

A Rare Soft-Tissue Tumor in a 15-Year-Old Boy With Tuberous Sclerosis Complex: Answer

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ANSWER

This is a folliculocystic and collagen hamartoma (FCCH), a rare benign collagen hamartoma strongly associated with tuberous sclerosis complex (TSC). Hamartomas in TSC with mutations in the *TSC1* (encodes for hamartin) and *TSC2* (tuberin) genes have high mTORC1 activity as a result of lack of inhibition by this TSC tumor suppressor complex. High mTORC1 activity stimulates proliferation of fibroblasts, keratinocytes, hair follicles, and sebaceous glands.¹ However, for the development of hamartomas, a second somatic event is required, in addition to the germline *TSC1/TSC2* mutation.²

DISCUSSION

TSC is an autosomal dominant disorder caused by mutations in the *TSC1* (30%) or *TSC2* (65%) gene.² In 5%–10% of TSC patients, no mutation can be identified, and some patients have low-level mosaicism.² For detailed information about the diagnostic and genetic criteria, we refer to the International Tuberous Sclerosis Complex Consensus conference, held in 2012.

FCCH was suggested as a new type of complex hamartoma related with TSC by Torrelo et al in 2012.³ They described 6 male patients with congenital/early childhood skin lesions consisting of large plaques with an irregular surface that became scattered with numerous comedo-like openings over time. Five of the 6 patients had a definite clinical diagnosis of TSC. After this initial description, only 4 additional case reports have been published, including 3 female patients^{1,4,5} and 1 patient without TSC.⁶

FCCH histopathologically resembles angiofibroma, shagreen patches, and TSC-unrelated collagen nevi. These lesions have in common that they show coarse, rather than delicate, collagen fibers, which are often haphazardly arranged through the dermis. In contrast to the previously mentioned lesion, FCCH shows collagen fibers that are

arranged in a concentric array around hair follicles. This perifollicular fibrosis is often associated with some distortion of the pilosebaceous units. Furthermore, infundibular cyst formation is a characteristic feature, which can only be observed in FCCH.⁶ Clinically, the case might also resemble plexiform neurofibroma (in NF1) or nevus sebaceous. In nevus sebaceous, the appearance of sebaceous gland hyperplasia with or without immature hair follicles in the dermis is the key feature. This is in contrast to the mature hair follicles surrounded by fibrosis and inflammation as can be seen in FCCH. Finally, fibrous hamartoma of infancy is a rare soft-tissue lesion that may enter the differential diagnosis. This lesion harbors a characteristic triphasic morphology of fat, mesenchymal tissue, and fibroblastic fascicles.⁴

The final diagnosis of FCCH requires familiarity with the clinical features and the 3 histopathological features of this lesion. Likely, FCCH is underrecognized because not many clinicians and pathologists are familiar with this relatively new entity. When FCCH is the presenting feature of TSC, early recognition is important for further clinical workup leading to a final diagnosis. In patients already diagnosed with TSC, early recognition of this benign entity within the spectrum of TSC could prevent distress and anxiety during the diagnostic process. Altogether, we think it is important to recognize this rare, relatively new entity and to further study its relation to TSC.

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