Case Report

DOI: 10.14235/bas.galenos.2017.1453
Bezmialem Science 2018;6(3):220-2

Birt-Hogg-Dube Syndrome

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ABSTRACT

Birt-Hogg-Dube syndrome is characterized by cutaneous findings, including fibrofolliculomas, angiofibromas, fibroepithelial polyps, and trichodiscomas. It is an inherited autosomal dominant disorder. This syndrome also includes extra-cutaneous findings, such as pulmonary cysts, spontaneous pneumothorax, and renal cancer. Because of the systemic involvement, early diagnosis and treatment are important. Here, we report the case of a 53-year-old man diagnosed as having Birt-Hogg-Dube syndrome.

Keywords: Trichodiscoma, Birt-Hogg-Dube syndrome, fibrofolliculoma

Introduction

Birt-Hogg-Dube syndrome (BHDS) is an autosomal dominant syndrome clinically characterized by fibrofolliculoma, trichodiscoma, lung cysts, spontaneous pneumothorax and kidney tumors. This syndrome is caused by the mutations in the folliculin (FLCN) gene. Here, we present a 53-year-old male patient with Birt-Hogg-Dubé syndrome.

Case Report

A 51-year-old male patient was admitted to our outpatient clinic with the complaint of wen on the face and neck. It was found out that the patient had a history of vertigo, cervical spondylosis and hypertension. In his family history, the mother had kidney disease (she did not know her exact diagnosis), and his father died of lung cancer. He stated that his brother also had similar lesions. Dermatological examination revealed common, whitish and dome-shaped papules of several millimeters in diameter in large numbers in the neck, and fewer on the cheeks and forehead (Figure 1a-c). Systemic examination, and hemogram, biochemistry, complete urine and stool tests of the patient were normal. Biopsy was obtained from the skin lesions of the patient and it was found histopathologically compatible with trichodiscoma (Figure 2, 3). Because the result of the skin biopsy was consistent with trichodiscoma, it was decided to perform advanced investigation considering Birt-Hogg-Dubé syndrome. In the examinations preformed in terms of systemic involvement, thorax-abdominopelvic tomography revealed no findings other than benign renal cysts. The patient was followed up and his brother with similar complaints was called to our clinic for diagnosis and screening.

Discussion

Birt-Hogg-Dubé syndrome (BHDS) which was first defined by Birt et al. (1) in 1977 shows autosomal dominant inheritance. This syndrome was found to be caused by multiple mutations in the folliculin (FLCN) gene located in the 14th exon of the p11.2 region of chromosome 17. Folliculin protein is predicted to have tumor suppressor function but it has not yet been confirmed. The tumors that are seen clinically support this. It is estimated that the diagnosis of the syndrome cannot be made most of the time and therefore its incidence has not been determined. Around 200 families with FLCN mutations have been reported worldwide (2, 3).

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Received: 11.10.2016
Accepted: 20.03.2017

Cite this article as: Emiroğlu N, Cengiz FP, Tosuner Z, Bahalı AG, Onsun N. Birt-Hogg-Dube Syndrome. Bezmialem Science 2018; 6(3): 220-2.

Birt-Hogg-Dube syndrome is characterized by skin-colored, asymptomatic, solid, soft, 2-4 mm, dome-shaped papules that usually appear on the face and in the upper body in the third decade of life. Ear involvement is very specific for BHDS. The classic triad of skin involvement in BHDS includes fibrofolliculomas, trichodiscoma and acrochordons. Other than these, although not frequent, skin tumors such as angiofibromas, lipomas, angiolipomas, oral polyps and collagenoma can also be seen (4). Other common non-cutaneous manifestations of BHDS include lung cysts, spontaneous pneumothorax, and renal tumors (4).

Due to the variety of skin and systemic involvement, the European Birt-Hogg-Dube Consortium has proposed some criteria for the diagnosis of the disease. In order to be able to make the diagnosis of Birt-Hogg-Dubé syndrome, patients should meet 1 major or 2 minor criteria from the following criteria. The major criteria are 1) ≥5 fibrofolliculomas or trichodiscomas at least one of which has been histopathologically diagnosed 2) Mutation in the FLCN gene. Minor Criteria are 1) Numerous lung cysts (bilateral and basal-located ± spontaneous pneumothorax) 2) Kidney cancer (before 50 years of age or multifocal, bilateral or mixed chromophobe, oncocytic histopathology) 3) Birt-Hogg-Dubé syndrome in first-degree relatives (5). As a result; without any accompanying systemic symptoms, at least 5 trichodiscomas which occur in adulthood and at least one of which is histopathologically diagnosed suggest the diagnosis of Birt-Hogg-Dubé syndrome. Our patient also had multiple trichodiscomas that were histopathologically confirmed. He had a family history; therefore, his brother was called for an examination, but he did not come. The patient, who had no systemic findings other than benign renal cysts, was subjected to long-term follow-up.

The risk of renal tumor increases 16-fold and the risk of spontaneous pneumothorax increases 50-fold in patients with Birt-Hogg-Dube syndrome in comparison to healthy population. Pneumothorax is probably associated with lung cysts (6). While the risk of renal tumor increases in advanced age and male gender, the risk of spontaneous pneumothorax decreases

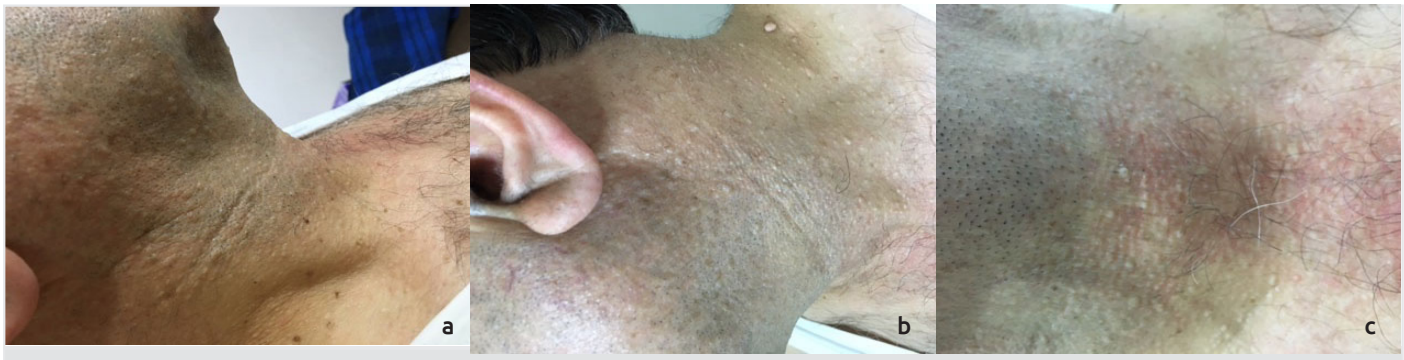

Figure 1a-c. Numerous common, whitish, dome-shaped papules of several millimeters in diameter in the neck

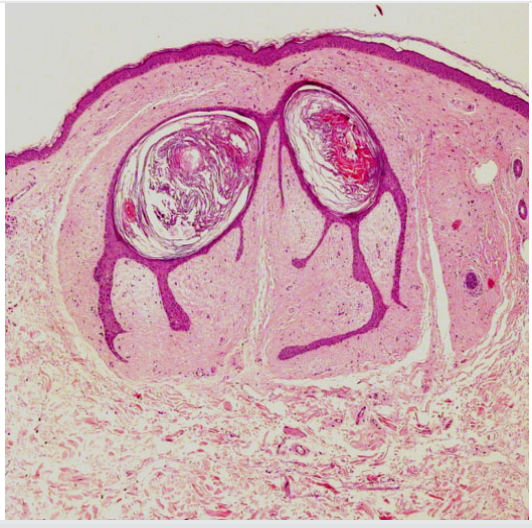

Figure 2. In histopathologic examination, a dome-shaped cystic lesion, which is surrounded by thin long follicular epithelium on both sides under atrophic epidermis. The cyst contains free hair shafts and lamella contains keratin. Hematoxylin Eosin x40

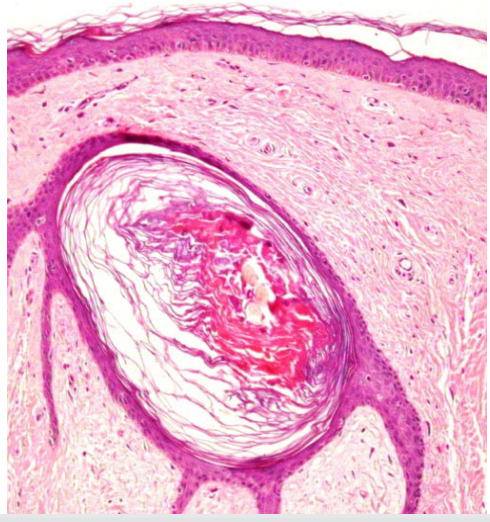

Figure 3. Increased fibrillar collagen, organized in irregular bundles, and increased star-shaped fibroblasts and mucinous stroma. Hematoxylin Eosin x100

with age (7). Therefore, routine imaging examinations in terms of early diagnosis of renal tumor can be started as of 40 years of age in patients under follow-up (7).

Intestinal polyps, thyroid nodules, thyroid cysts, parotid oncocytoma, parathyroid adenoma, choroidal melanoma, chorioretinopathy may be seen less frequently in patients with Birt-Hogg-Dube syndrome (8).

Trichodiscoma and fibrofolliculoma, the characteristic skin lesions observed in approximately 80% of patients, usually occur after the age of 35 and are the most important clue for the syndrome (9). These lesions, which are asymptomatic, skin-colored, dome-shaped, and which often involve the head, neck and the upper part of the body, can be confused with many other tumors. In the differential diagnosis of these tumors with mixed ectodermal and mesodermal origin, other hereditary diseases in which multiple facial papules are seen are in the foreground. These epithelial lesions are Cowden's syndrome in which trichilemmomas are seen, Brooke-Spiegler syndrome and Rombo syndrome in which trichoepitheliomas are seen, basaloid follicular hamartoma syndrome in which basaloid follicular hamartomas are seen and tuberous sclerosis in which angiofibromas are seen (9, 10).

Conclusion

Because our case is rare, it is important to report; in such syndromes, the recognition of skin findings is important for monitoring systemic involvement and facilitating early diagnosis especially in malignancies.

Informed Consent: Written informed consent was obtained from patient who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions

Design - N.E.; Resources - F.P.C.; Materials - N.O.; Data Collection and/or Processing - Z.T.; Analysis and/

or Interpretation - A.G.B.; Literature Search - N.E.; Writing Manuscript - N.E.; Critical Review - N.O.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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