

Multiple unilateral angiofibromas with a hypopigmented patch as a possible presentation of tuberous sclerosis complex (TSC)

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ABSTRACT

Tuberous sclerosis complex (TSC), known as Bourneville's disease or epiloia, is an autosomal dominant inherited disorder that may affect numerous organ systems. TSC has many forms of clinical presentation. The cutaneous features of TSC include facial angiofibromas, shagreen patches, ash leaf hypopigmented macules, periungual fibromas, forehead fibrous plaques, confetti hypopigmentation, and poliosis. Rarely, the angiofibromas in TSC have a segmental distribution. It has been suggested that the segmental expression of tuberous sclerosis may result from a postzygotic mutation. The aim of this concise communication was to describe a patient with unilateral angiofibromas associated with a hypopigmented patch. No other features of TSC were present. We think this could have been a rare presentation of TSC.

Key words: Angiofibroma, Hypopigmented patch, Loss of heterozygosity (LOH), Tuberous sclerosis complex (TSC)

INTRODUCTION

Tuberous sclerosis complex (TSC) is an autosomal dominant (AD), multisystem disorder characterized by hamartomas affecting numerous organ systems, including the skin, brain, kidneys, lung, and heart [1-12].

Skin lesions include facial angiofibromas, melanotic macules, and patches of connective tissue nevi [3-5].

Some of the cutaneous features, such as hypomelanotic macules, may appear at birth or early childhood and may regress, while others, such as angiofibromas, may appear later in life yet persist.

There is a wide clinical spectrum, and some patients may have minimal symptoms.

Multiple angiofibromas are present in most of patients with TSC, and they are usually of facial location [3-5].

In this short report, we describe a patient with multiple non-facial angiofibromas associated with a hypomelanotic macule, who we think, may have a new presentation of TSC.

CASE REPORT

A 32-year-old Pakistani male presented with multiple, asymptomatic skin lesions on the back of the neck persisting for many years. These have increased in number and size.

There was no history of chronic skin problems in him or in his family members, and his parents were

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not consanguineous. There was also no history of headaches, seizures, or other neurological symptoms.

On examination, there were non-scaly, skin-colored papules and nodules in a linear fashion on the right side of the posterior aspect of the neck. An associated non-scaly, hypopigmented patch, of about 4 cm in size, was present in the vicinity of the lesion (Fig. 1).

A Wood's lamp (UV light) examination did not reveal any additional hypopigmented spots.

Scalp examination did not reveal any area of gray hair (poliosis).

There were no other significant cutaneous findings, and his systemic examination was normal.

A punch skin biopsy of one of the nodules revealed dilated blood vessels in the upper dermis and prominent collagen bundles (Fig. 2) consistent with the diagnosis of angiofibroma.

Additional studies, including CT of the brain, chest X-ray, abdominal sonography, echocardiography, and fundus examination, were normal.

The nature of the disorder and the treatment options for the angiofibroma (including excision, cryotherapy, radiofrequency ablation, chemical peeling, topical sirolimus, dermabrasion, and lasers) and the potential complications of each therapeutic option were discussed with the patient.

The patient is currently under follow-up.

DISCUSSION

Tuberous sclerosis complex (TSC) is an autosomal-dominant neuro-cutaneous disorder. It is caused by a mutation of either of two genes, *TSC1* and *TSC2*, which code for the proteins hamartin and tuberin, respectively [1-12].

TSC affects multiple organs, with hamartomas developing in the brain, skin, kidneys, heart, and eyes. The cutaneous features include hypomelanotic macules, subungual fibromas, facial angiofibromas, fibrous plaques of the forehead, and shagreen patches. Not all patients with TSC have all systemic or cutaneous features [3-5].



Figure 1: Unilateral angiofibromas with an associated hypopigmented patch.

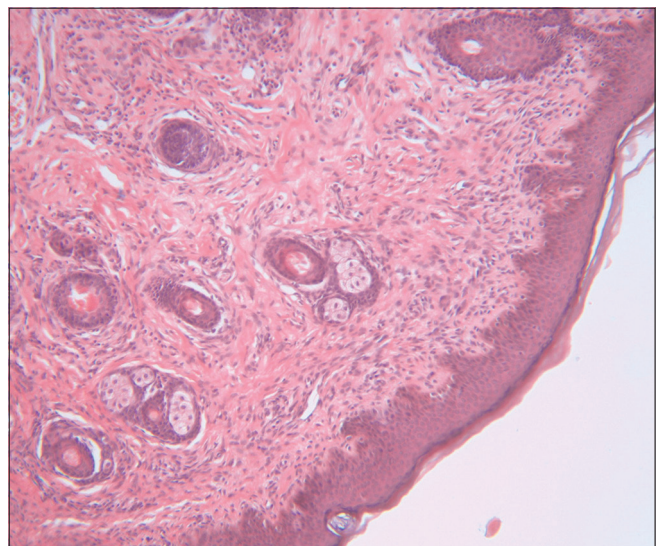


Figure 2: Concentric arrangement of collagen bundles around multiple hair follicles and dilated blood vessels in the upper dermis (H&E; 40x).

Angiofibroma is a benign cutaneous neoplasm. It may occur on the face (fibrous papules or adenoma sebaceum), on the penis (pearly penile papules), underneath the nail (periungual angiofibroma or Koenen tumors), and in the mouth (oral fibroma).

Multiple facial angiofibromas are classically found in TSC yet may also be found in other syndromes such as multiple endocrine neoplasia type 1 (MEN-1), Birt–Hogg–Dube syndrome, and Frank–Ter Haar syndrome [10].

Multiple angiofibromas have also been reported in a congenital and non-syndromic form [11].

The clinical differentials of facial angiofibromas include trichoepitheliomas, fibrofolliculoma, syringoma, and sebaceous hyperplasia.

Angiofibromas occur in the majority of patients with TSC.

Angiofibromas in TSC are typically present after five years of age and are of bilateral involvement. They may attain a very large giant size.

Rarely, these lesions occur unilaterally, as seen in our case. Segmental cutaneous presentation is known to occur in syndromes with generalized skin involvement such as neurofibromatosis. This is explained genetically by loss of heterozygosity (LOH) [7].

Some authors suggested that patients with isolated unilateral facial angiofibromas need to be followed up to look for the development of other extracutaneous manifestations of TSC.

Supekar et al. reported a patient with unilateral angiofibromas and reviewed similar cases in the literature [9].

All reported cases are male, except one case, and all of them have a facial involvement.

The location in the neck and the presence of an associated hypopigmented spot in our case has not been reported before.

We think that this case may represent a unique cutaneous presentation of a mosaic form of TSC.

TSC patients with mosaicism and asymmetric facial angiofibromas were shown to exhibit fewer findings, later onset, and lower Variant allele fraction (VAF) in the blood [7].

We think sharing similar cases of unilateral angiofibromas or unusual cutaneous features in TSC will help in recognizing these presentations and make diagnosis easier.

It will help also in enriching our understanding of angiofibromas and TSC, in particular, if conjoined by genetic studies.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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