Case Report

Delayed Diagnosis of Klippel-Trénaunay Syndrome in a 23-year-old African American Male

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Abstract

Description

Klippel-Trénaunay syndrome is a rare genetic disorder that typically presents as a triad of symptoms consisting of venous malformations (varicosities), capillary malformations (port-wine stain), and limb overgrowth. We followed a 23-year-old African American male with a past medical history of peripheral vascular disease, who was visiting the dermatology clinic for a persistent skin lesion on his thigh. During physical examinations, we noted a subtle port-wine stain on his right leg, right leg hypertrophy, and peripheral vascular disease. Skin findings were difficult to observe on his darker skin tone, Fitzpatrick skin type VI, which may have led to the delayed diagnosis of Klippel-Trénaunay syndrome. The lesion of concern was removed during a follow-up visit and was consistent with an angiokeratoma. Our patient had not suffered any serious complications from his new diagnosis of Klippel-Trénaunay syndrome; however, there was a concern for thrombotic events.

Keywords

Klippel-Trénaunay syndrome; angiomatosis; angio-osteohypertrophy syndrome; vascular diseases; congenital, hereditary, and neonatal diseases and abnormalities; skin pigmentation; dermatology; diagnosis; dermatology; skin of color; African; Indian

Introduction

Klippel-Trénaunay syndrome (KTS) is a rare genetic disorder that typically presents as a triad of symptoms consisting of venous malformations (varicosities), capillary malformations (port-wine stain), and hypertrophy of soft tissue or bone.[1] Lymphatic malformations may or may not be present.[1] At birth, the most frequently observed findings are port-wine stains on the affected extremity.[1] The soft tissue hypertrophy and venous insufficiency may become more evident as a child develops.[1] It is important to recognize the signs and symptoms of this condition as a delayed diagnosis can lead to complications. These include bone and joint involvement (limb length discrepancy, osteoporosis, knee arthropathy), visceral bleeding, venous thromboembolism, localized intravascular coagulation, and/or pulmonary arterial hypertension.[2] We present the case of a 23-year-old African American male who visited the clinic for a persistent skin lesion on his thigh, with an additional finding of port-wine stain (PWS). The difficulty in detecting the PWS in a patient with darker pigmented skin may have led to the delayed diagnosis of KTS.

Case Presentation

A 23-year-old African American male with a past medical history of peripheral vascular disease presented with a chief complaint of a persistent scaly skin lesion on his right thigh. The patient reported a 2-year history of itching, scaling, and growth of the lesion, which prompted the evaluation. He also reported receiving care for dilated blood vessels in his right leg that were present since birth. He complained of worsening edema when his right leg was in dependent positions for extended periods of time, or when he was non-adherent wearing a compression stocking. He was unaware of a specific cause of the dilated ves-

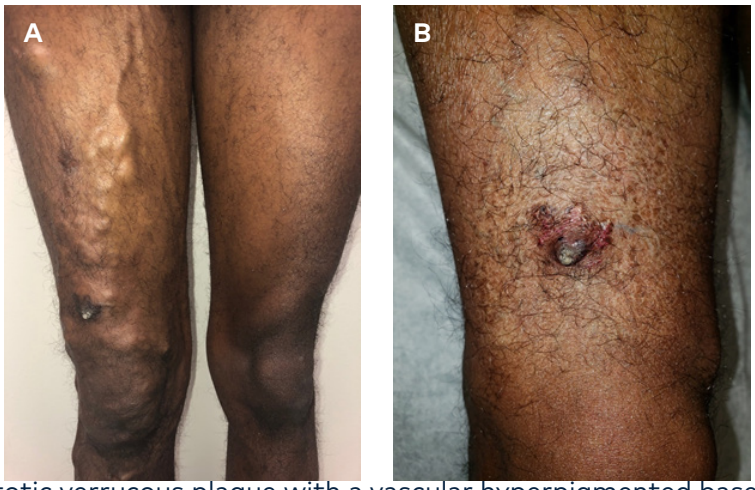

Figure 1. Hyperkeratotic verrucous plaque with a vascular hyperpigmented base is seen on the right anterior distal thigh. Also, visible on the lateral aspect of the right thigh is a subtle erythematous patch of varying degrees of pink, red, and violet colors on highly pigmented skin. **(A)** The patient shown at initial presentation. **(B)** The patient at a subsequent 3-month follow-up visit, after treatment with clobetasol 0.05% topical ointment.

sels in his leg. He had undergone multiple vein strippings by several different surgeons. On physical skin exam, a hyperkeratotic verrucous plaque (1.2 cm) with vascular hyperpigmented base was found on the right anterior distal thigh (**Figure 1**). The entire right leg had extensive tortuous and dilated venous vasculature (**Figures 1-3**). There was hypertrophy of the right limb that was prominent when comparing alignment of the knees (**Figure 2**). The entire right leg had increased length and girth in comparison to the left leg. Ill-defined, subtle red-violaceous, hyperpigmented patches and plaques were located on the right proximal lateral thigh extending to the distal lateral lower leg (**Figure 3**). A subtle thrill was palpated on the superior portion of the right thigh (femoral artery). The patient denied any previous thrombosis in the affected extremity.

We diagnosed the patient with KTS and suspected the new lesion to be pseudoverrucous hyperplasia. We informed the patient that he would need regular follow-up with his vascular surgeon, referred him to hematology for anticoagulation consideration, and recommended he continue wearing a compressive garment. We prescribed clobetasol 0.05% topical ointment for the thigh lesion, which the patient applied twice a day until follow-up. At his subsequent 3-month follow-up visit, we performed a biopsy on

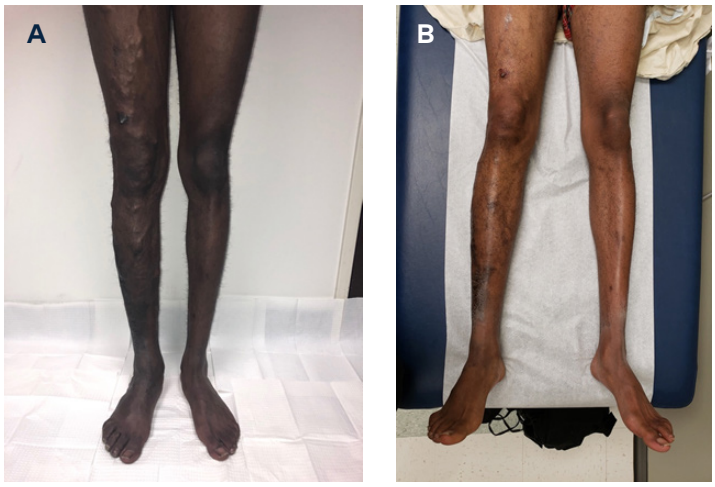

Figure 2. A hypertrophied right leg shows extensive tortuous and dilated vasculature with unaligned knees. **(A)** Patient shown at initial presentation, standing position. **(B)** Patient at a subsequent 3-month follow-up visit, supine position.

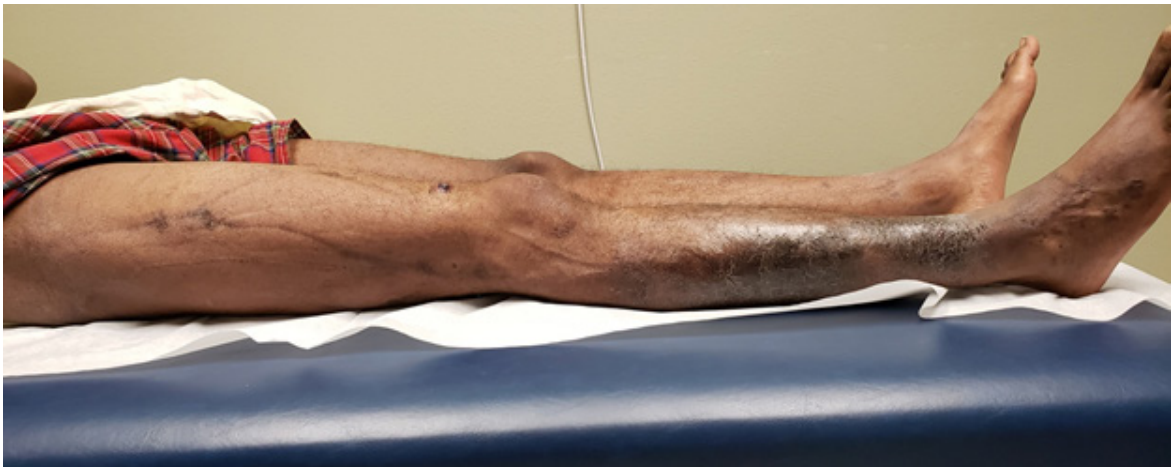

Figure 3. The patient shown at a subsequent 3-month follow-up with the lateral, right, lower extremity in supine position demonstrating varying degrees of pink, red, violet, and hyperpigmented patches and plaques.

the lesion. Histopathology showed irregular acanthosis with closely associated cavernous vascular spaces consistent with angiokeratoma. We obtained medical records, which showed lower extremity venous duplex completed 2 years prior, with findings of unilateral right leg reflux in the anterior accessory saphenous vein, greater saphenous vein below the knee, posterior tibial vein, and peroneal veins.

Discussion

KTS is part of the PIK3CA-related overgrowth spectrum and is a rare congenital disease that can be difficult to diagnose.[3] Two of the 3 items in the triad of port-wine stain, venous varicosities, and hypertrophy of soft tissue or bone are required to make the diagnosis.[1] Diagnosis can be made at birth; however, we suspect our patient had a delayed diagnosis at 23 years of age due to the rarity of this condition and/or his indistinct port-wine stain. The epidermal melanin unit biology helps explain the dilemma of visualizing erythema in darker pigmentation. Varying levels of pigmentation are due to differences in the amount and type of melanin in addition to the size, quantity, and distribution of the melanosomes.[4] Our patient's skin findings were difficult to observe on his darker skin tone, Fitzpatrick skin type VI.

Delayed diagnoses of KTS have been reported in 3 persons with darkly pigmented skin.[5-7] A 39-year-old African female, diagnosed with KTS at the age of 29, presented for pregnancy management with KTS. Her report did not comment on skin color findings in the presentation, while clinical photos were notable for a hyperpigmented patch.[6] In another case, an African American female was diagnosed at the age of 17 with descriptive findings of darkly pigmented macules and patches.[5] In a third case, an Indian patient presented with a port-wine stain described as a hyperpigmented patch and was diagnosed at 30 years old.[7] Classically, port-wine stain has been described as a pink to red or purple patch, which can become more nodular over time.[1] The cases highlighted above demonstrate different presentations of port-wine stains in darker pigmented skin.

KTS management is often complex requiring a multidisciplinary approach. Management can include compression stockings, anticoagulation, pulse dye laser treatment, orthopedic procedures, vascular surgery, sclerotherapy, or catheter embolization.[2] Complications of KTS have been fatal as illustrated by the case of a 20-year-old African American male who died from a massive pulmonary embolus.[8] In another case, an African patient with KTS who was pregnant was well-managed with a multidisciplinary approach, which led to a positive outcome.[6]

Conclusion

Earlier diagnosis, increased knowledge, and greater awareness of the various presentations in skin of darker pigmentation is vital for improved diagnosis and management of KTS.

Informed Consent

Written informed consent was obtained from the patient's guardian for their anonymized information to be published in this article.

Conflicts of Interest

The authors declare they have no conflicts of interest.

Drs Nguyen and Weis are employees of Medical City Fort Worth, a hospital affiliated with the journal's publisher.

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