GENETICS AND GENODERMATOSES

A CASE OF TUBEROUS SCLEROSIS COMPLEX WITH EXTENSIVE MULTIPLE ORGAN INVOLVEMENT

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Background: Tuberous sclerosis complex (TSC) is a rare multisystemic syndrome with variable presentation. This results from mutations in TSC1 or TSC2 genes that code for hamartin and tuberin. These act as tumor suppressor genes and inhibit various cellular activities via mammalian target of rapamycin complex 1 (mTORC1). Hence, mutations lead to continuous stimulation presenting as hamartomatous proliferations.

Observation: A 33-year-old female had multiple facial lesions that were present since birth. The brown plaque on the right mandible and temple and multiple skin-colored to brown papules on the paranasal area increased in size and number over several years. There were no seizures or developmental delays. No similar lesions were noted among family members. Physical examination revealed angiofibromas, shagreen patches, a fibrous plaque and periungual fibromas, fulfilling a definite diagnosis of TSC. Diagnostic tests confirmed the presence of parenchymal and subependymal calcifications, an echogenic mass with a consideration of cardiac rhabdomyoma, multiple hepatic foci, splenomegaly with splenic foci, bilateral renal masses, and pulmonary lymphangioleiomyomatosis. Biopsy of the plaque on the temple was consistent with a fibrofolliculoma, a type of follicular hamartoma not commonly seen in TSC.

Key Message: Studies have shown that apart from the genetic mutations, cutaneous hamartomas have a special structure that leads to the pathologic changes. These are the fibroblast-like cells commonly seen in those with TSC2-null mutations. These cells give off paracrine signals that lead to epidermal proliferation, angiogenesis and phagocytosis. These fibroblast-like cells also induce normal keratinocytes to form hair follicles and stimulate hamartomatous changes, making hamartomas like fibrofolliculomas possible in TSC patients. Despite its varied clinical presentation, identification of skin lesions may suffice in diagnosing TSC. Establishing the diagnosis as early as possible enables timely intervention and prevention of complications.