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# Answers to Medical Quiz

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A1. Figure 1: Multiple angiofibromas ("adenoma sebaceum"). A hypopigmented macule is also present.
Figure 2: Periungual/subungual fibromas
Figure 3: Ash leaf (hypopigmented) macule

A2. Tuberous sclerosis

TS is inherited in autosomal dominant fashion via loci on chromosomes 9 (TSC 1) and 16 (TSC 2). Two-thirds of cases are sporadic. The disorder is characterized by the triad of mental deficiency, epilepsy and angiofibromas of the face. The **angiofibromas** consist of numerous small, red papules in symmetrical distribution in the nasolabial folds, on the cheeks and on the chin. Other cutaneous manifestations include asymmetrical large brown **fibromas** on the face and scalp; **subungual and periungual fibromas**; **shagreen patches**, usually found in the lumbosacral region, and consisting of slightly raised and thickened areas of skin. Histologically they are connective tissue naevi; and **hypopigmented ("ash leaf") macules** which are usually the earliest cutaneous sign of tuberous sclerosis.

A3. **Tubers** – foci of cerebral gyral expansion in which there is glial overgrowth causing an unusual firmness ("sclerosis"), giant astrocytes, and architectural disarray.
**Subependymal giant cell astrocytoma (SEGA)** – a glioma classically associated with TS **"Candle gutterings"** – Miniature versions of SEGA in a periventricular location.

## DISCUSSION

Tuberous sclerosis-also called tuberous sclerosis complex (TSC) - is a rare, multi-system genetic disease that gives rise to tumors in the brain and in other organs such as the kidneys, heart, eyes, lungs, and skin[1]. It commonly affects the central nervous system and results in a combination of symptoms including seizures, developmental delay and behavioral problems.

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The disorder affects as many as 25,000 to 40,000 individuals in the United States and about 1 to 2 million individuals worldwide, with an estimated prevalence of one in 6,000 newborns. TSC occurs in all races and ethnic groups, and in both genders.

The name tuberous sclerosis comes from the characteristic ***tuber*** or root-like growths in the brain, which calcify with age and become sclerotic. The disorder-once known as ***epiloia*** or ***Bourneville's disease***- was first identified by a French physician more than 100 years ago.

TSC may be present at birth, but signs of the disorder can be subtle and full symptoms may take some time to develop. As a result, TSC is frequently unrecognized and misdiagnosed for years.

TSC is caused by mutations in two genes-TSC1 and TSC2. Only one of the genes needs to be affected for TSC to be present. The TSC1 gene, discovered in 1997, is on chromosome 9 and produces a protein called ***hamartin***[2]. The TSC2 gene, discovered in 1993, is on chromosome 16 and produces the protein ***tuberin***. Both genes are putative tumour suppressor genes.

Although some individuals may inherit the disorder from a parent with TSC (autosomal dominant transmission), most cases occur as spontaneous mutations. Some individuals acquire TSC through ***gonadal mosaicism***.

**Systemic lesions in TSC:**

a) **Kidney:** cysts, angiomyolipoma, oncocytoma, renal cell carcinoma.
b) **Brain:** cortical tubers, subependymal nodules, subependymal giant cell astrocytoma.
c) **Heart**: rhabdomyoma
d) **Eye**: retinal phakoma
e) **Skin:**

**Hypomelanic macules** ("ash leaf spots"), which are white or lighter patches of skin that may appear anywhere on the body.

***facial angiofibromas*** (also called ***adenoma sebaceum***), which appear on the face (sometimes resembling acne).

Raised, discolored areas on the forehead called ***forehead plaques***.

Areas of thick leathery, pebbly skin called ***shagreen patches***, usually found on the lower back or nape of the neck.

***ungual or subungual or periungual*** fibromas that grow around and under the toenails or fingernails and may need to be surgically removed if they enlarge or cause bleeding.

Other skin features that are not unique to individuals with TSC, include ***molluscum fibrosum*** or skin tags, which typically occur across the back of the neck and shoulders, ***café au lait spots*** or flat brown marks, and ***poliosis***, a tuft or patch of white hair that may appear on the scalp or eyelids.

**f)** Additional tumors and cysts may be found in other areas of the body, including the liver, lung, and pancreas. Bone cysts, rectal polyps, gum fibromas, and dental pits may also occur.

The prognosis for patients with TSC depends on the severity of symptoms, which range from mild skin abnormalities to severe mental retardation, uncontrollable seizures, and kidney failure. Those individuals with mild symptoms generally do well and live long productive lives, while individuals with the more severe form may have serious disabilities.

In rare cases, seizures, infections, or tumors may cause severe renal and cerebral complications that can cause death. However, with appropriate medical care, most individuals with the disorder can look forward to normal life expectancy.

**REFERENCES**


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