

## مقاله گزارش موردی

### سندرم بروک اسپیگلر

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#### چکیده

**معرفی:** سندرم بروک اسپیگلر یک بیماری اتوزومال غالب نادر است که توسط ایجاد تومورهای متعدد ضمام پوستی شامل سیلندروما، تریکوآپیتلیوما و اسپیرآدنوما مشخص می شود.  
**توصیف نمونه:** بیمار یک خانم ۴۹ ساله با سابقه ظهور تدریجی ندولهای متعدد که عمدتاً روی اسکالپ و صورت قرار داشته مراجعه کرده است. آزمایش پا تولوژیک ضایعات سیلندروما با کانونهایی از اسپیرآدنوما را نشان داد.  
**بحث:** سندرم بروک اسپیگلر توسط موتاسیون های مختلفی در ژن سیلندروماتوزیس که یک ژن سرکوب کننده تومور است، به وجود می آید. این جهشها منجر به سیلندروما و تریکوآپیتلیوما های متعدد میشود. تبدیل به بدخیمی در سیلندروما ی منفرد ممکن است رخ دهد. اما در نوع متعدد شایعتر است و نیاز به پیگیری دقیق طولانی مدت دارد.

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CASE REPORT

## Brooke-Spiegler Syndrome

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ABSTRACT

**Introduction:** Brooke-Spiegler Syndrome (BSS) is a rare autosomal dominant disease characterized by the development of multiple adnexal cutaneous tumors such as cylindromas, trichoepitheliomas and spiradenomas.

**Case Description:** A 49 years old female patient presented with a history of gradual appearance of multiple nodules situated predominantly on the scalp and face. Pathologic examination of lesions revealed cylindroma with foci of spiradenoma.

**Discussion:** Brooke-Spiegler Syndrome (BSS) caused by various mutations of the cylindromatosis gene (CYLD), a tumor suppressor gene resulting in multiple cylindromas and trichoepitheliomas. Malignant transformation may develop within solitary cylindromas, but more common in multiple variant and requires careful followup surveillance.

**Keywords :** *Brook-Spiegler Syndrome, Adenoid Cystic Carcinoma, Trichoepithelioma*

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## INTRODUCTION

The Brooke-Spiegler Syndrome (BSS) inherited by autosomal dominant transmission consists of multiple trichoepitheliomas, cylindromas and spiradenomas. The gene for this syndrome has been mapped to chromosome 16q12-13 (1). Mutations in cylindromatosis gene (*CYLD*), a tumor suppressor gene, are responsible for the manifestations of the disease. Cylindromas can present singly or in multiple format. Cylindromas may coalesce and form giant mosaic plaques on the scalp referred to as 'turban' tumor (2). Reported treatments of cylindromas include excision, dermabrasion, electrodesiccation, CO<sub>2</sub> laser, cryotherapy, and radiotherapy or topical applications of aspirin derivatives (3).

## CASE PRESENTATION

A 49 years old female patient presented with a history of gradual appearance of multiple scalp tumors since the age of 20. Her daughter, brother and aunt also had a history of similar cutaneous lesions. On examination, a group of round-to-oval skin-colored to pink papules and nodules measuring 5 to 15 mm in diameter was seen on the face, particularly in the forehead, nose, chin and less commonly on the cheek and periorbital region (Figure 1). Addition to this, multiple large exophytic tumoral and nodular lesions was also seen on the scalp. The tumors of the scalp were pinkish red, dome-shaped, firm, tender. They measured 2 to 4 cm in diameter (Figure 2). There was also a subcutaneous firm nodule with a size of 0.5x0.5 cm on the patient's left breast. Her general condition was good.

The histopathology of the scalp nodule revealed a well-defined dermal lesion composed of islands and cords of basaloid cells arranged in a jigsaw

puzzle-like pattern and surrounded by eosinophilic hyaline bands. Two populations of basaloid cells with, peripheral palisading cells and central large cells were suggestive of cylindroma with foci of spiradenoma (Figure-3).

The histopathology of a papule from the patient's forehead demonstrates nests of basaloid cells arranged in a jigsaw puzzle-like pattern and separated by hyaline basement membrane material, consistent with cylindroma.

Histopathologic examination of papule from the nose of patient's daughter revealed well-defined tumor composed of basaloid cell nest and sheet with keratin plug surrounded by fibroblastic stroma consistent of trichoepithelioma.

Her 40 years old brother had multiple small papules, predominantly on nasolabial fold. Multiple biopsy performed were typical for trichoepithelioma and cylindroma.

According to clinical features and histopathologic findings, a diagnosis of Brooke-Spiegler Syndrome (BSS) was made.

In this patient, a number of large cylindroma of the scalp were excised, and split-thickness skin graft was completed. For smaller lesions of face electrodesiccation was performed.

## DISCUSSION

The Brooke-Spiegler Syndrome inherited by autosomal dominant transmission consists of multiple trichoepitheliomas, cylindromas and spiradenomas resultant from mutations or loss of heterozygosity of the cylindromatosis gene (*CYLD*) located at 16q12-q13 (1). Other lesions reported with BSS include parotid basal cell adenomas, organoid nevi, syringomas, and basal cell carcinomas. The cylindromatosis gene is a tumor suppressor gene, and its product represses the tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) pathway. Activation of this pathway increases the expression of nuclear factor- $\kappa\beta$  (NF- $\kappa\beta$ ), a

transcription factor that regulates a number of anti-apoptotic genes involved in the proliferation of skin appendages. Mutations in the CYLD gene result in increased expression of NF- $\kappa$ B and lead to apoptotic resistance and tumors of the folliculosebaceousapocrine unit including cylindromas, trichoepitheliomas, and spiradenomas (4). The penetrance of the gene has been estimated to be between 60-100 percent (5).

The disease also demonstrated variable clinical and histopathological features among the affected members of a single family, in which older members tend to have larger lesions that are also greater in number as compared to the younger members (6). This condition was obvious in our patient's family, where the younger daughter (21 years old) had multiple trichoepithelioma lesions on her face. Rare lesions may occur in the breast sporadically or in association with Brooke-Spiegler Syndrome as in our patient (1). Although cylindromas are usually benign neoplasms, malignant transformation to cylindroma carcinoma is well documented. The malignant cylindroma is locally aggressive, often metastasizes, so follow-up care is also recommended (7).

The various modes of treatment which have been suggested for the adnexal tumors in BSS patients include excision of the tumor, dermabrasion, electrodesiccation, cryotherapy, and radiotherapy using argon and Co2 lasers (8). A study reported that treatment with erbium-YAG laser causes less scars and fewer recurrences(9). It has been proven that the Topical salicylic acid has been used with some success in patients with multiple cylindromas (10).

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