

# Tuberous sclerosis associated with a renal angiomyolipoma

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Sir,

A 27 year-old male hospitalized in the department of urology awaiting left nephrectomy, after presenting with a four month history of feeling a mobile mass in his left abdomen. CT angiography of the bilateral kidneys showed the following: the right kidney is of normal dimensions with multiple lipomas no greater than 7mm, while the left kidney is enlarged, with multiple heterogeneous lipomas in the cortex and medulla, most likely representing an angiomyolipoma (Fig. 1).

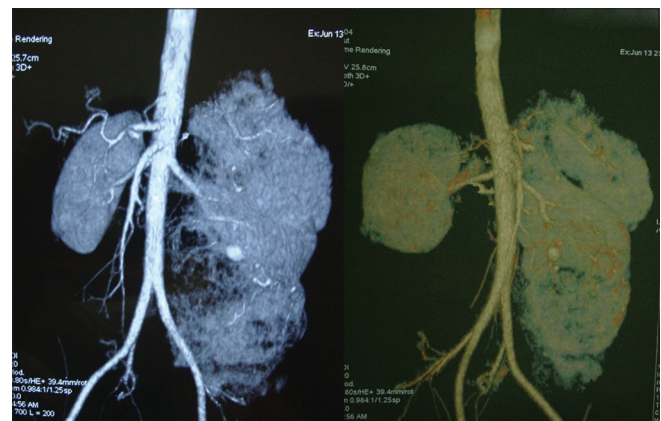
A through dermatologic examination demonstrated pink neoplasms in the proximal nail fold of the first, second, third and fourth toes of the left foot (Figs. 2 and 3), dermatoscopic view of the pink neoplasms of the proximal nail folds (Figs. 4ab and 5ab) and multiple, skin-colored neoplasms of the central face (Fig. 6). The remainder of the examination was within normal limits.

The patient reported that he has had the lesions on the face and left foot since he was very young. No other family member affected.

Past medical history and family history: negative and not consanguinity

With this clinical data, it was determined that the renal mass in this patient was associated with a diagnosis of tuberous sclerosis

The renal mass was surgically removed. Macroscopic and histological images of the kidney are observed on its outer surface, note the increase in size and abnormal



**Figure 1:** CT angiography of the bilateral kidneys showed the following: the right kidney is of normal dimensions with multiple lipomas no greater than 7 mm, while the left kidney is enlarged, with multiple heterogeneous lipomas in the cortex and medulla, most likely representing an angiomyolipoma



**Figure 2:** Pink neoplasms in the proximal nail fold of the first, second, third and fourth toes of the left foot

appearance (Fig. 7a) Cut surface of the macroscopic and histological images of the kidney are observed on its

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outer surface and at both poles, with some observable normal renal parenchyma (Fig. 7b), the microscopic image of the tumor shows that it is composed of neoplastic adipose tissue, smooth muscle and blood

vessels, correlating well with the gross image (H & E 10X) (Fig. 8) Increased magnification of the neoplasm shows a group of adipocytes surrounded by prominent blood vessels and bundles of smooth muscle (H & E 40X) (Fig. 9).

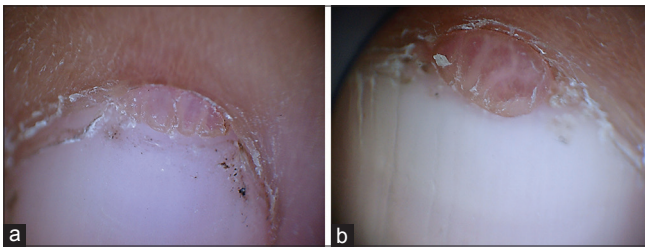
Prior to the study, patient gave written consent to the examination and biopsy after having been informed about the procedure.

What is interesting about this case is the association of tuberous sclerosis with a renal angiomyolipoma, which is not a very common clinical presentation.

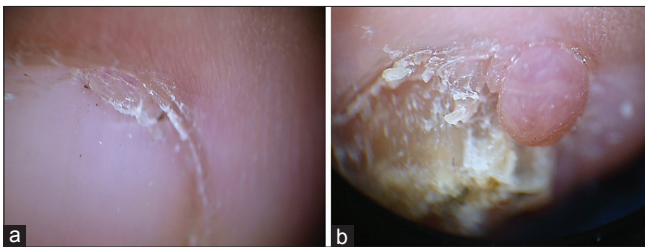
Tuberous sclerosis is an autosomal dominant genodermatosis, historically characterized by epilepsy,



**Figure 3:** close up of the Koenen's tumors of the proximal nail fold



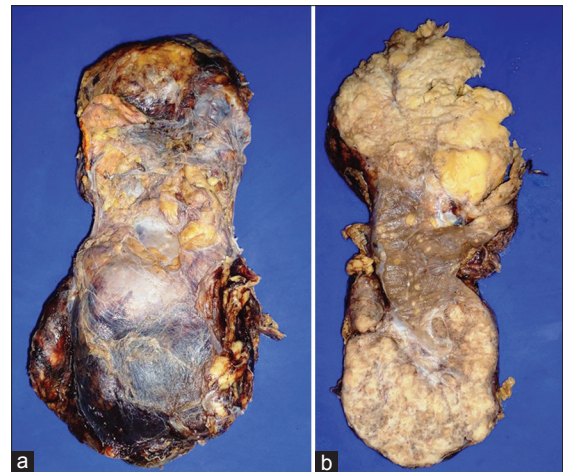
**Figure 4:** (a and b) Dermoscopic view of the neoplasms of the proximal nail fold



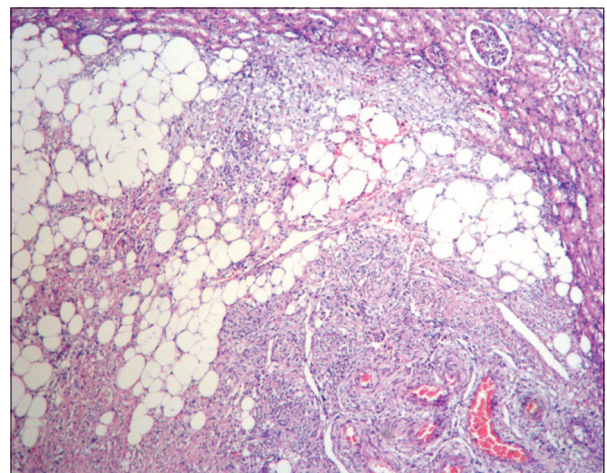
**Figure 5:** (a and b) Dermoscopic view of the neoplasms of the proximal nail fold



**Figure 6:** Angiofibromas of the face



**Figure 7:** (a) Macroscopic and histological images of the kidney are observed on its outer surface and increase in size and abnormal appearance (b) Macroscopic and histological images of the kidney are observed on its outer surface and at both poles, with some observable normal renal parenchyma

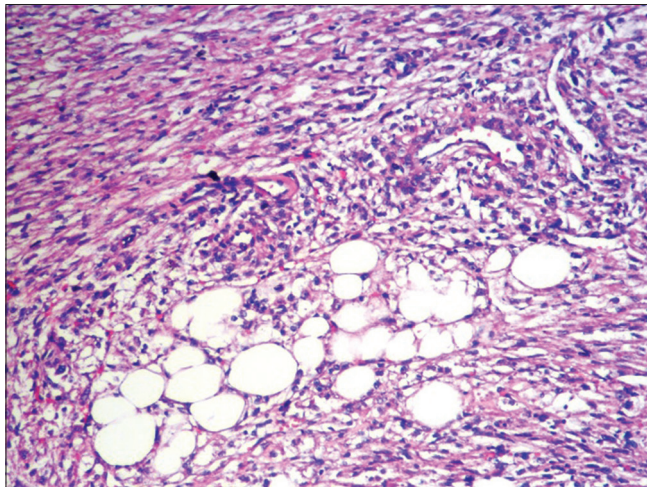


**Figure 8:** The microscopic image of the tumor shows that it is composed of neoplastic adipose tissue, smooth muscle and blood vessels, correlating well with the gross image (H & E 10X)



**Table 1:** Different manifestations of the tuberous sclerosis

Skin/nails	Renal	Neurological	Cardiovascular	Ocular	Oral cavity	Pulmonary
Facial angiofibroma	Angiomyolipoma	Cortical tuber	Rhabdomyoma	Retinal hamartoma	Gingival hyperplasia	Pulmonary lymphangioleiomyomatosis
Shagreen patch	Cystic disease	Giant cell astrocytoma		Optic nerve hamartoma	Oral papillomatosis	
Hypomelanotic macule	Fibroadenoma	Subependymal nodule			Enamel pitting	
Periungual fibroma	Mixed tumor					
	Renal cell carcinoma					

**Figure 9:** Increased magnification of the neoplasm shows a group of adipocytes surrounded by prominent blood vessels and bundles of smooth muscle, (H & E 40X)

low intelligence, and hamartomatous lesions in many organs, including facial angiofibromas. Although reported as roughly 1 in 10,000, the exact prevalence of this disease is unknown, due to the fact that the classic triad mentioned above is only found in a minority of cases, making the diagnosis difficult [1]. Clinically, greater than 90 percent of affected patients have one or more classic skin finding, including facial angiofibromas, hypomelanotic macules, periungual fibromas, and Shagreen patches [2]. The percent of patients with tuberous sclerosis that present with the above-mentioned lesions are 90, 85, 50, and 40, respectively. Facial angiofibromas, or adenoma sebaceus, tend to first appear around four years of age, and are usually found symmetrically on the cheeks, nose, and forehead. They consist of 1-3 mm yellowish-red, discrete, waxy papules. Ash leaf, or hypomelanotic macules, may range in number from 1 to 100, commonly present in the first few decades of life, and tend to fade in late adulthood. “Knobby” patches or plaques of connective tissue, Shagreen Patches usually develop in the first decade of life. They vary in size from 1 to 8 cm in diameter, and are most found on the trunk, particularly the lumbosacral area. Periungual fibromas, also called Koenen tumors when associated with tuberous sclerosis, are small digitate,

protruding neoplasms that tend to manifest during adolescence or adulthood, and despite their name, can be periungual and/or subungual (Table 1) [1,3]. In addition to cutaneous involvement, the kidneys are often affected in Tuberous Sclerosis. In one study, renal lesions were found in 80% of patients, with roughly 80% of those being angiomyolipomas (AML), 20% renal cysts, and 25 case reports of an associated renal cell carcinoma. It is a mutation in a tumor suppressor gene, either TSC1 or TSC2, which causes tuberous sclerosis. In general, both alleles of a tumor suppressor gene must be mutated to lead to disease, and hamartomas in tuberous sclerosis patients typically demonstrate this loss of heterozygosity. Interestingly, angiomyolipomas and renal cysts are more commonly associated with mutations in the TSC2 gene than the TSC1 gene. The diagnosis of tuberous sclerosis is usually suspected clinically, with confirmation by genetic testing. However, evidence of a mutation in TSC1 or TSC2 confirms the diagnosis even in the absence of physical findings. Biopsy is rarely needed, and is usually performed when the clinical picture is not classic for the disease [1,3,4]. When considering alternative diagnoses, the presence of multiple facial papules may indicate other genodermatoses, such as Cowden, Brook-Spiegle, or Birt-Hogg-Dubé syndrome [3]. Schaffer et. al describe a case of a patient with Birt-Hogg-Dubé syndrome, a rare autosomal dominant genodermatosis with an increased risk of renal tumors, whose major presenting sign was multiple facial angiofibromas [5]. Historically, surgery was considered to be the only viable option for treating the cutaneous lesions of tuberous sclerosis. More recently, topical rapamycin has been shown to improve the appearance of subungual fibromas and facial angiofibromas, lessening the need for surgery and subsequent scarring. In addition to topical treatment, systemic everolimus, approved for patients with tuberous sclerosis who have subependymal giant-cell astrocytomas or renal angiomyolipomas, has also proven to have positive effects on skin lesions [1,3,6,7].

## CONSENT

The examination of the patient was conducted according to the Declaration of Helsinki principles. Written informed consent was obtained from the patient for publication of this article.

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