A Report of Kyrle’s Disease (Hyperkeratosis Penetrans) in a 43-Year-Old Male with End-Stage Renal Disease

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Abstract

Kyrle’s disease, also known as hyperkeratosis penetrans or hyperkeratosis follicularis et parafollicularis in cutem penetrans, is a rare condition, classified as one of the perforating dermatoses. Clinical presentation is typically numerous red-brown nodules with a scaly crust and central hyperkeratotic plug. Although an identifiable cause has yet to be established, there appears to be a strong relationship with end-stage renal disease and diabetes mellitus. In this report, we present a case of Kyrle’s disease in a 43-year-old male with multiple comorbid medical conditions and provide a review of efficacious treatments.

Introduction

Perforating dermatoses, including Kyrle’s disease (or hyperkeratosis follicularis et parafollicularis in cutem penetrans), perforating folliculitis, elastosis perforans serpiginosa, and reactive perforating collagenosis, are disorders of transepithelial destruction of dermal structures, commonly occurring secondary to chronic renal disease or diabetes mellitus.1,2 Kyrle’s disease was first described in 1916 and usually presents as an extensive, painless papular eruption with a hyperkeratotic central plug. It most commonly involves the lower extremities but can also involve the upper extremities and trunk.3 There is no involvement of the acral surfaces or mucous membranes.4 Histologically, there is epidermal atrophy with extension into the papillary dermis and the presence of a hyperkeratotic plug.4

The etiology of Kyrle’s disease is unknown, and although in some cases it appears to be a primary perforating skin disorder, in others it occurs secondary to chronic kidney disease, liver disease, congestive heart failure or diabetes mellitus.4 Treatment is focused on managing underlying medical conditions, if present, as well as keratolytic agents, although no one treatment option has proven to be efficacious in improving the appearance of lesions.4
Case Presentation
A 43-year-old African American male presented to our clinic with a chief complaint of bilateral pruritic papules on his upper and lower extremities of two to three months’ duration. He initially treated the lesions using a topical antifungal cream prescribed by his primary care physician, which was unsuccessful. His past medical history consisted of end-stage renal disease, diabetes mellitus, hypertension, thyroid disease, anxiety, and depression. Dialysis was initiated for five months prior to this cutaneous event due to worsening renal failure.

On clinical exam, the patient had numerous hyperpigmented, excoriated papules, with occasional hyperkeratotic central plaques, on the bilateral upper and lower extremities (Figures 1 and 2). A punch biopsy was obtained from a lesion on the right forearm, and pathology revealed epidermal hyperplasia surrounding areas of neutrophilic debris and fragmented elastic fibers in the epidermis and dermis (Figures 3 and 4). The appearance of the lesions, co-existing medical conditions, and pathologic findings confirmed a diagnosis of Kyrle’s Disease. The patient was given potent topical corticosteroids, and narrowband UVB therapy was recommended, but the patient failed to follow up.

Discussion
Kyrle’s disease is classified as one of the perforating dermatoses along with elastosis perforans serpiginosa, perforating folliculitis, and reactive perforating collagenosis. It was first described by Austrian pathologist and dermatologist Josef Kyrle in 1916 as “hyperkeratosis follicularis et parafollicularis in cutem penetrans.” Despite efforts to identify a cause for the disease, it has yet to be determined whether there are any underlying hereditary links or if it is idiopathic in nature. The strongest associations thus far are with chronic renal failure and diabetes mellitus; it is estimated that about 10% of patients on hemodialysis will eventually develop Kyrle’s disease. In a study by Papali et al., 21 patients with Kyrle’s disease, 12 were found to have diabetic nephropathy as well as elevated serum phosphorus levels. They proposed that because the skin lesions appeared to improve following dialysis, it is possible that hyperphosphatemia and uremic toxin buildup could be contributing factors to development of the lesions; however, further investigation of this relationship is needed.

Kyrle’s has also been linked to various other diseases, including, but not limited to, hepatic dysfunction, liver carcinoma, hypothyroidism, myelodysplastic syndrome, congestive heart failure, and tuberculosis lymphadenitis. In one case report of two Indian siblings affected with Kyrle’s Disease, ages 7 and 10, a possible autosomal-recessive genodermatosis was proposed, although evidence for a familial predisposition is still not well-studied.

Kyrle’s lesions typically manifest as a generalized eruption of multiple red-brown nodules with a scaly crust and central hyperkeratotic plug. In some instances, the lesions may coalesce to form larger plaques. Although the lower extremities are the primary sites of involvement in the majority of cases, the trunk may also be affected. Typically there is sparing of the mucous membranes, palms, and soles. The lesions are usually painless, but can be intensely pruritic and cosmetically bothersome.

Histologically, the lesions are characterized by a keratotic plug with basophilic cellular debris filling epithelial invaginations. Additionally, there may be parakeratosis in some parts of the plug as well as abnormal keratinization involving the entire epidermal thickness, leading to contact between keratinized cells and dermis. In some cases, there are neutrophils located where the keratinized cells contact the dermis. Lympohcytic and histiocyctic infiltrates may also be seen.

Treatment targets the presumed underlying associated disease processes, such as adequate blood glucose control for diabetes mellitus and dialysis for end-stage renal disease, as well as direct treatment to the lesions and symptom relief with topical agents. One study showed that with better glycemic control, where fasting blood glucose was < 75 mg/dL, post-prandial plasma glucose was < 131 mg/dL, and HbA1c was < 7.5, the lesions completely healed in about eight weeks and left behind only a hyperpigmented scar. Other documented effective therapies include topical salicylic acid, oral isotretinoin, tretinoin cream, and hypoallergenic emollients to soften the skin. To control pruritus, topical lotions including methanol or camphor may be soothing, and oral antihistamines like hydroxyzine, which can be sedating, may aid in symptom control at night. UV therapy can be helpful for those with diffuse skin involvement and individuals with renal or hepatic disease. The proposed mechanism of UV therapy is modification of pruritogens presenting in the skin. Carbon dioxide laser or cryosurgery can be used for smaller lesions; however, there are risks of skin hypopigmentation in individuals with darker skin, as well as the possibility of inducing diabetic foot infections in patients with diabetes mellitus or peripheral vascular disease. There is no randomized data to indicate a primary modality of treatment, and a variety of therapies can be implemented with special attention to the underlying comorbidity, if one is present.

Conclusion
In this report, we describe the case of a patient with end-stage renal disease and diabetes mellitus, currently undergoing dialysis treatments, who presents with Kyrle’s disease (hyperkeratosis penetrans). Although the disease has been presented in various case studies and associated with many systemic illnesses, there is no well-established cause or genetic link identified to date. However, because of the greater association with renal dysfunction and diabetes mellitus, it is important for physicians evaluating perforating dermatoses in patients with comorbid illnesses to be aware of this relationship to provide efficacious therapy and appropriate referrals for the management of underlying disease. Future studies are needed to further investigate the role of renal disease and diabetes in the development of Kyrle’s disease.

References