lesions (APL)

Presented for interest
DISCUSSION: Atrichia with papular lesions (APL) is a rare, autosomal recessive genodermatosis characterized by complete and irreversible alopecia with multiple follicular cysts. Patients with APL present with normal lanugo hairs present at birth and then rapidly progress to an alopecia universalis-like phenotype once these neonatal hairs are shed. This process of permanent alopecia is present by age 2-3 years. Around age 2-10 years, patients often begin to develop follicular papules and cysts filled with keratin that arise at the mid-portion of the follicle. APL has been associated with mutations in the hairless gene (HR), which encodes a transcriptional co-repressor involved in the wnt signaling pathway in the hair growth cycle. Patients with APL may be misdiagnosed as having alopecia universalis, which is an important distinction to make in order to avoid unnecessary treatment. Clinical diagnostic criteria have been proposed, although genetic testing ultimately confirms the diagnosis in suspected cases.

REFERENCES:

CASE # 7

NOTE: Axilla, inframammary, abdomen

PATIENT INITIALS: CH AGE: 72 SEX: F RACE: Caucasian

PRESENTED BY: Shehla Admani, MD, Tissa Hata, MD

HISTORY: CH is a 72-year-old female with a history of breast cancer and nonmelanoma skin cancer, who presented for evaluation of a dark spot on the right underarm. The lesion had been present for at least one year, not growing or changing and asymptomatic.

PAST MEDICAL HISTORY: Cancer of right breast, treated with radiation in 1985, then with recurrence and mastectomy in 2009; nonmelanoma skin cancer (pigmented basal cell carcinoma) in area of prior radiation

MEDICATIONS: Calcium-Vitamin D

ALLERGIES: Penicillin, Sulfa, Ciprofloxacin

FAMILY HISTORY: Noncontributory

PHYSICAL EXAMINATION:
- Pink/brown patch/minimally elevated plaque on right axilla
- Brown papule with a stuck on appearance with some erythema on the umbilicus
- No oral mucosal lesions

LABORATORY DATA: N/A

PATHOLOGY: 2 shave biopsies from the A) right axilla and B) umbilicus both showed hyperkeratosis, epidermal effacement, hypergranulosis, liquefaction degeneration and a band like infiltrate of lymphocytes and histiocytes in the superficial dermis also with melanophages in the dermis. The diagnosis was consistent with lichen planus.

DIAGNOSIS: Lichen planus (inverse variant)

CLINICAL COURSE: At one year follow-up, the patient had developed new lesions on the right axilla, left inframammary area and left pannus fold. The lesions were asymptomatic and she elected not to treat.

Presented for interest and any comments on diagnosis and treatment

DISCUSSION: Lichen planus (LP) can have a variety of clinical variations that are categorized based on morphology and distribution. In inverse LP the majority of the lesions are located in intertriginous areas. Due to the location and occlusion, inverse LP lesions can have an atypical morphology and often will have associated hyperpigmentation.
Lichen planus in general, not specifically the inverse subtype, has been seen in patients with a history of radiation. There are three variants that can be seen: localized, generalized, and progressive (localized at onset and then generalizes). There are a limited number of cases of lichen planus associated with radiation in the literature; the majority are localized and time to onset ranges from during radiation therapy to 15 months after treatment.

The isoradiotopic response is a term used to describe any skin disorder on an irradiated, photoexposed or burned skin area. Development of LP at a radiation site is considered an isoradiotopic response. Other skin conditions that can have a similar response are pemphigoid, pemphigus, Stevens-Johnson, erythema multiforme, lichen sclerosus et atrophicus, graft-versus-host disease and scleroderma. Another variant of the isoradiotopic response is radiation recall, which notably has been reported up to 15 years after treatment.

Regarding our patient’s course, her LP initially developed in a previously irradiated area (right axilla) and then also developed on above mentioned “inverse” areas. Her radiation was over 25 years prior to the onset of her LP lesions and it is possible that there is no association between the two; however, as other forms of isoradiotopic response can be seen many years after the radiation exposure, our patient may have a unique progressive form of this response with lesions being limited to inverse areas only.

REFERENCES:
CASE # 8

NOTE: Dorsal hands, ankles

PATIENT INITIALS: SD    AGE: 45    SEX: M    RACE: Caucasian

PRESENTED BY: David Cotter, MD, PhD, Zhe Jessie Hou, MD PhD, Wynnis Tom, MD

HISTORY: SD is a 45-year-old man with a history of HIV, prior IV drug use, neuropathy, bipolar disorder, and renal transplant who presents for a pruritic rash on the dorsal hands and ankles for the last three to six months. He reports tiny blisters that are extremely pruritic. When he scratches, they tend to bleed and subsequently scar. Hydrocortisone 1% cream provided no relief for the condition. He normally wears shorts and sandals and does not adhere to sun protection measures. He denies any other lesions elsewhere on the body. Of note, for chronic neuropathic pain he takes naproxen 500 mg PO BID since approximately January 2015. In addition, he applies capsaicin cream as needed.

PAST MEDICAL HISTORY: HIV (CD4 count 1472, no detectable viral load), bipolar disorder, history of renal transplant, neuropathy. No history of Hepatitis C (HCV) and HCV antibody testing non-reactive as of 8/28/14.

MEDICATIONS: Abacavir-dolutegravir-lamivudine 600-50-300 mg PO daily, capsaicin 0.1% cream, hydrocortisone 1% cream, loperamide 2mg PO daily, loratadine 10mg PO daily, naproxen 500mg PO daily, pregabalin 100mg PO TID, risperidone 1mg PO TID, venlafaxine XR 150mg PO daily

ALLERGIES: No known drug allergies.

SOCIAL HISTORY: No alcohol consumption; ½ ppd smoker. Previous IV methamphetamine use 3.5 years ago.

FAMILY HISTORY: Non-contributory

PHYSICAL EXAMINATION:

• Fitzpatrick Skin Type 2
• A solitary 2mm vesicle was present on the left dorsal wrist and multiple 1-2mm rusted scars and erosions were present on the dorsal hands and ankles.
• A linear excoriation was present on the left lateral malleolus.

LABORATORY DATA: CBC and CMP are WNL. HIV-1 RNA is not detected. CD4 count is normal. Hep C Ab, HBsAg, and HepBcAB IgM are all non-reactive. Syphilis EIA Screen and Chlamydia/gonorrhea PCR urine are non-reactive.

PATHOLOGY: Punch biopsy of the left dorsal wrist showed an intact Paucicellular subepidermal bullae. The overlying blister cavity contained numerous necrotic keratinocytes in linear array (so-called caterpillar bodies) and the papillary dermis revealed an undulating pattern, especially at the apices of the superficial vascular plexus (so-called festooning). Rare eosinophils were present in the connective tissue away from the blister.
cavity. Direct immunofluorescence testing from perilesional skin lacked immunoreactant deposition.

**DIAGNOSIS:** Pseudoporphyria secondary to naproxen

**CLINICAL COURSE:**
We recommended appropriate sun protection, to stop naproxen, and to seek alternative options to control foot pain. We told the patient that if no adequate alternative could be found, that he should apply triamcinolone 0.1% ointment twice daily to the vesicles, should they recur. At his last follow up visit, he had only been off of naproxen for 3 days. At that time, he had developed only one new vesicle with the use of SPF alone. His next follow up appointment is in October.

*Presented for interest.*

**DISCUSSION:** Porphyria is a heterogeneous group of disorders united by abnormalities of heme metabolism. They can be sub-categorized as acute or subacute/chronic, based on their proclivity to present with acute flares or attacks, and alternatively subdivided as cutaneous or non-cutaneous variants.

The cutaneous porphyrias often manifest as photodistributed bullous disorders. The most common porphyria, porphyria cutanea tarda (PCT), presents with hallmark skin findings. It may be commonly acquired (type 1), or rarely, inherited with autosomal dominance (type 2). PCT presents in the 3rd-4th decade with photosensitivity, photodistributed skin fragility in the form of vesicles and bullae, milia/scarring, hyperpigmentation, and hypertrichosis. Acquired PCT may be triggered by alcohol, estrogens, polychlorinated hydrocarbons, dialysis, iron, and viral infection, namely HIV and hepatitis C. Suspicion for the underlying disease should prompt a skin biopsy for H&E and direct immunofluorescence (DIF), along with 24-hour urine porphyrin studies. Histopathology may reveal a paucicellular subepidermal vesicule with festooning of dermal papillae, and superjacent aminophilic basement membrane (caterpillar bodies) in the roof of the blister cavity. DIF often shows IgG, IgM, C3, and fibrinogen at the DEJ and around vessels in the papillary dermis. Urine porphyrin studies may show increased excretion of uroporphyrin, hepta-carboxylated porphyrins, and coproporphyrin. Examination of the patient’s urine under Wood’s lamp may show pink to red fluorescence, while exposure to natural light for a few hours may turn it red or brown.

Pseudoporphyria mimics PCT clinically, but lacks biochemical abnormalities of porphyrin metabolism. Pseudoporphyria retains the clinical features of skin fragility, erosions, and blisters on sun-exposed skin, but tends to lack hypertrichosis and milia. It can be drug-induced and associated with chronic kidney disease and hemodialysis. Naproxen is the most common cause of pseudoporphyria. Pseudoporphyria is histologically indistinguishable from PCT with the same pattern of immunoreactant deposition on DIF. Treatment includes discontinuation of the causative medicinal agent and adherence to sun protection.
Our patient lacked hypertrichosis and milia and had only mild disease activity. Therefore, urine porphyrin studies and Wood’s lamp of his urine were not pursued. Should he not improve with empiric avoidance of naproxen and sun protection, additional diagnostic workup may be pursued.

REFERENCES:
HISTORY: NZ, is a 63-year-old woman with a history of an eruption on the back and right arm for at least the past 3-years. At the time of evaluation in our clinic, she reported a large, painful area of skin thickening with redness on the back and less so on the right forearm. She described white scale or crust that was easily picked off, occasionally weeping fluid. In the past, she reported that long periods of sunlight appeared to exacerbate the skin lesions, particularly after prolonged swimming. Over time the condition has become progressively worse, circumferential enlargement of the lesion on the back. Although she complained of fatigue, she denied any weight loss, fevers, or night sweats. Previously she trialed over-the-counter and prescription topical and intralesional corticosteroids without much improvement, including most recently topical betamethasone 0.05% BID. Patient underwent ~9-10 Narrow-band UVB sessions, and had a flaring of lesions on back, prompting discontinuation of light therapy. In December 2015, two punch biopsies were obtained by an outside dermatologist. The report suggested the possibility of [pseudolymphomatous] tumid lupus erythematosus. Two additional biopsies from the same lesion on the back were repeated in January 2016, again showing a dense lymphocytic [B-cell] infiltrate with negative B-cell gene rearrangement. UCSD Hematopathology reviewed this material upon referral to UCSD Oncology, and the consensus was that this represented a reactive B-cell process.

PAST MEDICAL HISTORY: Nephrolithiasis, Hypertension, aortic regurgitation, fibroid uterus.

MEDICATIONS: Aspirin 81mg PO daily, lisinopril 2.5mg PO daily, metoprolol succinate 100mg PO daily, Betamethasone 0.05% ointment topically BID, tacrolimus 0.1% ointment topically BID

ALLERGIES: Iodine

FAMILY HISTORY: None

PHYSICAL EXAMINATION:
- 4.5cm x 2.5cm well-defined erythematous to plum-colored plaque with induration and numerous telangiectases, with a surrounding rim of hypopigmentation and subtle atrophy on the right mid-back
- 3.5cm x 1.5cm erythematous ill-defined plaque with well-defined borders and central erosion and crusting on the right forearm
- No lymphadenopathy
LABORATORY DATA: CBC w/ diff, CMP, LFTs are grossly WNL; outside records from 05/29/2015—all negative: ANA, Anti-DS DNA, Anti smith, Anti scleroderma-70, Anti-ssa, anti-ssb, antichromatin, anti-jo, anti-centromere, RNP; RA factor 7.3 (wnl), normal ESR, normal CRP, Apolipoprotein 80 (normal 0-79 mg/dL).

PATHOLOGY:
- 7/25/2016: Sections of a 4mm punch biopsy from the right mid-forearm showed an ulcer with subjacent granulation tissue and mixed inflammation without atypicality of lymphocytes.
- 8/8/2016: A 5mm punch biopsy from the right upper back revealed a pan-dermal lymphoid infiltrate comprised of cleaved small-medium sized lymphocytes that are present in germinal center-like aggregates in a nodular and diffuse pattern within the dermis. Some of the latter have retained mantles rimming the periphery of the lymphoid follicles. CD20 and CD3 immunostaining highlights widely scattered nodules of CD20+ B cells that vary in size and shape, with an encompassing infiltrate of CD3+ T cells in the interstitium. CD23 immunohistochemistry labels distinct meshworks of follicular dendritic cells. Many of these foci are positive for centrally positioned aggregates of Bcl-6 positive cells, with numerous Bcl-6 positive cells present outside of the meshworks. Chromogenic in situ hybridization for kappa and lamda light chains revealed a polytypic infiltrate. A diagnosis of mixed type follicular B-cell lymphoma was rendered.

DIAGNOSIS: Cutaneous follicle center [B-cell] lymphoma

CLINICAL COURSE: Prior to establishing this diagnosis, we recommended stopping the topical corticosteroids in anticipation of repeat biopsy. On follow-up visit the lesion on back was less indurated and more pink in color, but the same size. Patient also found to have new diffuse erythematous, non-blanching patches on bilateral lateral arms, and bilateral pretibial areas, posterior calves and lateral thigh. Upon establishing the diagnosis, she was referred to Oncology for repeat evaluation of primary malignant process, but is unable to receive further care at UCSD due to insurance restrictions. Patient is in the process of scheduling an Oncology appointment.

Presented for interest

DISCUSSION: The incidence of primary cutaneous lymphoma is 0.5-1 case per 100,000 people annually. Of these, 20% represent primary cutaneous B-cell lymphoma (PCBCL). Primary cutaneous follicle center lymphoma (PCFCL) is the most common PCBCL, accounting for ~60% of all cases. It usually affects non-Hispanic White M>F, with median age of 50.

Clinically, PCFCL presents as firm erythematous, painless, non-pruritic papules/plaques/tumors on the head/neck/trunk. While overlying scale is certainly possible, ulceration is rare. The progression is often slow, representing an indolent process many times developing over 20 years. Unlike systemic disease, “B” symptoms are rarely observed in cutaneous variants of B-cell lymphoma.
If left untreated, skin lesions may disseminate to extra-cutaneous sites in approximately 10% of patients. Radiation therapy has been used for solitary lesions with some success. Scattered lesions which would not fit into a radiation field have been treated with excision or chemotherapy. Widespread disease has been treated with rituximab, radiation therapy and/or chemotherapy (CHOP-like). Intralesional interferon alpha has also been reported as a therapeutic option.

The overall prognosis for PCFCL is very good with 95% survival rates at 5-years. Select studies of PCFCL have reported relapse rates approaching 30% after radiation therapy. Patients with cutaneous follicle center lymphoma, however, should always undergo a full-body skin examination with palpation for lymphadenopathy with subsequent staging workup to exclude the possibility of node-based disease.

REFERENCES:
• Bolognia JL, Jorizzo JL, Schaffer JV. Dermatology 3rd edition 2012 Elsevier
CD is a 50-year-old woman with a history of diabetes, chronic sinusitis, and prior diagnosis of sarcoidosis since 2012, on adalimumab. She initially presented to our clinic in October 2014 with brown papules and plaques on the face (right nasal ala, right infraorbital area) and upper back. A biopsy of a single papule on the back showed lichenoid granulomatous dermatitis consistent with sarcoidosis. At that time, a chest x-ray showed linear interstitial opacities in the bilateral lower lobes. A subsequent CT scan about one-year later in December 2015 demonstrated mediastinal/hilar adenopathy consistent with ongoing pulmonary sarcoidosis.

While on adalimumab (40mg sc q2weeks), the lesions on the back improved, while her facial disease remained recalcitrant. In April 2015, she was started on clobetasol 0.05% cream daily to apply strictly onto lesions on the face, but it caused a burning sensation and was self-discontinued after 1-week of use. The patient received intralesional triamcinolone injections on two consecutive visits (November 2015 & January 2016) for facial lesions, but this only led to minimal improvement. Topical tacrolimus 0.1% ointment BID was started thereafter with a clinical response.

While being seen by dermatology, the patient developed worsening dyspnea. Bronchoscopy in January 2016 showed 50% lymphocytes in the lung parenchyma, but cytology was negative for granulomas or malignant cells. Per pulmonology recommendations, adalimumab was discontinued in the setting of worsening pulmonary symptomatology. In June 2016, the patient was restarted on methotrexate (2.5mg tablets, 4 tablets PO qweek). Her pulmonary symptoms improved on methotrexate, but with no major improvement in facial lesions.

Past treatments included hydroxychloroquine, minocycline, prednisone, methotrexate, topical clobetasol, and intralesional Kenalog. She was started on adalimumab 40mg sc q2weeks, and was only on this medication for her sarcoidosis when first presenting at UCSD. At UCSD, topical clobetasol 0.05% cream daily (with appropriate topical steroid breaks) and intralesional Kenalog injections x 2 did not offer much improvement. Topical tacrolimus 0.1% ointment BID provided some benefit. As mentioned above, adalimumab was discontinued in the setting of worsening pulmonary symptoms, and the patient resumed methotrexate.

Past medical history: Chronic sinusitis, diabetes mellitus, benign hypertension, hyperlipidemia

Medications: Albuterol inhaler 1 puff q12h PRN wheezing, atorvastatin 20mg PO nightly, metformin 1g PO BID, insulin (100 units/ml) 50 units SQ nightly, biotin 1mg PO daily, cholecalciferol 800 units PO daily, vitamin E 400 units PO daily
ALLERGIES: No medication allergies known to date

FAMILY HISTORY: Noncontributory

PHYSICAL EXAM:
- Hyperpigmented papules coalescing into plaques on the cheeks, right nasal ala, bilateral upper extremities, and upper back
- Dark red scaly papules and hyperpigmented papules along the right nasal ala

LABORATORY DATA: Serum ACE level 89 units/L (high, normal: 9-67), CBC/BMP/LFT wnl. An ECG showed normal sinus rhythm. Pulmonary function tests in 2014 revealed an FEV1/FVC ratio wnl (73%), DLCO moderately reduced. PFTs in 2015 showed an FEV1/FVC ratio 69% (mild obstructive ventilatory defect), DLCO moderately reduced.

PATHOLOGY: Biopsy specimen from the upper back showed noncaseating granulomas with Langhans and occasional foreign body giant cells. There are foci of lichenoid interface change with apoptotic cells and sclerotic collagen in the stroma. Perineural involvement is present. No polarizable material is identified. Special stains including AFB, Fite, GMS, and PAS are negative for organisms. A diagnosis of sarcoidosis was rendered.

DIAGNOSIS: Cutaneous sarcoidosis

Presented for Interest

DISCUSSION: Sarcoidosis is a systemic granulomatous disease of unknown etiology that develops in the skin and many internal organs, including the lung, liver, and spleen. In so-called lupus pernio, the lesions are generally brown-to-violaceous smooth papules and plaques on the nose, ears, cheeks, lips, and forehead. Involvement of the nasal mucosa/underlying bone may occur and contribute to nasal perforation. Patients have concurrent chronic fibrotic respiratory tract involvement in about 75% of cases. Lupus pernio is usually seen in women in their 4th or 5th decade. The skin lesions rarely spontaneously involute.

Early treatment of lupus pernio may help reduce and prevent disfigurement from scar formation. Local and systemic corticosteroids are typically first line treatments. However, steroid-sparing agents such as antimalarials, methotrexate, and tetracycline antibiotics may be used. TNF-alpha antagonists, such as infliximab and adalimumab, have proven successful in cases refractory to standard therapies. TNF-alpha has been shown to play a crucial role in the formation and maintenance of granulomas in sarcoidosis. For unclear reasons, there are cases of etanercept contributing to the development of sarcoidosis.

REFERENCES:
- Bolognia, Jean, Joseph Jorizzo L., and Julie Schaffer V. Dermatology. Philadelphia:


HISTORY: A 25-year-old male with no prior medical history presented to the dermatology clinic for evaluation of persistently dry skin. The man complained of dry, scaly skin covering a significant portion of his body since early childhood despite regular use of topical emollients and keratolytics. He was otherwise healthy, and a review of systems revealed no visual deficits, and no history of undescended testes or testicular masses. He noted his maternal grandfather and his brother were affected with similar scaly, dry skin.

Subsequent genetic testing confirmed a microdeletion on the X chromosome at the steroid sulfatase gene locus, consistent with a diagnosis of X-linked ichthyosis. He received counseling about the diagnosis, possible associated abnormalities including corneal deficits, cryptorchidism and testicular cancer, and treatment options. His current treatment includes tazarotene 0.05% gel daily and liberal application of ammonium lactate 12% lotion and urea 20% cream. A subsequent ophthalmology consultation revealed no corneal opacities; a urology consultation is currently pending.

PAST MEDICAL HISTORY: Exercise induced asthma and allergic rhinitis

MEDICATIONS: Tazarotene 0.05% gel daily, ammonium lactate 12% lotion PRN, urea 20% cream PRN, acetaminophen PRN

ALLERGIES: NKDA

FAMILY HISTORY: Similar findings in brother and maternal grandfather

PHYSICAL EXAMINATION:
• Brown, rhomboid scales on the extensor surface of extremities
• Fine brown scaling on the trunk and neck
• Sparing of the face, flexural surfaces, and palms and soles

LABORATORY DATA: FISH chromosomal analysis confirming steroid sulfatase gene (STS) microdeletion on X chromosome

PATHOLOGY: N/A

DIAGNOSIS: X-linked ichthyosis

DISCUSSION: X-linked ichthyosis is a heritable disorder of keratinization with a prevalence of 1 in 6000, mostly in males. This disorder characteristically manifests as thick, brown, polygonal scales over the extensor surfaces that develop within the first few
weeks of life. It is inherited in an X-linked recessive fashion due to abnormalities in the steroid sulfatase gene (STS), most commonly due to a chromosomal deletion of the entire 146 kb gene. Steroid sulfatase (STS) catalyzes the hydrolysis of aryl and alkyl steroid sulfates to produce biologically active steroids.

In the skin, deficiency of STS results in the abnormal accumulation of cholesterol sulfate within the stratum corneum, thereby preventing normal desquamation. In utero, fetuses with STS deficiency have diminished placental estrogen levels, potentially resulting in prolonged labor (in up to one third of patients). Other associated abnormalities include asymptomatic corneal opacities (classically described as “comma-shaped”) that develop during adolescence (approximately 50% of patients); cryptorchidism (up to 20%); and an increased risk of testicular germ cell cancer that occurs independently of cryptorchidism.

X-linked ichthyosis may present as an isolated disorder or as a component of several well-characterized syndromes resulting from contiguous chromosomal deletions. These syndromes include X-linked chondrodysplasia punctata, Rud syndrome (congenital ichthyosis, hypogonadism, mental retardation, retinitis pigmentosa and hypertrophic polyneuropathy) and Kallmann syndrome (hypogonadotropic hypogonadism with anosmia).

The diagnosis of X-linked ichthyosis is often based on family history and clinical findings. Confirmatory tests include genetic techniques and biochemical assays such as protein electrophoresis (confirmed by increased mobility of the beta-lipoprotein fraction). Prenatal screening labs include amniocentesis, showing low estriol in the amniotic fluid, or maternal urinalysis, showing low levels of estrogen and increased levels of nonhydrolyzed sulfated steroids.

Treatment typically includes topical emollients, keratolytics and topical retinoids. Systemic retinoids are rarely indicated. All patients should be referred for ophthalmology evaluation, genetic counseling, and urologic evaluation.

REFERENCES:

LP is a 35-year-old woman who presented to our dermatology clinic with a 6-week history of three slowly enlarging subcutaneous nodules on her back. Review of systems was positive for periodic low-grade fevers, but negative for other B symptoms. There was no preceding trauma, discharge, or pain associated with the skin lesions.

The patient was status-post left-sided renal transplantation secondary to focal segmental glomerulosclerosis twelve years prior, followed by right-sided papillary renal cell carcinoma in 2010. Of note, she developed nodal post-transplant lymphoproliferative disorder (PTLD) in 2011 while on oral prednisone and tacrolimus, without evidence of skin disease. Immunosuppression was reduced and concurrent administration of rituximab led to complete response at 3-months follow-up. She was believed to be in remission at the time of presentation to our clinic.

FSGS s/p left kidney transplant in 2004 complicated by PTLD in 2011, renal cell carcinoma of the right kidney s/p right nephrectomy, hypertension, gastroesophageal reflux.

Tacrolimus 2 mg daily, prednisone 7.5 mg daily, allopurinol 100 mg daily, amlodipine 5 mg daily, calcium-D500 daily, metoprolol tartrate 50 mg BID, omeprazole 20 mg BID, valacyclovir 500 mg BID

Contrast media, iodine, lidocaine

Non-contributory

Three mobile subcutaneous nodules with a plum hue were present on the back with maximum size of 2cm x 3cm and without overt surface change. Nodules measured

No palpable lymphadenopathy or other detectable skin abnormalities.

CBC w/ diff: WBC 11,500 with elevated absolute lymphocyte count (3,600), Hemoglobin 14.9 and platelet count of 319,00, Flow cytometry of blood showed no clonal B-lymph proliferation, CMP: Cr 1.5 (her baseline 1.46-1.58, normal range 0.7-1.1), LDH within normal limits, Epstein-Barr Virus, Quant PCR serum – detected (previously undetectable)
IMAGING

- PET/CT 5/10/16: Multiple hypermetabolic subcutaneous nodules consistent with malignancy (including several nodules on the back). Hypermetabolic right pleural densities and right pelvic sidewall lymph node are also suspicious for malignancy.

PATHOLOGY: Sections show a large cohesive bulbous nodule with a deep center of gravity with marked expansion of the subcutaneous compartment. Sheets of cells are present with pale zones that contain small to medium sized cells with a monocytoid apperance. Some larger cells are admixed at the periphery of these areas. Mitotic figures are easily identified within many of the constituent cells. Pax-5 (B-cell marker)/CD3 (T-cell marker) showed a predominance of T-lymphocytes with large intervening zones of cells that lacked positivity. CD10 expression and CD21 expression were lackin. Bcl-2 was weakly positive, corresponding to mixed T and B-cells, and c-myc showed similar weak and patchy expression. Chromogenic in situ hybridization avidly labeled the plasmacytoid cells with kappa light chain, whereas lambda light chain expression is lacking. EBV in situ hybridization was diffusely positive in the majority of the lymphocytes.

DIAGNOSIS: Cutaneous post-transplant lymphoproliferative disease (PTLD), polymorphic B-cell variant with kappa light restriction

Presented for interest

DISCUSSION: Post-transplant lymphoproliferative disease (PTLD) is a rare but potentially fatal complication after solid organ transplantation. PTLD is the most common malignancy associated with organ transplantation (both solid and bone marrow), excluding non-melanoma skin cancers. PTLD occurs in 0.4-10% of recipients (more common in the pediatric population). The most common type of lymphoproliferative disorder in PTLD is non-Hodgkin lymphoma. One study found that HLA A2, CMV and EBV infections were risk factors associated with developing PTLD. In fact, a majority of cases (>90%) are associated with Epstein Barr virus (EBV), which drives the proliferation of B cells. It is believed that the loss of CD8+ T cell regulation due to the immunosuppressive medications permits reactivation of EBV. Reducing immunosuppression and treating the lymphoproliferative disease are the mainstays of treatment. With this recurrence of PTLD, our patient was restarted on rituximab, and her immunosuppressive agents were also continued. Both the Hematology and Nephrology teams felt that she could tolerate both regimens and that this would be the most beneficial treatment for this patient. Her most recent PET/CT showed a reduction in the size and activity of the subcutaneous FDG avid nodules indicating a response to treatment. Interestingly, some work has been done showing a decreased incidence of PTLD in patients on antimetabolites (mycophenolate mofetil) compared to those on typical immunosuppressant like tacrolimus (Caillard et al).

REFERENCES: