

Klinefelter's Syndrome with a Cutaneous Manifestation of Lower Limb Ulceration

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Abstract

Klinefelter's syndrome (KS) is considered the most common type of male hypogonadism. The majority (80-90%) of patients are seen to have 47 XXY karyotype. Leg ulceration has been described as a complication of Klinefelter's syndrome. A young 21 year old male presented with a non-healing ulcer of the lower extremity of three years duration. Doppler studies and autoimmune workup was negative. However, clinical and further laboratory findings were consistent with Klinefelter's Syndrome. This case report highlights the importance of screening for chromosomal abnormalities besides evaluating for peripheral vascular disease, venous stasis and diabetes mellitus especially in a young male patient with chronic leg ulceration.

Keywords: Klinefelter's syndrome; Chronic leg ulceration

Key Messages

Klinefelter's syndrome the most common type of male hypogonadism. Leg ulceration has been described as a complication of Klinefelter's syndrome. In a young patient with chronic leg ulceration it is important to screen for chromosomal abnormalities besides evaluating for peripheral vascular disease, venous stasis and diabetes mellitus.

Introduction

A young male with a chronic non healing ulcer was evaluated for the presence of peripheral vascular disease, venous stasis, diabetes mellitus and autoimmune diseases as possible causes for the limb ulcer. The normal neurovascular examination supported by normal arterial and venous Doppler findings, normal blood sugar and glycosylated haemoglobin values ruled out the possibility of peripheral vascular disease, venous stasis and diabetes mellitus. The clinical profile including lack of secondary sexual characters, poorly developed testis, elevated FSH levels, presence of Barr bodies on buccal smear and karyotyping confirmed hypergonadotrophic hypogonadism which was consistent with features of Klinefelter's syndrome.

Case Report

A 21 year old male presented with non-healing ulcer over the lower one-third of the left leg for duration of three years which was associated with pain and persisted irrespective of whether he was ambulant or at rest. There was no history suggestive of trauma, intermittent claudication pain or neuropathic pain of the legs. He did not report any joint pains, fever or photosensitivity. Treatment with local wound care had been ineffective.

He is a non-smoker, gave history of mild learning difficulty during childhood and adolescence and did not report any increase in testicular size during puberty.

The patient was examined and found to have a tall stature with a height of 177 cms, weighed 82 kgs and a BMI of 28.4. He possessed an arm span of 182 cms which was greater than his height. His cardiovascular system, respiratory system and abdomen were found to be within normal limits. On closer examination he was found to have poorly developed secondary sexual characteristics namely scanty pubic, body and axillary hair, absence of beard and moustache, bilaterally small testis and gynaecomastia was noted (Figure 1).



Figure 1: Photograph shows tall stature with poorly developed secondary sexual characteristics.

Cutaneous examination revealed an ulcer was seen measuring 4 cms × 3 cms over the medial aspect of the lower one third of left leg with the floor covered by scab and surrounded by hyperpigmented skin. The limb revealed no neurovascular deficits or venous varicosities. Small, tender left inguinal lymph nodes were palpable (Figure 2).



Figure 2: Lower limb ulceration shows the floor covered by scab and surrounded by hyperpigmented skin.

The clinical findings were followed by investigations as to determine the etiology of the limb ulceration, the tests revealed a blood sugar value of 97, HbA1C of 6.1, he had a hemoglobin of 11.1, total count of 7800, ESR of 48. Arterial and venous Doppler studies revealed no abnormalities. His limb and chest X ray were normal. Biopsy from the ulcer did not show features of vasculitis.

In view of poorly developed secondary sexual characters and sparse body hair he was further evaluated by the endocrinologist and found to have elevated FSH of 29.08 (N: 1.4-18.1 IU/ml) and TSH was normal at 1.13. Buccal smear revealed the presence of a Barr body and karyotyping showing 47 XXY enabled us to arrive at a diagnosis of hypergonadotrophic hypogonadism which is consistent with Klinefelter's Syndrome.

Discussion

Venous thromboses in young patients resulting in chronic leg ulcers can be caused by underlying hereditary haemostasis disorders like deficiencies of anti-thrombin III, protein C, and protein S, and activated protein C resistance, increased plasminogen activator inhibitor levels, as well as deficiencies of tissue plasminogen activator or other congenital syndromes [1]. Klinefelter's syndrome and hyperhomocysteinaemia are rare disorders associated with an elevated risk of thrombosis in young individuals.

Klinefelter's syndrome (KS) is considered the most common type of male hypogonadism. The majority (80-90%) of patients are seen to have 47, XXY karyotype while mosaicism is seen in about 10-20% of patients [2].

Harry F. Klinefelter first described the condition in 1942 as the most common congenital abnormality affecting 1 in 500 live births [3]. It is a condition with more than one X chromosome due to non dysjunction or mosaicism showing hypergonadotrophic hypogonadism presenting phenotypically in males with obesity, tall stature, scant facial, axillary and pubic hair, small firm testis and infertility [4].

Leg ulceration has been described as a complication of Klinefelter's syndrome [5]. The possible pathogenesis could be obesity which increases the expression of Plasminogen activator inhibitor 1 which inhibits tissue plasminogen activator and promotes thrombosis by reducing fibrinolysis. In addition low testosterone levels have been associated with higher levels of PAI-1 activity which can cause skin ulceration [6]. Androgen replacement or testosterone therapy has been observed to show to help wound healing in venous ulcers [2]. The PAI-1 levels were not tested in this patient due to resource constraints. This case report thus highlights the importance of screening for chromosomal abnormalities like Klinefelter's syndrome in young men with chronic limb ulceration.

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