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Case Report

From Tuberous Sclerosis to Brooke-Spiegler Syndrome: A Diagnostic Challenge Based on a Clinical Case

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Abstract

Brooke-Spiegler Syndrome (BSS) is a rare autosomal dominant condition characterized by multiple adnexal skin neoplasms such as spiradenomas, cylindromas, and trichoepitheliomas. These tumors typically emerge during puberty and progressively increase in number and size throughout life. Due to clinical similarities with other dermatological conditions, diagnosis is challenging and requires skin biopsy and histological examination.

We report a 56-year-old woman with a 34-year history of asymptomatic cutaneous lesions on her face and scalp, unresponsive to topical tacrolimus and corticosteroids. Physical examination revealed several well-defined, skin-colored papular lesions on the central facial region and scalp. Biopsies confirmed the presence of trichoepithelioma and spiradenoma. The patient also had a significant family history of the same condition affecting multiple relatives.

This case underscores the importance of considering BSS in patients presenting with multiple adnexal tumors and a familial pattern of skin neoplasms. Early diagnosis is crucial due to the potential for malignant transformation in 5–10% of cases. Treatment remains challenging; although various modalities like surgical excision and laser therapy are used, recurrence and excessive scarring are common. Our patient responded favorably to erbium laser therapy.

ABBREVIATIONS

BSS: Brooke-Spiegler Syndrome; CYLD: Cylindromatosis Gene

INTRODUCTION

Brooke-Spiegler Syndrome (BSS) is a rare autosomal dominant hereditary condition characterized by the development of multiple adnexal skin neoplasms, most commonly spiradenomas, cylindromas, and trichoepitheliomas (also known as cribriform trichoblastomas) [1,2]. The first tumors typically appear during puberty, with a slight predilection for females [3]. Throughout life, these tumors increase in both number and size [4]. Clinical differential diagnoses include several conditions involving multiple skin and/or scalp tumors, making this syndrome a diagnostic and histological challenge.

CASE REPORT

A 56-year-old female patient with a medical history of chronic kidney disease, hypertension, diabetes mellitus, and hypothyroidism. For the past 34 years, she has developed cutaneous lesions on her face and scalp, which have progressively increased in size and number. The lesions are asymptomatic. She has received topical treatments with tacrolimus and corticosteroids without any clinical improvement.

Physical examination revealed several well-defined, skin-colored papular neoformations located in the central facial region (Figures 1-3). Additional isolated, skin-colored papules with regular borders were observed on the scalp (Figure 4). A skin biopsy was performed, resulting in diagnoses of trichoepithelioma and spiradenoma, respectively (Figure 5A,B).

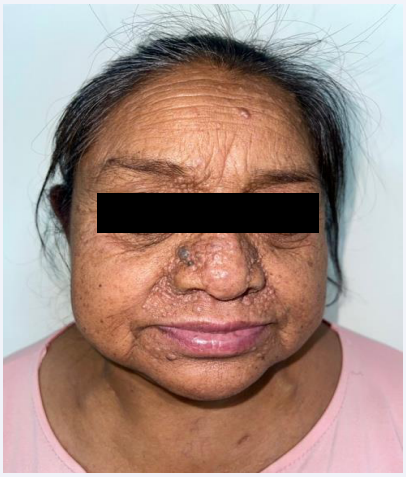

Figure 1 Well-defined, skin colored popular neoformations located in the central facial region.

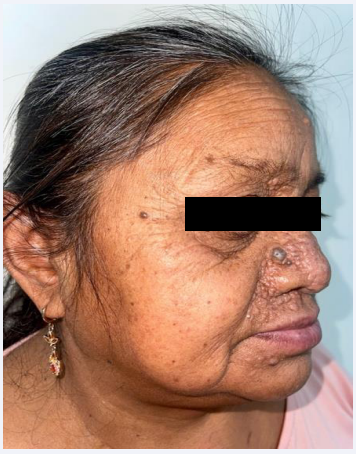

Figure 2 The neoformations are of varying sizes, with the largest measuring 0.8mm in diameter, located on the right nasal wall.

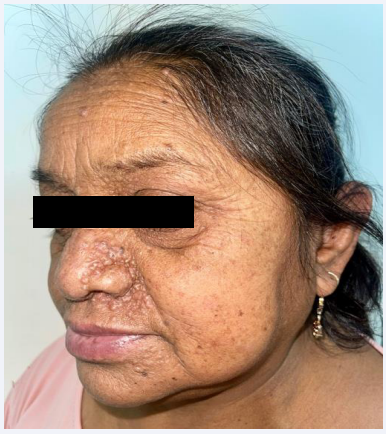

Figure 3 Skin-colored papules with regular, well-defined borders, grouped to from a large plaque affecting the supra- and infra-palpebral regions, nose, and perioral area.

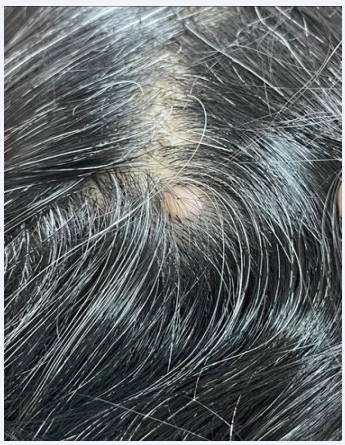

Figure 4 Isolated skin-colored papules with regular, well-defined borders located on the scalp.

The patient reports a significant family history of the same dermatological condition, affecting several relatives, including her father (deceased), four siblings, three children, and five nephews (Table 1).

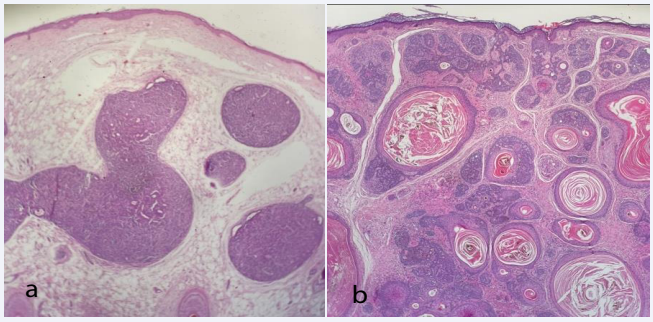

Figure 5 A: Benign adnexal tumor characterized by a pattern in which numerous small glandular lumina are observed, lined by a single layer of basophilic epithelial cells and surrounded by another group with paler cytoplasm. It exhibits a trabecular pattern, encircled by eosinophilic cell chains. Compatible with spiradenoma.

B: Benign adnexal characterized by infundibular cysts filled with basophilic lamellar keratin intermingled with basaloid cords. Surrounding these cords and epithelial nests, rings of eosinophilic, sclerotic collagen can be observed. Compatible with trichoepithelioma.

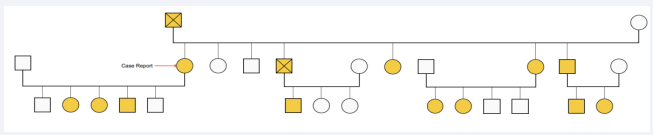

Table 1 Family tree showing her father (deceased), four siblings, three children, and five nephews affected with BBS.

DISCUSSION

Brooke-Spiegler Syndrome (BSS) is a rare genodermatosis caused by germline mutations in the Cylindromatosis Gene (CYLD), a tumor suppressor located on chromosome 16q12-q13 [1,5].

The disease is characterized by multiple cutaneous adnexal neoplasms such as cylindromas, trichoepitheliomas, and/or spiradenomas; in fact, these constitute its diagnostic criteria [6]. Clinically, they are indistinguishable, making skin biopsy and histological identification crucial for diagnosis. These lesions present as multiple papules or nodules on the head and neck but can also appear on the trunk, genitals, and axillae [7].

Although the tumors are usually considered harmless, but there are case reports where malignant transformation can occur in 5–10% of all patients with BSS. For example, spiradenoma may evolve into spiradenocarcinoma, cylindroma into cylindrocarcinoma, and trichoepithelioma may develop into basal cell carcinoma [2,8], highlighting the importance of early diagnosis [3].

To date, over 200 cases of Brooke-Spiegler syndrome (also known as CYLD cutaneous syndrome or CCS) have been documented, with an estimated incidence of approximately 1 per 100,000 in the United Kingdom [5].

Differential diagnoses include Birt-Hogg-Dubé syndrome, neurofibromatosis type 1, Cowden syndrome, tuberous sclerosis complex, Marie-Unna hypotrichosis, basal cell nevus syndrome,

pilar cysts, and multiple syringomas [4]. Our patient had been treated for over 30 years with a diagnosis of tuberous sclerosis, despite not meeting the diagnostic criteria for this disease and without skin pathology. A biopsy performed at our hospital led to the identification of the array of adnexal tumors that define this condition. Furthermore, the history of multiple affected family members directed suspicion toward this diagnosis.

Brooke-Spiegler syndrome is a devastating disease with no consensus standard of treatment. Various modalities have been employed, including surgical excision, electrocauterization, CO_2 laser ablation, dermabrasion, and radiofrequency [9] however, nodule recurrence is common, and excessive scarring may occur. With the diagnosis established, we initiated erbium laser therapy for our patient with favorable results.

CONCLUSION

Brooke-Spiegler Syndrome is a rare genodermatosis characterized by the appearance of multiple adnexal skin neoplasms, which poses a diagnostic challenge due to its similarity to other skin diseases. Confirmation of the diagnosis through biopsy and histological identification is essential, as there is a 5-10% risk of malignant transformation in these tumors. Despite the various treatments available, such as surgical excision and laser ablation, there is no standard approach, and recurrence is common, highlighting the importance of early diagnosis and appropriate follow-up.

ACKNOWLEDGMENTS

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ETHICAL PERMISSION

The patient has given informed consent during his treatment for the publication of this article.

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