Cutaneous Manifestations of Tuberous Sclerosis

Dear Editor,

Tuberous sclerosis (TS) is an autosomal dominant multisystem disease, which occurs due to genetically determined hyperplasia of ectodermal and mesodermal cells. Clinical manifestations present on the skin and in the nervous system, kidneys, heart, and other organs. Recent studies estimate the incidence of TS at 1/6000 to 1/10,000 live births, and a prevalence in the general population of approximately 1 in 20,000 (1). There are two different genetic loci responsible for TS: 9q34 (TSC1-hamartin) and 16p13.3 (TSC2-tuberin) (2). Cutaneous manifestations occur in about 96% of patients (3). Neurological disorders occur in 50% of patients in the form of seizures and motor and psychomotor symptomatology (4).

A 19-year-old male patient was hospitalized for clinical and diagnostic evaluation in February 2016 year in Clinic for Nephrology, Clinical Center of Montenegro, Podgorica, Montenegro. Polycystic kidney changes were verified by ultrasound when the patient was three years old, with the presence of several calcified nodules in lateral ventricles and supraventricularly in the brain as well as the existence of several hypopigmented maculae on the skin. During the last hospitalization in February 2016, the following tests were performed: cranial magnet resonance imaging (MRI) findings showed the existence of visible changes in the signal in the form of ectopic tuber tissue in the region of the cortex and subcortical white matter of the brain, but without neurological and psychomotor abnormalities; ultrasound of the urinary tract showed that both kidneys were enlarged with multiple cysts, with dominant cysts at the lower pole of the right kidney with a size of 55 mm and at the upper pole of the left kidney, approximately 40 mm. Reduced functional capacity of kidneys was found on dynamic scintigraphy, slightly more in the left kidney (41%) compared with the right (59%). Electroencephalography, X-ray of the lungs and heart, and echocardiography were also performed, but without any pathological findings.

Dermatological examination found numerous fibroma up to 0.5 cm in diameter, the largest located nasolabially, periorally, and on the chin skin (Figure 1) at the age of seven, whereas a fibroma and several white maculae were present from birth on the skin of the forehead. They were now also present on the skin of the trunk and on the upper and lower extremities (Figure 2), accompanied by surrounding

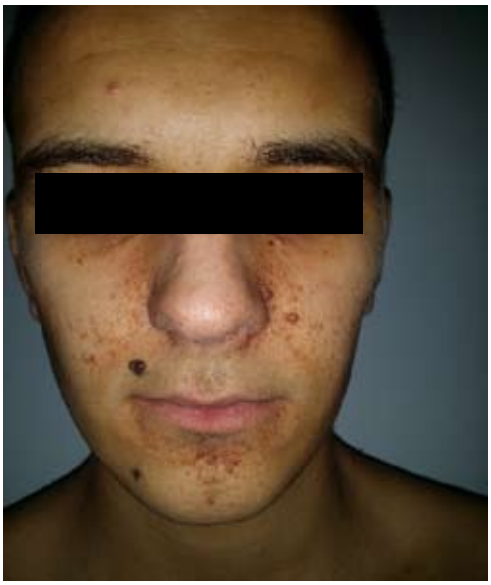

Figure 1. Facial angiofibromas.

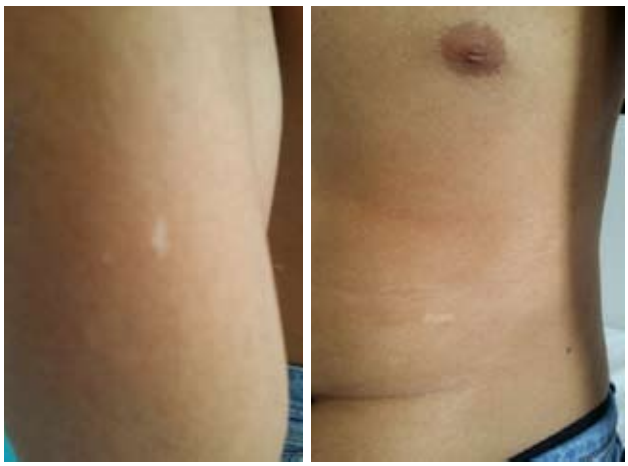

Figure 2. Hypomelanotic macules.

minor changes in the form of confetti-like maculae. A subungual fibroma was present on the third finger of the right hand. Collagen nevus (shagreen patch) (5), i.e. a subepidermal fibrosis as a mildly elevated, palm-sized area is also characteristic of TS, which is described in literature, in most cases in the lumbosacral region. In our case, such a fibrosis about 3 cm in diameter, and with the consistency of an orange peel, was discovered on the right shoulder. Subungual fibromas (Koenen tumors) (6), which can develop in adolescence, were present in our patient on the third finger of the right hand**.**

The diagnosis of TS was established based on genetic testing, physical examination, ultrasound-verified polycystic kidney disease and reduced global renal functions, intracranial MRI, many hypomelanotic changes, and angiofibromas found with dermatological examination (7).

There is no specific therapeutic approach for TS, and the treatment is symptomatic. Angiofibromas of the skin can be removed by dermabrasion or laser. Recent data show a good therapeutic effect of applying 0.1% rapamycin (8), which leads to a reduction of angiofibromas in patients with TS. On dermatological follow up after five weeks of application of tacrolimus, angiofibromas of the face were in regression. Some studies suggest the simultaneous topical applications of both of those drugs (9). In adolescents and adults of reproductive age, genetic counseling is recommended (10).

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