

Facial and Upper Body Papules in a Patient With a Family History of Recurrent Pneumothorax

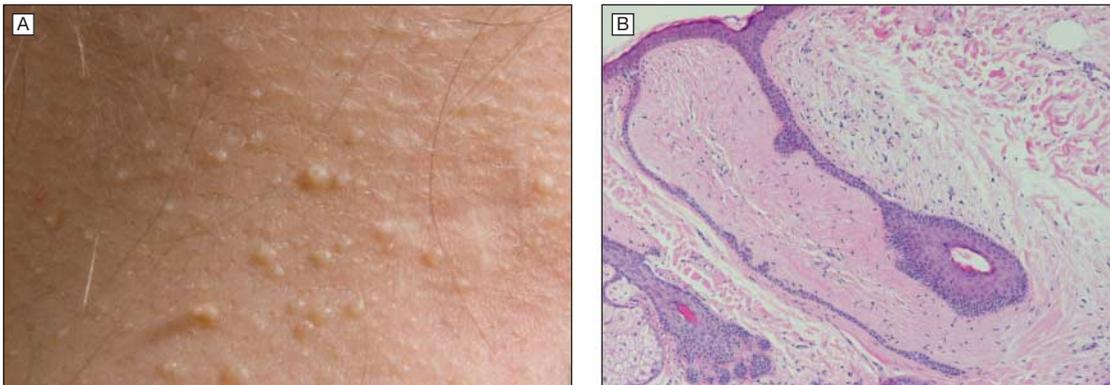


Figure. A, Close-up of papules on the patient's upper back. B, Skin biopsy from representative lesion showing follicular distortion and a thin band of follicular epithelium extending into fibrous stroma (hematoxylin-eosin, original magnification $\times 10$).

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A 31-YEAR-OLD WOMAN PRESENTS WITH A 10-YEAR HISTORY OF PROGRESSIVE development of small, whitish/skin-colored papules across her forehead, neck, and upper back (FIGURE, A). She also has scattered skin tags in this distribution. The patient also reports that her brother and father have similar papular facial rashes, and her father has had recurrent pneumothoraces in the past, necessitating pleurectomy. A skin biopsy obtained from a representative lesion confirms the presence of fibrofolliculomas (Figure, B).

What Would You Do Next?

- A. Schedule colonoscopy
- B. Schedule cranial computed tomography
- C. Schedule pleurectomy
- D. Schedule renal tract ultrasonography

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Diagnosis

Birt-Hogg-Dube syndrome

What to Do Next

D. Schedule renal tract ultrasonography

The key feature in this case is the adult-onset papular facial rash, with a histological diagnosis of fibrofolliculomas. This is indicative of Birt-Hogg-Dube syndrome and is supported by the positive family history. The most important work-up to perform in suspected or confirmed cases of Birt-Hogg-Dube syndrome is a renal tract ultrasound because of the increased risk of associated renal cell carcinoma.

Comment

Birt-Hogg-Dube syndrome is a rare autosomal dominant disorder, originally described in 1977, that predisposes individuals to cutaneous fibrofolliculomas, pulmonary cysts (and thus pneumothorax), and an increased risk of renal carcinoma.¹ It is attributable to mutations within the *FLCN* (folliculin) gene on chromosome 17, and the folliculin protein is present in many tissues including the skin, lungs, and kidney.² Diagnostic criteria include adult onset of at least 5 fibrofolliculomas and trichodiscomas confirmed on skin biopsy, or a demonstrable mutation in *FLCN*, supported by a positive family or personal history of bilateral lung cysts or renal carcinoma.³ Skin lesions typically appear as multiple, 2- to 4-mm, smooth, whitish papules on the face, neck, and upper trunk during the third and fourth decades and usually increase in size and number with age. A later onset of cutaneous lesions tends to correlate with a milder skin phenotype.

More than 80% of affected adult patients have lung cysts on high-resolution computed tomography.⁴ These cysts are usually bilateral and

multifocal. While most individuals are asymptomatic, the risk of spontaneous pneumothorax is thought to approach 30%.⁵ The most important complication of Birt-Hogg-Dube syndrome is the development of renal tumors. Tumor types vary and include chromophobe, chromophobe-oncocytic hybrid tumor, and clear cell renal cell carcinoma; they may be multiple and bilateral.⁵ One study reported renal tumors in 12% of the 115 patients studied; one-third of the patients had metastatic renal cancer.⁶

There are no guidelines regarding the age or frequency at which to screen for renal cancer in Birt-Hogg-Dube syndrome, but early screening should be considered, ideally also involving a urologist. Renal ultrasound is an acceptable first-line modality for screening purposes and if in doubt or where available, magnetic resonance imaging can also be used, with the particular advantage of superior visualization to identify early or small lesions. Other medical problems associated with Birt-Hogg-Dube syndrome include medullary thyroid cancer, thyroid adenoma, parathyroid adenoma, multiple lipomas, sarcoma, and intestinal polyposis and colorectal cancer. Investigating for these associations, including colonoscopy for intestinal polyposis, should be guided according to patient symptoms and clinical suspicion. Patients should be referred to a genetic counselor, with whom genetic testing to confirm the *FLCN* mutation and screening of potentially affected relatives can be organized. A geneticist may also discuss the possibility of prenatal testing in those starting a family.

Regarding treatment, removal of fibrofolliculomas and trichodiscomas is difficult. Laser ablation may produce substantial improvement, but relapse

can occur. Treatment of pneumothorax is the same as in the general population. Prophylactic pleurectomy is not recommended; however, high ambient pressures and smoking (independent risk factors for pneumothorax) should be avoided. For renal tumors, nephron-sparing surgery should be preferred as appropriate.

Patient Outcome

In this patient, renal tract imaging results were normal and she and her brother were referred for genetic counseling. An initial test patch with carbon dioxide laser to a small area of forehead skin resulted in improvements in skin texture and appearance. Laser treatments are now continuing every 12 weeks until papule clearance.

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