Kyrle Disease

A Rare Dermatologic Condition Associated with the Diabetic Foot

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We report two cases of biopsy-confirmed Kyrle disease. Kyrle disease is one of the perforating dermatoses associated with diabetic patients undergoing renal dialysis. In this report, we describe the clinical and histopathologic features, the differential diagnoses, and successful treatment of this unusual disorder. (J Am Podiatr Med Assoc 105(5): 451-455, 2015)

The first reported case of Kyrle disease was written by J. Kyrle in 1916.[1] He described a 22-year-old woman with diabetes mellitus who had "hyperkeratosis et parafollicularis in cutem penetrans."[1] The perforating dermatoses are 1) elastosis perforans serpiginosa, 2) reactive perforating collagenosis, 3) perforating folliculitis, and 4) Kyrle disease.[2] Kyrle disease has been primarily linked to patients with diabetes and renal disease with an even higher predilection for dialysis.[2-4] There have been reports of Kyrle disease also having an association with hepatic deficiency and congestive cardiac failure.[5] This dermatologic disease has been more commonly seen in individuals aged 35 to 70 years, but there have been a few case reports of patients as young as 4 years old.[5] The female to male ratio has been reported to be 2 to 1 to 6 to 1.[3-5] A genetic trait has been suggested as a predisposing factor for the development of Kyrle disease.[3] Constantine and Carter[6] in 1968 first proposed the histologic criteria of 1) a keratotic plug filling an epithelial invagination, 2) parakeratosis in parts of the plug, 3) basophilic cellular debris, and 4) abnormal keratinization of all of the epidermal cells. Kyrle's original clinical criteria consisted of 1) chronic, scattered, generalized, papular eruptions that have hyperkeratotic cone-shaped plugs; 2) with or without follicle involvement; 3) lesions may coalesce into hyperkeratotic verrucous plaques; and 4) lesions do not involve the mucous membranes, palms, or soles.[1]

Since the initial report of J. Kyrle there have been other cases reported in the literature describing the diagnosis and treatment of the disease.[7] However, most of the reported treatments had limited success in healing the lesions. We present two cases of histologically proven Kyrle disease that were successfully treated with a regimen of a topical corticosteroid and keratolytic therapy.

Case 1

A 57-year-old black man presented with a hyperkeratotic, well-circumscribed nodule on the medial aspect of the distal ankle of the left foot (Figs. 1 and 2). The patient reported that the ankle lesion presented several months previously. He denied any pain or pruritus but admitted minor discomfort to the area. He could not recall any trauma. Many similar asymptomatic lesions were found on the extensor aspects of both elbows and forearms (Figs. 3 and 4).

The patient had a 15-year history of diabetes mellitus with peripheral neuropathy and a 10-year history of home peritoneal dialysis therapy performed three times a day after bilateral nephrectomies for renal carcinoma. Additional medical

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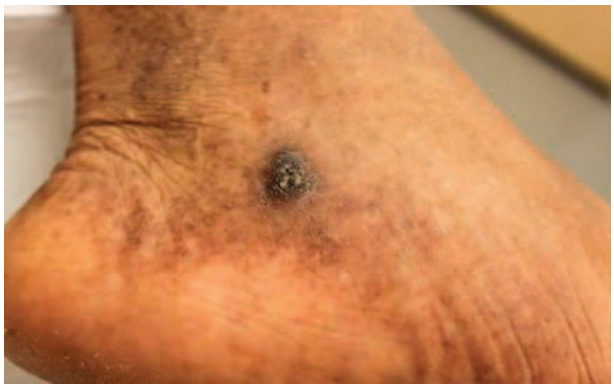


Figure 1. Case 1: a horny nodule on the medial aspect of the left foot.

history included benign prostatic hypertrophy, peripheral arterial disease, obesity, and gout. Medications included sevelamer and calcium acetate for hyperphosphatemia, esomeprazole for gastroesophageal reflux, lorazepam, insulin (Humulin; Eli Lilly & Co), and erythromycin. The patient denied medication allergies and other surgical history. The patient's mother is also diabetic, with similar but undiagnosed lower-leg lesions. The patient is a former tobacco user but denies any alcohol or illicit drug use. The patient is currently retired.

Physical examination revealed palpable pedal pulses but decreased protective sensation when tested with the 5.07 Semmes-Weinstein monofilament. The musculoskeletal examination found mild hallux abducto valgus deformity bilaterally. On the medial left ankle, a sensitive, hyperpigmented, hyperkeratotic eruptive nodule measured 1.2 × 1.2 cm. Some tenderness to palpation was noted.

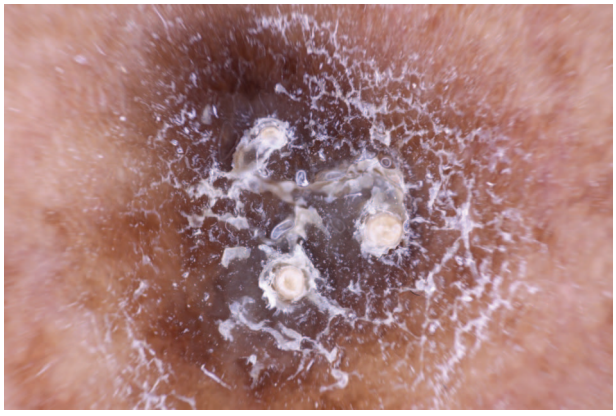


Figure 2. Case 1: dermoscopic examination reveals brown and deeper gray amorphous hyperpigmentation surrounding multiple horny plugs.



Figure 3. Case 1: right elbow with hyperpigmented papules.

Similar but smaller lesions were found on both forearms ranging from 4 mm to 1.5 cm in diameter. Histopathologic examination of a 2-mm punch biopsy sample revealed a large hyperkeratotic plug embedded in an epidermal invagination associated with adjacent epidermal hyperplasia characteristic of Kyrle disease (Fig. 5).



Figure 4. Case 1: left elbow with hyperpigmented papules.

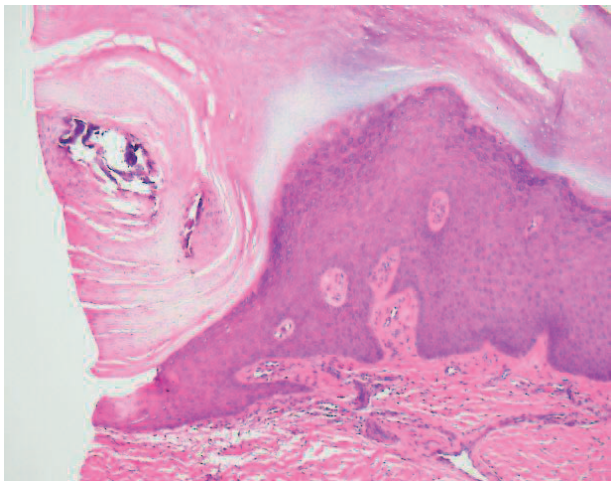


Figure 5. Case 1: medial left foot punch biopsy sample stained with H&E (x100).

Case 2

A 44-year-old black woman presented to the clinic with a concern about painful papules and plaques on both lower extremities. The multiple lesions were located about the medial and lateral ankles and the Achilles tendon and extended proximally to the thigh. The patient denied a specific incident that triggered the lesions. She first noticed them approximately 1 year before her presentation to the clinic. The lesions progressively had grown in size, and her symptoms worsened. She had seen a dermatologist approximately 6 months before presentation, with treatments consisting of multiple corticosteroid creams. After several conservative treatment options were exhausted and after limited efficacy she was referred to the clinic by her primary care physician for a second opinion. The review of systems was unremarkable besides intermittent claudication-type symptoms.

The medical history was significant for insulin-dependent diabetes mellitus, multiple sclerosis, depression, hypertension, and asthma. Medications included insulin lispro (Humalog; Eli Lilly & Co), budesonide/formoterol (Symbicort; AstraZeneca), omeprazole, zolpidem tartrate (Ambien; sanofi-aventis US), albuterol, sertraline hydrochloride (Zoloft; Pfizer Inc), loratadine, and montelukast. Medication allergies to cephalosporins and macrolides were reported. The family history was significant for diabetes and hypertension, but no history of similar lesions could be found. The surgical history was unremarkable. She had a 30–pack-year smoking history and worked as a homemaker.

On physical examination her neurovascular status was grossly intact. The dermatologic examination revealed multiple hyperpigmented and hyperkeratotic plaques measuring 1.5 × 1.0 cm each. No erythema or blanching was noted. The lesions were very painful on direct palpation. Two lesions were noted on the anterior thigh, three on the left posterior Achilles region, one on the left medial malleolus, and another overlying the right lateral malleolus.

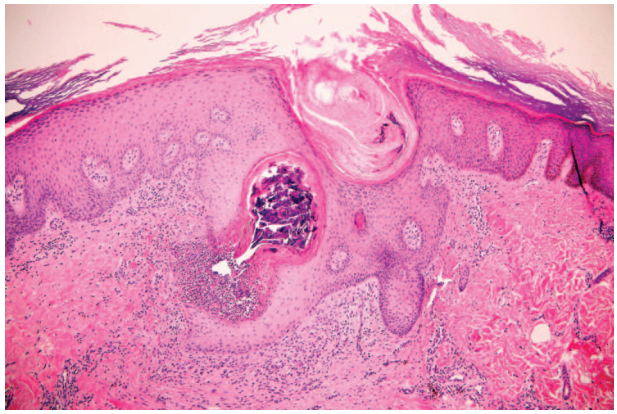


Figure 6. Case 2: an epithelial invagination with a parakeratotic plug, which contains basophilic debris and neutrophils; the parakeratotic plug meets the dermis at the base of the invagination (H&E, x100). Courtesy of Christine Jaworsky, MD, Professor of Dermatology, Case Western Reserve University School of Medicine, Cleveland, Ohio.

Two 3.0-mm punch biopsy samples were obtained from one of the lesions. The histopathologic examination showed acanthotic epidermis with an effaced or thinned rete ridge pattern (Fig. 6). There was a broad zone of superficial dermal fibrosis with interstitial lymphocytic inflammatory infiltrates. Additional slides revealed characteristic endophytic epithelial invaginations and discrete focal epithelial necrosis. There were overlying collections of parakeratin with cellular debris and neutrophils in the vicinity. Periodic acid–Schiff stains showed no evidence of yeast or hyphal elements.

The histology reports for both patients presented a working diagnosis of Kyrle disease. Both patients were started on local topical treatment of triamcinolone, 0.5%, ointment applied every 12 hours. The patients were instructed to apply the triamcinolone ointment 6 of 7 days per week for 30 days to avoid tachyphylaxsis.

In addition, the second patient was prescribed 40% urea cream under occlusion every night. The lesions on the weightbearing surfaces were offloaded in the standard manner for symptomatic

relief. The patient was referred back to her primary care physician for evaluation of abnormal renal and hepatic function tests. The first patient reported significant improvement without any discomfort at the lesion site. After a 30-day course of the triamcinolone, 0.5%, ointment, there was nearly complete clearance of the lesion (Fig. 7). The medial left foot lesion remained clear at 9 months.

Discussion

Clinically, the differential diagnosis for our patients consisted of prurigo nodularis, multiple keratoacanthomas, verruca vulgaris, and nodular melanoma. Although both patients did follow the clinical criteria of Kyrle disease, it was difficult to base a diagnosis on the clinical appearance alone. It was not until the punch biopsy samples were obtained that the differential list was narrowed to Kyrle disease. The histology reports echoed the criteria set forth by Constantine and Carter.[6] What further strengthened the final diagnosis of Kyrle disease was that both patients reported a medical history of diabetes and the first patient was undergoing peritoneal dialysis. These characteristics supported the diagnosis of Kyrle disease. A genetic link may be associated with patient 1 because he reported similar-looking lesions to the lower extremities that were never fully investigated. Patient 2 denied any family history of similar dermatologic conditions. Although these two patients were symptomatic, it has been thought that Kyrle disease is most often asymptomatic.

Although the pathogenesis is multifactorial and not well understood, there is increasing evidence that immune system dysfunction and an elevated proinflammatory pattern are involved in chronic kidney disease–associated pruritus.[6] Localized scratching could trigger a sequence of localized lichen simplex chronicus, progressing in some patients to prurigo nodularis and in the genetically predisposed patient to Kyrle disease.



Figure 7. Case 1: complete resolution after 1 month.

Reported treatment of Kyrle disease has ranged from vitamin A to surgical removal of the lesion, with little success reported in terms of full clearance of the lesion.[6] As a result, the goal of treatment for the disease has been centered on symptomatic relief. In the few successful case reports in the literature that noted clearance of the lesions, the lesions did return within 6 months of initial clearing. There was one report of clearance of the lesions after the use of oral clindamycin for an associated cellulitis and no report of the lesions returning.[3] In that case report, it was noted that both the new active lesions and the old chronic lesions had responded to an oral antibiotic drug course. Review of the literature did not reveal previous topical corticosteroid therapy to clear the lesions of Kyrle disease.

Topical corticosteroids have anti-inflammatory, antipruritic, and immunosuppressive properties that potentially pave the way for clearing the lesion and providing symptomatic relief for the patient.[8] For our patients, topical corticosteroids provided a decrease in inflammation and broke the itch/scratch cycle that accompanies the perforating diseases. It is thought that blocking the inflammatory process allows dermal debris to be shed through epidermal channels, resulting in resolution of the lesions. We postulate that the immunosuppressive activity of the vasoconstrictive corticosteroid blocks the abnormal immune reaction in the skin, helping to suppress new lesion formation.

Topical corticosteroids provide multiple potent pharmacologic effects for the clinician to exploit in the treatment of many conditions, but as with any medication there is the potential for adverse reactions. Overuse of topical corticosteroids increases the risk of skin atrophy, hypopigmentation, and telangiectasia. These adverse drug reactions can largely be avoided by limiting applications to only 6 of 7 days.[8] Although rare, hypothalamic-pituitary-adrenal axis suppression with the overuse of topical corticosteroids can occur; the risk is lessened with application regimens that have low surface to volume ratios and shorter durations.[9] Focal application of corticosteroids lessens the possibility of systemic adverse effects.

Kyrle disease has been a dermatologic condition that has once been proved difficult to treat. As we saw with the present patients, the use of topical corticosteroids can provide the clinician with an effective treatment strategy and a favorable adverse effect profile. The exact period of regression

of the lesion once treated with topical corticosteroids is unknown. These two patients reported no recurrent symptoms 9 months after initiation of treatment.

Financial Disclosure: None reported.
Conflict of Interest: None reported.

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