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### Title

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### Permalink

<https://escholarship.org/uc/item/62w694s1>

### Journal

Dermatology Online Journal, 23(8)

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### Publication Date

2017

### DOI

10.5070/D3238036007

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Peer reviewed

# Folliculin mutation-negative trichodiscomas in a patient with multiple endocrine neoplasia type I syndrome

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## Abstract

Multiple endocrine neoplasia (MEN) type I, an autosomal dominant disorder caused by mutations in the *MEN1* gene, is classically associated with parathyroid, pituitary, and pancreatic tumors. Patients with MEN type I also frequently exhibit multiple cutaneous lesions, specifically facial angiofibromas and collagenomas. Herein we describe a patient with genetically confirmed MEN type I syndrome who presented with trichodiscomas, skin tumors characteristic of Birt-Hogg-Dubé (BHD) syndrome. Although BHD is associated with mutations in the folliculin (*FLCN*) gene, this patient with trichodiscomas was negative for the *FLCN* mutation.

*Keywords: multiple endocrine neoplasia, trichodiscoma*

## Introduction

Multiple endocrine neoplasia (MEN) type I, an autosomal dominant disorder caused by mutations in the *MEN1* gene, is classically associated with parathyroid, pituitary, and pancreatic tumors. Patients with MEN type I also frequently exhibit multiple cutaneous lesions, specifically facial angiofibromas and collagenomas [1]. Herein we describe a patient with genetically confirmed MEN type I syndrome who presented with trichodiscomas, skin tumors characteristic of Birt-Hogg-Dubé (BHD) syndrome. Although BHD is associated with mutations in the *FLCN* gene, this patient with trichodiscomas was negative for the *FLCN* mutation.

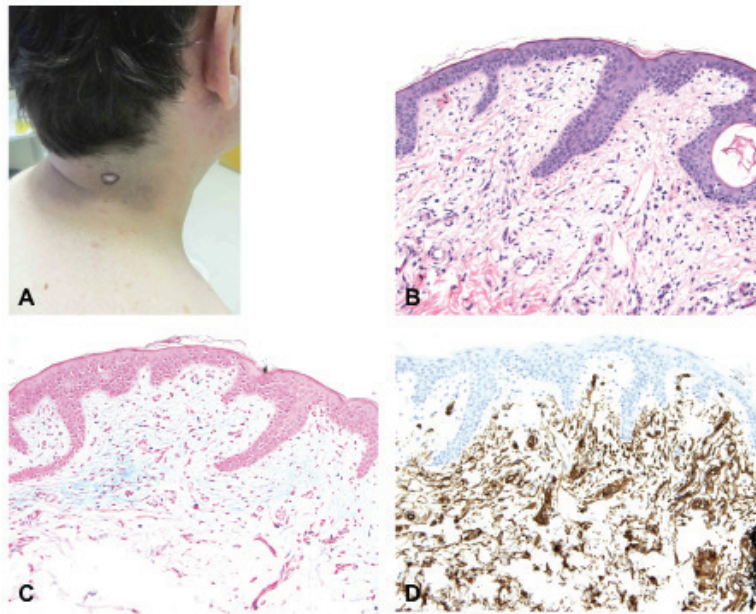
## Case Synopsis

A 47-year-old man with MEN type I and a history of parathyroid adenomas, hyperthyroidism, a pheochromocytoma, and a gastrinoma presented to the dermatology clinic for screening for skin findings of MEN type I. Family history was positive for a history of MEN type I in the patient's father. Genetic testing confirmed the presence of a *MEN1* gene mutation. On physical examination, the patient appeared well and comfortable. Scattered angiofibromas were noted on his face and no collagenomas or lipomas were seen. Many atypical nevi were noted and the patient has since returned regularly to dermatology clinic for follow-up of these nevi. At a recent visit, a number of white papules varying in size from 1 to 4 mm were noted on his posterior neck (**Figure 1A**).

A shave biopsy of one of the white papules revealed a CD34-positive spindled cell proliferation in the upper dermis with focal stromal mucin consistent with trichodiscoma (**Figure 1B-D**). Biopsy of another of these lesions showed similar features. Given this diagnosis of multiple trichodiscomas, the patient was referred for genetic testing for BHD syndrome but was found to be negative for the *FLCN* gene mutation.

## Case Discussion

Trichodiscomas are benign follicular tumors, specifically mesenchymal hamartomas of the mesodermal portion of the hair disk, that occur on the head and neck of adults as small, slow-growing papules [2]. Trichodiscomas may be solitary or multiple. The presence of multiple trichodiscomas has been associated with two syndromes. BHD syndrome



**Figure 1.** Clinical and pathologic images of a patient with trichodiscoma. A) Representative white papule (white arrow) on patient's posterior neck at initial presentation. B) Hematoxylin and eosin stained section of white papule showing proliferation of slender spindled cells in the upper dermis (200x). C) Alcian blue stained section of white papule showing focal stromal mucin in the lesional stroma (200x). D) By immunohistochemistry the lesional spindled cells are uniformly positive for CD34, characteristic of trichodiscoma (200x).

is a rare autosomal dominant disorder associated with germline mutations (17p11.2 and 17p12-q11.2) in *FLCN*, which encodes the folliculin tumor-suppressor protein. *FLCN* mutations, reported in 60-80% of patients with BHD syndrome [2], predispose patients to trichodiscomas, fibrofolliculomas, acrochordons, lung disease (cysts, pneumothorax), and renal carcinoma [3]. Histologic overlap between fibrofolliculomas and trichodiscomas have been noted, and acrochordons may show similarities to fibrofolliculomas on histopathology [4]. Another syndrome with similar cutaneous findings but no clear association with the *FLCN* locus is familial multiple discoid fibromas (FMDF), an inherited disorder characterized by well-circumscribed elliptical fibrovascular tumors [5]. Although there may be some overlap in the histology of trichodiscomas and discoid fibromas, the lesion in our patient lacks the superficial telangiectasias, peripheral hair follicle, and dense collagen typically described for discoid fibromas [5]. In addition, this patient presents at a later age, has a characteristic centrally located follicle, and shows less prominent centrafacial and pinnae involvement. These nuances in histologic features and anatomical site together favor the diagnosis of trichodiscoma.

This patient with multiple trichodiscomas tested negative for the *FLCN* gene mutation and lacked pulmonary and renal involvement, making the diagnosis of BHD unlikely. Moreover, his clinical presentation was not typical of FMDF. Therefore we considered the possibility that his trichodiscomas were related to his underlying MEN type I disease.

## Conclusion

This case of a patient with genetically confirmed MEN type I but *FLCN* mutation-negative trichodiscomas suggests that trichodiscomas, in addition to facial angiofibromas, may be a key skin finding in MEN type I rather than being limited to BHD syndrome. These additional cutaneous manifestations may facilitate earlier diagnosis and management of MEN type I.

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