CASE REPORT

Brooke-Spiegler syndrome

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ABSTRACT

Brooke- Spiegler syndrome is an uncommon autosomal dominant disorder, only few cases have been reported. Herein, we report a patient with this rare condition. A 26 year old woman with Brooke-Spiegler syndrome (BSS) has multiple cutaneous adenxal neoplasms on her face and scalp. Clinical features, histopathogical spectrum, pathogenesis, malignant transformation and treatment modalities are reviewed.

INTRODUCTION

Brooke- Spiegler syndrome is an uncommon autosomal dominant disorder.This syndrome is named after the two men who first described these neoplasms. Brooke reported on trichoepitheliomas in 1892 and Spiegler who gave the description in 1899 of cylindromas.[1] It is characterized by high affinity to form multiple adenxal neoplasia. Only few cases have been reported in literature. Herein, we report a patient with this rare condition.

CASE REPORT

A 26 year old woman presented with numerous lesions on her face and scalp. It started 6 years ago as an isolated, small bump on her face, and slowly numerous similar eruptions appeared over the period of time. About 3 years later, she noticed nodular growths on her scalp and experienced continual appearance of new lesions with increase in size of the individual nodules. All lesions were asymptomatic. She had no known underlying disease and her general condition was good. Her father had similar facial lesions although rest of the family was unaffected.

Cutaneous examination revealed multiple facial lesions 0.5-3mm smooth, firm, skin-colored non tender papules and nodules mainly on mid-face particularly around nasolabial folds (Fig.1). Scalp showed multiple, smooth, firm, pink to red, dome shaped non tender nodules varying in size from 0.5 to 2 cm. Some of the nodules were pedunculated and devoid of hair whereas some showed telangiectasia on the surface (Fig.2,3).Routine blood and urine investigations revealed no abnormality.

Biopsy of scalp lesion (Fig. 4, 5) showed rounded outline with basaloid masses in the dermis, composed of closely set mosaic-like masses, separated by hyalinized stroma formed of fibrotic collagen with high vascularity. The nodules showed the classical jigsaw-puzzle architecture. These masses formed of two types of cells-central pale and peripheral dark cells. Some masses had more cystic appearance with more hyaline stroma. The histopathological picture leads to the diagnosis of cylindroma. Biopsy of facial lesion (Fig.6, 7) showed large well circumscribed deeply basophilic tumour masses in upper dermis without connection to epidermis, formed of dark and pale cells. The center of the masses showed large amorphous collection and lobules were surrounded by lymphohistiocytic infiltrate and dilated blood vessels, promoting the diagnosis of spiradenoma. Correlating clinical features and histopathologic findings of the patient, a diagnosis of Brooke-spiegler syndrome

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(BSS) was made. We treated our patient by surgically excising the cylindromas of the scalp and large spiradenomas on the face.

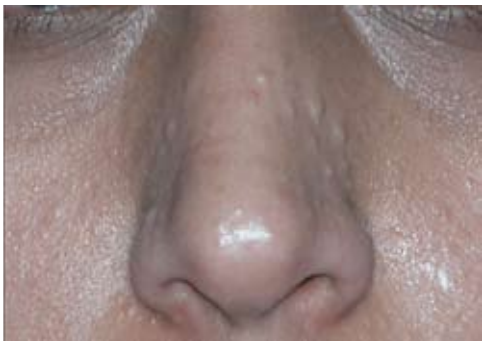
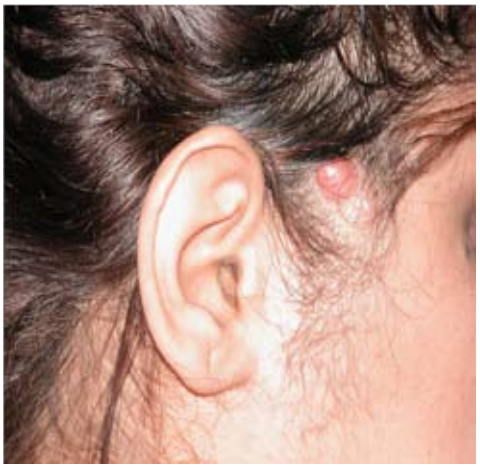


Fig. 1 Papules on nose and nasolabial areas



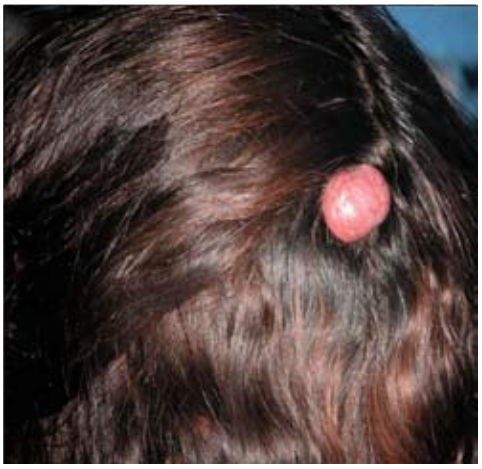


Fig. 2,3 Pinkish red, smooth surfaced, dome-shaped tumor, with surface telangiectasia

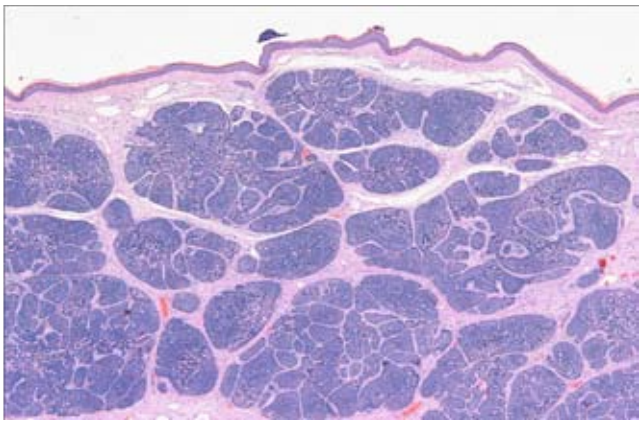


Fig. 4 The nodules are arranged in a jigsaw puzzle pattern and surrounded by a thick, homogeneous, eosinophilic basal membrane.

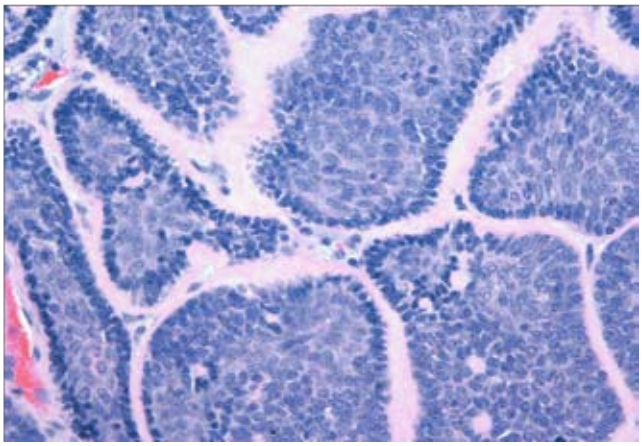


Fig. 5 The cells at the periphery show small, dark staining nuclei and a small amount of cytoplasm and

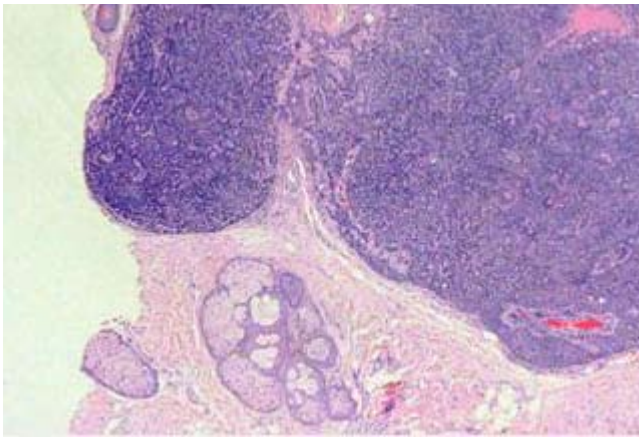


Fig. 6 Well-circumscribed, larger aggregates of dark and pale cells surrounded by a thin basement membrane.

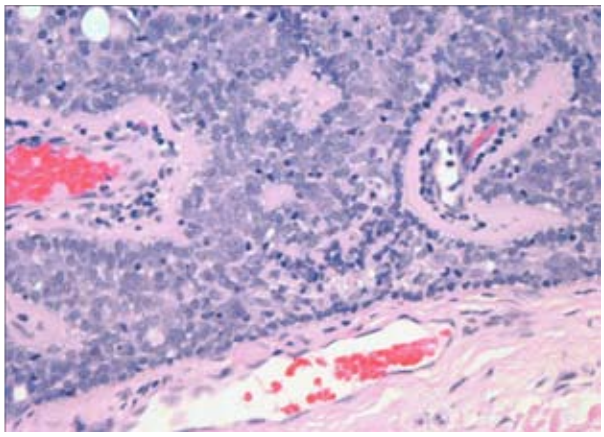


Fig. 7 Tubular structures and lymphocytes are apparent within the epithelial aggregations.

DISCUSSION

Brooke–Spiegler syndrome is a rare autosomal dominantly inherited disease characterized by high affinity to form multiple adenxal neoplasia, particularly cylindromas, trichoepitheliomas and spiradenomas typically located on the head and neck.[2] Women are more often affected, usually in the second or third decades of life.[2] There is a predisposition to develop other cutaneous adnexal neoplasms as BCC, trichoblastomas, follicular cysts, organoid nevi, and malignant transformation of pre-existing tumors. Also patients are at risk for developing tumors of salivary glands, such as basal-cell adenomas and adenocarcinomas of the parotid glands.[3, 4]

Cylindromas are pink, smooth-surfaced nodular lesions, with surface telangectesia, varying in size from few millimeters to several centimeters. They are usually located on head, mainly on the scalp and are occasionally painful. Less than 10% can be found on face, trunk and upper limbs. When multiple lesions cover the scalp, they form a disfiguring mass known as "Turban tumour".[5, 6] The larger lesions are generally pedunculated and hairless. Although cylindromas are usually benign neoplasms and malignant transformation is rare, but well documented. It needs close follow up as the malignancies are often locally aggressive and can metastasize.[6, 7, 8]

Eccrine Spiradenomas (ES) is a rare benign tumor, usually manifests as a solitary, gray, pink or blue nodule about 1cm. in diameter,[9] which usually occurs in persons aged 15 -35 years and can be multiple, giant, linear, zosteriform, nevoid or blashkoid.[10, 11] It can be painful, often in paroxysms and tend to arise on head, neck or the upper part of trunk. Eccrine spiradenoma is usually a benign tumor, but malignant transformation has been reported.[12]

Occurrence of both types of lesions in Brooke-Spiegler syndrome support the assumption that spiradenomas and cylindromas have been regarded as variants of the same neoplasm.[12, 13] Genetic studies have demonstrated that mutations in the CYLD[14] gene located on band 16q12-q13 are responsible in Brooke–Spiegler syndrome.[15] The penetrance of the gene has been estimated to be between 60% and 100%. Mutation in the genes that regulate stem cell proliferation and differentiation can cause defect in differentiation of the folliculo-sebaceous apocrine unit, which gives rise to the different combinations of adnexal skin tumors.[16, 17]

BSS syndrome was initially defined by the association of multiple familial cylindromas and trichoepitheliomas, later observations extended its histopathological spectrum by describing spiradenomas, spiradenocylindromas, trichoblastomas, basal cell carcinomas, follicular cysts, organoid nevi, and malignant transformation of pre-existing tumors in the affected individuals.[1, 13] Cylindromas composed of small, rectangular, triangular and polyhedral aggregations of basaloid cells arranged in a jigsaw puzzle pattern. The cells at the periphery possessed small, dark staining nuclei with a small amount of cytoplasm and were arranged in a palisade fashion.[2] The epithelial aggregates were surrounded by a thick, homogeneous, eosinophilic, PAS-positive basal membrane. Some epithelial aggregates were punc-

tuated by globules of homogeneous eosinophilic material. Lymphocytes were scant to none.[2, 6] Spiradenoma formed of large, well-circumscribed, variably sized aggregates of dark and pale cells. Some epithelial aggregates were surrounded by a thin basement membrane, while other epithelial aggregates lacked it. Tubular structures and lymphocytes were apparent within the epithelial aggregations. Lymphocytes were scattered in the paucicellular stroma. Rare epithelial aggregates contained globules of homogeneous eosinophilic material, which sometimes replaced the whole epithelial nodule.[1, 9]

A lack of lymphoid tissue is a histological feature that differentiates cylindromas from spiradenomas. Spiradenomas show prominent presence of lymphocytes. Cylindromas, on the other hand, show prominent dendritic cells, most likely langerhans cells that permeate the tumour.[13] The histolopathologic spectrum in BSS is broad and encompasses benign adnexal neoplasms of apocrine, follicular, and sebaceous differentiation, which can occur independently and conjointly.[12] The most unusual findings are neoplasms with hybrid features, such as spiradeno-cylindromas, spiradenoma-trichoepitheliomas,cylindroma-trichoepitheliomas, and even the concurrence of all three adnexal tumors in one lesion suggesting a common embryonic relationship between the follicles and the apocrine glands.[18]

The most common composite tumor was spiradenocylindroma. Co-occurrence of several tumors with apocrine, sebaceous and trichoblastic differentiation in spiradenocylindroma is a proof that spiradenoma and cylindroma are neoplasms of the folliculosebaceous-apocrine unit.[12]

Whether the cell-type of origin of BSS, is eccrine or apocrine, is a topic of debate. For cylindroma and spiradenoma both the apocrine and eccrine differentiation have been suggested.[1] The distinction is usually based upon enzyme histochemistry, and microscopic assessment. There is strong immunohistochemical similarity between cylindromas and spiradenomas.[19] Immunohistochemical studies linking cylindromas to eccrine differentiation include positive expression of cytokeratins 19 and 1-10-11. IKH-4 a marker to differentiate eccrine from apocrine tumours, is positive in eccrine cylindromas and spiradenomas. On the other hand immunohistochemical studies linking cylindromas to apocrine differentiation include the expression of alpha 1 antichymotrypsin, alpha smooth actin and cytokeratins 8 and 18.[2, 4] The presence of cylindroma and eccrine spiradenoma in one clinical nodule is not unusual and contributes circumstantial evidence for the similar derivation of both tumors.[1, 13]

Different treatment methods have been suggested for adenxal tumours in BSS which include surgical excision, dermabrasion, electrodesiccation, cryotherapy, lasers such as CO2, and Erbium:Yag with CO2. [3, 20, 21] It has been proven that the administration of aspirin and its derivatives can result in the rapid formation of new lesions.[20]

CONCLUSION

We report a case of Brooke-Spiegler syndrome in a 26 years old woman with multiple cylindromas of the scalp and spiradenomas that developed on her face. BSS is a clinically and histopathologically heterogeneous disorder with a common genetic background. The occurrence of different adnexal neoplasms in the same patient and in some cases in same biopsy specimen reflects the kinship of the elements of the folliculosebaceousapocrine unit. Malignant transformation rarely occurs. Due to its unpredictable biological behaviour, it should be regarded as a potentially lethal neoplasm. Close follow up and appropriate interventions are essential.

REFERENCES

1. Wevers W, Nilles M, Eckert F, Schill WB. Spiradenomas in Brooke-Spiegler syndrome. Am J dermatopathol.1993 Apr;15(2):156-61.
2. Gerretsen A, Beemer F, Deenstra W, *et, al*. Familial cutaneous cylindromas: investigations in five generations of a family.J Am Acad Dermatol1995; 33: 199-206.
3. Roberto Adrián Retamar, F. Stengel, M. E. Saadi, *et, al*. Brooke–Spiegler syndrome – report of four families: treatment with CO 2 laser, International Journal of Dermatology 2007,46, 583-86.
4. Putte S. The pathogenesis of familial multiple cylindromas, trichoepitheliomas, milia, and spiradenomas. Am J Dermatopathol 1995;17: 271-80
5. Elena Roche, María Luisa García-Melgares, José Luis Sánchez, *et, al*. Cylindrocarcinoma developed in a patient with Brooke–Spiegler syndrome. JAAD 2007 , 56, Issue 2, Supplement 2.
6. Gerretsen AL, Beemer FA, Deenstra W, van Vloten WA. Cutaneous cylindroma with malignant degeneration. Cancer. Sep 11993;72(5):1618.
7. Pizinger K, Michal M. Malignant cylindroma in Brooke–Spiegler syndrome. Dermatol 2000;201: 255-57.
8. Doherty SD, Barrett TL , Joseh AK. Brooke-Spiegler syndrome :report of a case of multiple cylindromas and trichoepitheliomas .Dermatol Online J 2008 Jul 15;14 (7):8.
9. Kaleeswaran AV, janaki VR, *et, al*. Eccrine spiradenoma. Indian J dermatol Venereol Leprol 2002;68: 236-7.
10. Criton S, Aravindan KP. Zosteriform network of spiradenoma. Indian J dermatol Venereol Leprol 1996;62:185.
11. Khalid Alhawsawi, Khalid Alaboud, Eccrine spiradenomas following lines of blaschko. JAAD 2005;52(3):50.
12. Dmitry V. Kazakov, Roman Soukup, *et, al*. Brooke-Spiegler Syndrome Report of a Case with Combined Lesions Containing Cylindromatous, Spiradenomatous, Trichoblastomatous, and Sebaceous Differentiation. Am J Dermatopathol 2005;27: 27-33.
13. Goette DK, McConnell, MA,Fowler VR. Cylindroma and eccrine spiradenoma coexistent in the same lesion. Arch Dermatol 1982 Apr; 118 (4): 274.
14. Hu G,*et, al*. A novel missence mutation in CYLD in a family with Brooke–Spiegler syndrome. J Invest Dermatol 2003; 121:732.
15. Fenske C, Banerjee P, Holden C, Carter N. Brooke–Spiegler syndrome locus assigned to 16q12-q13. J Invest Dermatol 2000; 114 : 1057-58.
16. *et, al*. A Novel Missense Mutation in the CYLD Gene in a Spanish Family With Multiple Familial Trichoepithelioma Arch Dermatol. 2007;143(9):1209-10.
17. Bowen S, Gill M, Lee DA, Fisher G, Geronemus RG. Mutations in the CYLD gene in Brooke-Spiegler syndrome, familial cylindromatosis, and multiple familial trichoepithelioma: lack of genotype-phenotype correlation. J Invest Dermatol. 2005 May;124(5): 919-20.
18. Kim C, Kovich OI, Dosik j. Brooke–Spiegler syndrome Dermatol Online J. 2007 Jan 27; 13 (1):10.
19. Layegh P, Sharifi-Sistani N, *et, al*. Brooke-Spiegler syndrome. Indian J Dermatol Venereol Leprol 2008;74: 632-4.
20. Martins C, Bartolo E. Brooke–Spiegler syndrome: treatment of cylindromas with CO2 laser. Dermatol Surg 2000;26: 877-80.
21. Rallan D, Harland CC.. Brooke-Spiegler syndrome: treatment with non ablative laser. Clin Exp Dermatol 2005;30: 355.