Familial myomatosis cutis et uteri, segmental type 2

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ABSTRACT

Reed's syndrome or familial myomatosis cutis et uteri, an autosomal dominant inherited condition with incomplete penetrance, is characterized by multiple cutaneous and uterine leiomyomas.[1] Uterine leiomyomas usually commence earlier compared to that in the general population and cutaneous leiomyomas may precede, follow or occur concurrently. Few patients may have associated renal cell carcinoma. Herein we report a case of a 50-year-old female with multiple, painful cutaneous leiomyomas and who had undergone hysterectomy owing to large uterine fibroids. Her 18-year-old daughter also has uterine fibroids.

Key words: Cutaneous leiomyomas, Reed's syndrome, segmental type 2, uterine leiomyomas

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INTRODUCTION

Leiomyomas are benign tumors of skin presenting as solitary and/or multiple papules and nodules. Reed's syndrome refers to the onset of uterine leiomyomas with cutaneous leiomyomas, the latter occurring segmentally or affecting a particular dermatome, that are classified into type 1 and 2. Type 1 is caused by a novel postzygotic segmental mutation; type 2 reflects an additional postzygotic loss of heterozygosity of the gene locus responsible for cutaneous leiomyomatosis in an initially heterozygous embryo. Loss of heterozygosity is a genetic process when a heterozygous cell becomes homozygous or hemizygous by loosing the corresponding wild-type allele. This phenomenon can be regarded as a precondition for tumor growth in type 2 cases, the segmental manifestation is more distinctive with additional disseminated disease because of a germline mutation with heterozygosity of all somatic cells outside the strongly affected area.[2] A subset of individuals with Reed's syndrome is predisposed to develop papillary renal cell carcinoma.[2] Herein, we report such rare occurrence of familial myomatosis cutis et uteri with type 2 segmental variety.

CASE REPORT

A 50-year-old female presented to us with history of developing multiple brown painful lesions which appeared initially over her left leg. They extended to appear insidiously over trunk, chest, and upper limbs about 25 years back which extended to appear insidiously despite excision of the left leg lesion. Pressure and exposure to cold aggravated the pain. She also underwent hysterectomy, owing to menorrhagia and multiple uterine fibromas, 25 years ago. Dermatological examination revealed multiple tender, hyperpigmented papulonodules over the left lower limb, trunk, right side of the chest, and bilateral upper limbs [Figures 1a,b and 2a,b]. A clinical suspicion of leiomyomas was confirmed by histopathological findings of a circumscribed tumor in the dermis composed of bundles of smooth muscles cells arranged in an interlacing and whorled pattern, having abundant eosinophilic cytoplasm and

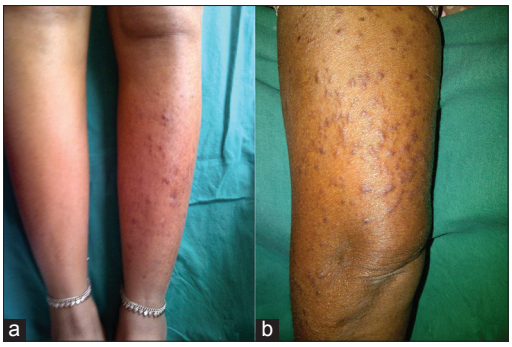

Figure 1: (a) Unilateral distribution of leiomyomas on the left leg, (b) Multiple papulonodules on the extensor aspect of the left arm

elongated nuclei with blunt ends. Deep red color with Masson's Trichome confirmed smooth muscle fibers [Figure 3a,b]. Mild lymphocytic infiltrate was present in the interstitial fibrous tissue. Gynecological consultation for her daughter's complaints of menorrhagia revealed uterine fibroids. A diagnosis of familial myomatosis cutis et uteri, segmental type 2 was made. She experienced pain relief with nifedipine and gabapentin.

DISCUSSION

Leiomyoma, a rare benign tumor of smooth muscle derived from arrector pili muscle, media of blood vessels, smooth muscle of scrotum, labia majora, and nipples, can be of pilar, genital (dartoic), and angioleiomyomic type. Pilar leiomyoma originating from the arrector pili is the most common type of cutaneous leiomyoma and usually occurs in early adult life.[3] Patients with multiple tumors have a familial background. Both the sexes are affected equally. It classically presents as a collection of pink, red or dusky brown firm nodules of varying size. Extremities are most commonly involved. Multiple lesions may be segmental and unilateral. The gene that predisposes to multiple pilar leiomyomas has been mapped to chromosome 1q 42.3-q 43. Multiple cutaneous leiomyomas, with inherited predisposition, are linked to uterine leiomyoma (Reed's syndrome), and increased incidence of renal cell carcinoma.

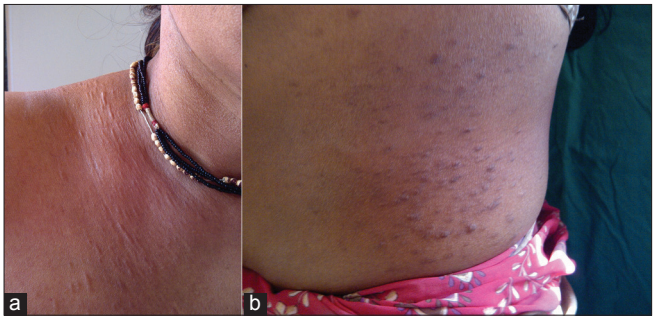

Figure 2: (a) Multiple papulonodules distributed over the right side of chest, (b) multiple leiomyomas distributed over the trunk

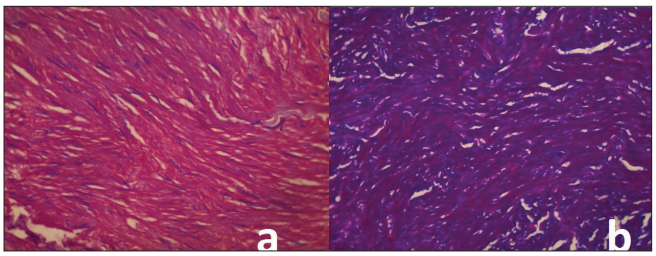

Figure 3: (a) Histopathology shows eosinohillic smooth muscles arranged in interlacing and whorled pattern (H and E, 40×), (b) Histopathology showing red color stained smooth muscle fibers (Masson's Trichome, 40×)

Two types of segmental manifestation of the autosomal dominantly inherited disease are postulated. Type 1 reflects heterozygosity for the underlying mutation, with a clinical picture similar to that in a nonmosaic phenotype. The lesions are restricted to one segment.[4] In type 2, loss of heterozygosity leads to homo- or hemizygosity, with a pronounced segmental manifestation of lesions in the affected segment.[1] This results in pronounced lesions superimposed on the disseminated tumors of the ordinary phenotype.[5] Though the exact molecular etiopathogenesis of multiple cutaneous leiomyomas is not known, recent studies have demonstrated the involvement of a classical tumor suppressor gene encoding fumarate hydratase, in the pathogenesis of multiple leiomyomas.[1] The lesions are often sensitive to touch, cold, emotional stress, or spontaneous pain. The pathogenesis of pain associated with these lesions is not clearly understood. It could be attributed to the local pressure exerted by the tumor on cutaneous nerves. Other hypothesis includes infiltration of mast cells or contraction of the arrector pili muscle. The excitation of these muscles occurs via the sympathetic nervous system resulting in contraction with the influx of calcium ions. Hence, nifedipine, a calcium channel blocker, has a role in relieving pain associated with cutaneous leiomyoma.[6]

There are a few cases reported on familial cutaneous myomatosis et uteri. This case of familial cutaneous myomatosis et uteri is reported for its rare occurrence and is rarer for being segmental type 2 variety.

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