propose that MP be renamed miliaria alba, following the pattern of the clinically descriptive names for miliaria crystallina and miliaria rubra.

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Birt-Hogg-Dubé Syndrome in an African Patient and a Novel Mutation in the FLCN Gene

Birt-Hogg-Dubé syndrome (BHDS), an autosomal dominant condition caused by mutations in the FLCN gene, is characterized by fibrofolliculomas, spontaneous pneumothorax, and renal cell carcinoma. Herein, we report the first case to our knowledge of BHDS in an African patient.

Report of a Case | A 53-year-old man from Somalia with a history of hypertension presented with multiple asymptomatic bumps on his face that appeared progressively over time. He denied having a personal or family history of similar lesions, renal cell carcinoma, spontaneous pneumothorax, or other pulmonary disease. Physical examination revealed diffuse flesh-colored, dome-shaped and pedunculated papules on the face, neck, upper back, chest, arms, and axillary folds (Figure 1). Histopathologic analysis of biopsy specimens taken from the left jawline (Figure 2) and left forearm were consistent with fibrofolliculoma and trichodiscoma, respectively. Genetic test results were positive for a novel nonsense heterozygous mutation p.Glu410Stop (E410X) in exon 11 of the FLCN gene. The patient was treated with shave removal of the lesions that were particularly disfiguring. At last follow-up, he was undergoing evaluation for renal and pulmonary disease.

Discussion | Birt-Hogg-Dubé syndrome was originally characterized by the triad of fibrofolliculomas, trichodiscomas, and acrochordons. The lesions usually appear after the second decade of life. Clinically, fibrofolliculomas and trichodiscomas are indistinguishable; both present as firm dome-shaped papules predominantly involving the face, scalp, and neck. However, skin findings may be absent in some patients. One of 2 major criteria proposed to diagnose BHDS is the presence of 5 or more fibrofolliculomas or trichodiscomas with 1 confirmed histologically. Histologically, fibrofolliculomas, trichodiscomas, and acrochordons were initially described as separate entities. However, many authorities now believe that all 3 are variants of a
fibrofolliculoma, and the histopathologic distinction is related to differences in sectioning techniques. Fibrofolliculomas are characterized by anastomosing epithelial strands radiating from a dilated hair follicle within a fibrous stroma.

Birt-Hogg-Dubé syndrome has an autosomal dominant pattern of inheritance and is caused by germline mutations in the FLCN gene, which is located on chromosome 17p11.2. This gene encodes for the folliculin protein, the role of which has not been fully elucidated; however, it appears to function as a tumor suppressor. Studies have found that folliculin interacts with FLCN-interacting protein 1 and is involved in 5′-AMP-activated protein kinase and mTOR signaling dysregulation.

Renal tumors and spontaneous pneumothoraces are strongly linked to BHDS. There is a 50-fold increased risk of spontaneous pneumothorax, and recurrent disease is common. Pneumothorax is probably related to the presence of multiple lung cysts, which have been reported in more than 80% of adult patients and are typically found at the lung bases.

Patients with BHDS have a 16% risk of developing renal cell carcinoma by age 70 years, which is often bilateral and multifocal. Chromophobe renal carcinoma and oncocytomas are most commonly reported. Although there is no consensus on screening guidelines, renal magnetic resonance imaging surveillance beginning at age 20 years has been recommended.

Treatment for the cutaneous manifestations of BHDS is difficult. Multiple modalities, including ablative lasers, electrodesiccation, and surgical excision have been reported. While surgical excision is the only definitive treatment for individual lesions, the scarring risk makes this an unreasonable option for multiple lesions. A recent double-blind placebo-controlled randomized trial using topical rapamycin yielded disappointing results. Most importantly, appropriate imaging studies for renal tumors and lung cysts should be obtained in all patients with BHDS as well as at-risk relatives.

To our knowledge, this patient is the first reported case of BHDS in an individual of African ancestry and is associated with an FLCN gene mutation that has not been previously described.

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COMMENT & RESPONSE

Indications and Limitations of Afamelanotide for Treating Vitiligo

To the Editor | I read with great interest the study by Lim et al1 on the use of afamelanotide in combination with narrowband UV-B for treating vitiligo. So far, there is no truly satisfactory treatment for vitiligo, so any new approach is most welcome. However, this study raises several issues. Afamelanotide binds with the melanocortin-1 receptor (MC1R), which is the receptor upstream of one of the key pathways for melanogenesis.3 Unfortunately, MC1R is not expressed by melanocyte stem cells, and thus afamelanotide can stimulate pigmentation and increase proliferation of melanocytes but cannot have any effect on the differentiation of melanocyte stem cells.

Phototherapy is required for induction of melanoblast differentiation. As a result, afamelanotide can increase the speed and the extent of repigmentation in patients who respond to phototherapy, but it cannot by itself induce differentiation and increase the rate of response.

This study also shows better results in dark-skinned individuals, which can be explained by the potent MC1R response in these patients.4 In December 2012, Clinuvel completed a similar study in Europe (NCT01382589), and the results do not seem to have been reported, or at least they are not yet posted on clinicaltrials.gov. These findings would be of great interest to the dermatologic community and patients.

In addition, afamelanotide usually induces potent tanning. While this is not an issue for those with dark skin, the increased contrast induced in fair-skinned individuals between healthy and lesional skin can increase the visibility of the vitiligo lesions and have a negative impact on the quality of life of treated people. Two of the patients in the study by Lim et al1 dropped out for this very reason. Quality of life is now recognized as a key criterion of evaluation in vitiligo treatment.5 This factor was listed in the secondary outcome measures in the registration of this study (NCT01430195), but it is not reported in the article. This outcome should be given by the authors for the entire population and for patients with type III skin in particular.

In conclusion, this therapeutic approach appears potentially interesting, especially in dark-skinned patients, but additional studies are clearly required to confirm these results and to determine the indications and limitations of this new treatment.

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