

Tuberous Sclerosis Complex and Diffuse Lipomatosis: Case Report of a Rare Association

Abstract

Lipomatosis is characterized by diffuse infiltration of adipocytes in a tissue. A young male patient presented for evaluation of unilateral limb swelling. On evaluation, he was found to have tuberous sclerosis complex with diffuse lipomatosis of the right leg. To the best of the authors' literature search, only two previous reports of association of tuberous sclerosis complex with diffuse lipomatosis were found. The molecular mechanisms behind the co-occurrence of these two entities have not been studied in detail. Abnormalities in lipolysis and lipogenesis pathway may underlie the co-occurrence of tuberous sclerosis complex and diffuse lipomatosis.

Keywords: Diffuse lipomatosis, macrodystrophica lipomatosis, tuberous sclerosis complex

Introduction

Lipomatosis is a group of conditions characterized by diffuse infiltration with adipose tissue. Histologically, lipomatosis is composed of normal adult-type adipocytes with no evidence of cellular pleomorphism. There have been only rare case reports of diffuse lipomatosis. Here, we report a case of diffuse lipomatosis with tuberous sclerosis complex.

Case Report

A 24-year-old male presented with gradually progressive diffuse swelling of the right lower limb since childhood. It was not associated with any paresthesia or sensory/motor function impairment. Apart from limb swelling, there was history of multiple, asymptomatic facial papules since early childhood. His sister also had similar facial lesions and seizure disorder.

On physical examination, there was diffuse swelling of the right lower limb extending from the groin up to the mid leg [Figure 1]. Multiple dilated tortuous veins were seen on the right thigh and leg. No visible capillary or venous malformations could be appreciated. There were multiple firm, discrete, reddish-brown, telangiectatic papules on the face involving the nasolabial furrows and cheeks [Figure 2a]. Multiple ash leaf-shaped hypopigmented patches of variable sizes were seen on trunk [Figure 2b]. Soft,

skin-colored papules were coalescing to form plaque on the left lateral trunk [Figure 2b]. On oral mucosal examination, dental pits and gingival fibromas were also seen [Figure 2a].

Fine needle aspiration smears from multiple passes from the right thigh swelling showed lobules of mature adipose tissue. On magnetic resonance imaging (MRI) of the right lower limb, there was altered signal intensity (T1-weighted hyper and T2-weighted hyperintense) involving the musculature of all compartments of the right thigh and leg suggestive of fatty infiltration and multiple prominent, tortuous vessels suggestive of venous channels [Figure 3]. There was associated cortical thickening of right femur and tibia with anterior bowing deformity of femur. On Doppler scan, multiple incompetent perforators along great saphenous vein territory were noted.

Discussion

Diffuse lipomatosis is a rare tumorous condition characterized by progressive growth and extension of mature adipose tissue to involve the skeletal muscle of the trunk and extremities. Rarely, osseous involvement may also be a feature.^[1] Its etiology is not known although genetic factors have been suggested. It is a benign entity and normally has no clinical significance except for the cosmetic disability. Young children are predominantly affected, however, presentation may become

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apparent in adulthood. Our case had typical clinical features of diffuse lipomatosis, which was further confirmed by cytology and MRI.

The clinical differentials considered in our patient were Klippel–Trenaunay syndrome, Proteus syndrome, Parkes–Weber syndrome, and macrodystrophica lipomatosa. However, there was no capillary, lymphatic, or arteriovenous malformation to suggest Klippel–Trenaunay syndrome or Parkes–Weber syndrome and epidermal naevi or cerebriform plantar naevi to suggest Proteus syndrome. Macrodystrophica lipomatosis is a close differential of diffuse lipomatosis with a few overlapping clinical and radiological features. However, macrodystrophica lipomatosis typically shows hypertrophy of nerves with

proliferation of fat on MRI. Other differences between these two conditions are listed in Table 1.

Multiple angiofibromas, shagreen patch, and more than three ash leaf macules fulfill the diagnosis of definite tuberous sclerosis complex in our case. To the best of our knowledge, there are only two previous reports of association of tuberous sclerosis complex with diffuse lipomatosis.^[2,3] The case reported by Klein *et al.*^[2] had lower limb involvement, whereas Alcazar *et al.*^[3] reported dorsal transthoracic involvement.

Constitutive activation of mTORC1 (Mammalian Target of Rapamycin Complex 1) is a major pathological consequence of mutations in *TSC1* or *TSC2* seen in tuberous sclerosis complex. Inhibition of mTOR pathway using rapamycin has been shown to be effective in treating various cutaneous manifestations of tuberous sclerosis complex.^[4,5] It has been shown that mTORC1 suppresses lipolysis, stimulates lipogenesis, and promotes fat storage.^[6] In addition, activating mutations in *PIK3CA*, part of mTOR pathway acting upstream of TSC complex, has been found in facial infiltrating lipomatosis.^[7]

Conclusion

In conclusion, the association of diffuse lipomatosis with tuberous sclerosis complex needs further assessment because it is difficult to explain the asymmetrical involvement of lipomatosis when all cells carry *TSC* mutation. Additional genetic mutations or complex pathways may be involved and requires further characterization.



Figure 1: Diffuse swelling of right lower limb extending from groin up to the mid leg. Multiple varicosities are visible on the surface



Figure 2: (a) Multiple discrete, reddish-brown, telangiectatic papules involving the nasolabial furrows and cheeks. Dental pits and gingival fibromas are appreciable. (b) Skin-colored papules coalescing to form plaque and single hypopigmented patch visible on the left lateral trunk

Table 1: Differences between diffuse lipomatosis and macrodystrophica lipomatosa

	Diffuse lipomatosis	Macrodystrophica lipomatosa
Sites involved	Proximal extremities and trunk	Distal extremities usually 2 nd or 3 rd digit of hand or foot
Age of onset	First decade of life, usually before 2 years of age	Usually noticed at birth or neonatal period
Overgrowth pattern	Overgrowth occurs diffusely	Overgrowth appears to develop in a specific sclerotome region (along the median nerve and plantar nerve distribution)
Growth pattern	Progressive, no plateau phase at puberty	Progressive growth till plateau phase at puberty
Nerve involvement	No	Yes, nerve hypertrophy, nerve function impairment
Magnetic resonance imaging	Imaging show diffuse infiltration of muscle mass by adipose tissue and osseous hypertrophy	Imaging shows diffuse infiltration of muscle mass by adipose tissue, nerve hypertrophy, and prominent bone changes

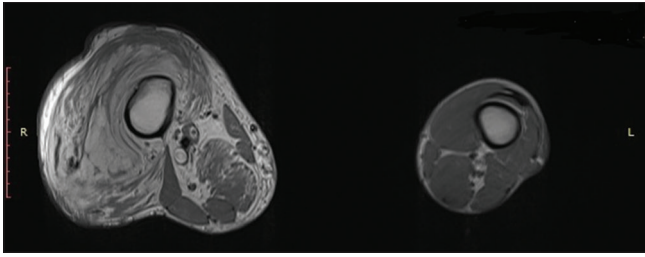


Figure 3: MRI of the right lower limb showing altered signal intensity involving the musculature of all compartments of the right thigh and leg suggestive of fatty infiltration

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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