

BRIEF ARTICLE

Sclerotic Fibroma in a Patient with Birt-Hogg-Dubé Syndrome

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ABSTRACT

Birt-Hogg-Dubé syndrome (BHD) is a rare genetic disorder characterized by cutaneous lesions and systemic findings such as renal neoplasms, pulmonary cysts, and spontaneous pneumothoraces. Fibrofolliculomas, trichodiscomas, and acrochordons are the most common cutaneous lesions associated with BHD. Some cases with mucocutaneous lesions have also been reported. We report a sclerotic fibroma that developed over a previous thoracotomy scar of a patient with BHD.

INTRODUCTION

Birt-Hogg-Dubé (BHD) syndrome is an uncommon autosomal dominantly inherited disorder caused by mutations in the Folliculin (FLCN) gene located on chromosome 17. Clinical manifestations of the syndrome include pulmonary cystic lesions, pneumothoracies, various renal tumors, and fibrofolliculomas. Other cutaneous lesions, such as benign skin hamartomas, angiofibroma, epidermal cysts, acrochordons, and cutaneous collagenomas, have also been reported.¹

Sclerotic fibromas (SF), also known as circumscribed storiform collagenomas, are rare benign soft tissue neoplasms that usually affect middle-aged individuals and have a slight female predominance.² SFs usually occur sporadically as a solitary lesion but sometimes may be seen as multiple lesions in patients affected by multiple hamartoma syndrome (Cowden's disease).³ Clinically, the lesions present as firm, flesh-

colored, keloid-like nodular lesions. Histopathologically, they are characterized by well-circumscribed, non-encapsulated dermal hypocellular nodules composed of eosinophilic hyalinized bundles of whorled or "storiform" collagen with clefting.³⁻⁵ As SFs are generally associated with Cowden's disease, it is important to note that they may also occur in BHD.

CASE REPORT

A 70-year-old female with a family history of Birt-Hogg-Dubé syndrome and a past medical history of spontaneous pneumothorax was diagnosed with BHD after testing positive for a mutation in the folliculin gene. She presented at our clinic with a new, asymptomatic, 6mm, pink-flesh-colored papule on an upper back thoracotomy scar from bleb removal. (**Figure 1**) Skin examination also revealed multiple fibrofolliculomas on the face (**Figure 2**) and medium-sized brown papules scattered on the trunk and extremities. A shave biopsy of



Figure 1. Pink-colored and well-demarcated papule about 6 mm in diameter on the previous thoracotomy scar.



Figure 2. Multiple skin-colored papules on the left nasolabial fold were consistent with fibrofolliculomas.

the new lesion on the back was performed. Histopathological examination revealed a well-circumscribed, hypocellular dermal nodule composed of sclerotic and hyalinized collagen with scattered, spindled fibroblasts, consistent with sclerotic fibroma (**Figure 3**). Loss of elastic fibers on the Verhoeff-Van Gieson (VVG) elastic stain was also noted (**Figure 3**). No further management was planned because of the lesion's benign nature and lack of symptoms.

DISCUSSION AND REVIEW

BHD was first described in 1977 by Birt, Hogg, and Dubé. In the study, 70 patients with a family history of hereditary medullary thyroid carcinoma were also reported to have multiple fibrofolliculomas, trichodiscomas, and acrochordons distributed on different sites of the body;⁶ however, cases with similar multiple small papular lesions involving the face, neck, chest, and upper

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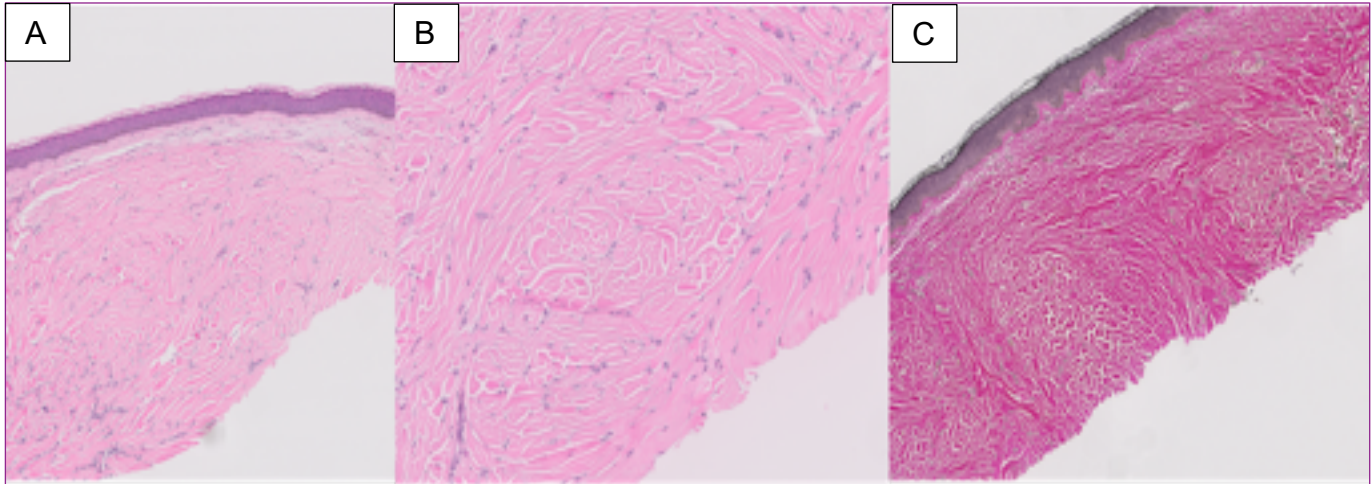


Figure 3. (A) and (B) are a shave biopsy from the lesion in Figure 1 showing a well-circumscribed, sclerotic, and hypocellular dermal nodule consisting of storiform and hyalinized collagen bundles with scattered, spindled fibroblasts consistent with SF (H&E, x100, x400). (C) demonstrates the loss of elastic fibers. (Verhoeff-van Gieson stain, x100).

back were first reported in 1925 by Burnier and Rejsek, and later in 1960 by Pinkus, respectively. The lesions were named perifollicular fibromas at the time of diagnosis.⁶

Multiple systemic manifestations have been described in BHD. Pulmonary manifestations such as multiple pulmonary cysts and blebs are usually seen in early to mid-adulthood and may be the only manifestation of the syndrome.^{7,8} Pneumothoraces may also be reported as both radiological and clinical findings. Renal neoplasms are also observed in patients with BHD. Unlike most of the other inherited renal cancer syndromes, BHD is not associated with one specific histologic renal tumor type, although oncocytomas predominate. Individuals with BHD are predisposed to a broad spectrum of renal tumors, including hybrid oncocytic tumors, chromophobe renal cell carcinoma, clear cell renal cell carcinoma, and renal oncocytomas.⁹ Although there have been some reported cases of colonic neoplasms with BHD, a definite association between colonic neoplasms and BHD has not been established.⁹

The diagnosis of BHD usually relies on family history and clinical presentation. Skin manifestations such as fibrofolliculomas are reported to be seen at the age of 25-35 years and can be missed when subtle; however, the development of renal neoplasms is usually observed after age 40. Hence, patients with spontaneous pneumothorax or a family history should be carefully examined for skin lesions that may be characteristic of BHD. High-resolution CT scans of the chest may be performed for further diagnosis of pulmonary cysts, and patients should be screened for renal neoplasms.¹

SF, also known as circumscribed storiform collagenoma, is an uncommon, fibrotic, benign tumor that usually occurs sporadically as an asymptomatic solitary lesion. SFs are pink or flesh-colored waxy papules or nodules measuring less than 1 cm in diameter. Multiple lesions can be observed in patients with Cowden's disease. Sporadic cases, unassociated with Cowden's disease, may also be seen in the oral mucosa.¹⁰

Histopathologically, SFs are unencapsulated but are well-circumscribed dermal nodules.

They are bland and hypocellular lesions composed of homogenized eosinophilic collagen bundles with prominent clefts. Storiform and whorled patterns of collagen may also be present. Stromal mucin and the absence of elastic fibers may be observed. CD34, factor XIIIa, and vimentin typically highlight the spindle cells.¹⁰

Differential diagnoses for SF include other well-circumscribed skin tumors such as dermatofibroma, pleomorphic fibroma, fibrolipoma, hypertrophic scar, and giant cell collagenoma.² Our preoperative differential diagnoses also included hypertrophic scar and keloid since the lesion was observed on a surgical incision scar; however, distinctive features of hypertrophic scar and keloid were not observed on histopathology.¹⁰

Literature shows various SF associated with scars. Kim et al. reported a keloid-like SF developing on a scar. Their patient had a well-circumscribed firm nodule removed from the thigh on a previously picked-up lesion, with a clinical differential diagnosis of keloid considering the patient's picking habit; however, the histopathological examination revealed storiform patterns of collagenous bundles separated by prominent clefts, which were found to be consistent with an SF.¹¹ Furthermore, Zavras et al. reported another case of SF associated with scar formation in a patient with Rubenstein-Taybi syndrome. The patient underwent surgeries for the transposition of the great vessels and undescended testes. A hypertrophic scar and keloid formation were observed on the chest incision. Additionally, a multilobulated, pink mass with crypts and fissures was identified on the left groin incision scar. Histopathology revealed collagen bundles arranged in a storiform pattern, intermixed with fibroblasts, separated by elongated clefts, diagnosing the nodule as an SF.¹²

Surgical excision is considered the standard treatment for solitary SFs. Once the histopathological diagnosis is confirmed, no treatment or further investigation is usually required.² We report a sclerotic fibroma in a patient diagnosed with BHD. Since SFs are distinctive lesions usually observed sporadically and sometimes with Cowden's Disease, our case underscores that SFs may also be a warning lesion for undiagnosed BHD.

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