International Clinical and Medical Case Reports Journal
Case Report (ISSN: 2832-5788)

Brooke-Spiegler Syndrome: A Case Report

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Citation: *Khudheeja Ahmed, Juwayria Ahmed, Mohammed Habeeb Ahmed. Brooke-Spiegler Syndrome: A Case Report. Int Clinc Med Case Rep Jour. 2024;3(3):1-2.*

Received Date: 20 March, 2024**; Accepted Date:** 25 March, 2024**; Published Date:** 27 March, 2024

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ABSTRACT

Brooke-Spiegler Syndrome (BSS or BRSS), refers to a genetic disorder marked by diverse dermatological neoplasms. BSS, found across all ethnic groups with an unknown incidence and prevalence, impacts both genders equally. A 53-year-old female diagnosed with BSS sought cardiac consultation due to complaints of palpitations. Upon examination, multiple pinkish-colored, firm papulonodular lesions were observed on mainly the central forehead and nasal area. This case is presented due to the rarity of BRSS, emphasizing the need to document and share information about this infrequently encountered syndrome.

Keywords: Case Report; Lesions; Brooke-Spiegler; Dermatology

INTRODUCTION

Brooke-Spiegler syndrome (BSS) has several names, often being called CYLD cutaneous syndrome.[1] It is an uncommon condition in which cutaneous tumors including “cylindromas, spiradenomas, and trichoepitheliomas" are observed.[2] These benign tumors are more so located on the head and neck.[1] “Trichoblastoma, basal-cell carcinomas, follicular cysts, and organoid nevi” are also reported neoplasms.[2] Classic BRSS manifests often with various cutaneous tumors such as “spiradenoma, cylindroma, and trichoepithelioma”.[1] A variant called multiple familial trichoepithelioma (MFT1), is identified in cases where solely trichoepitheliomas are observed.[1,3] Familial cylindromatosis represents a type of BRSS marked by cylindromas alone.[1,3] Additionally, cases documenting “spiradenomas or spiradenocylindromas only” have been noted.[1]

The skin tumors associated with BRSS can exhibit a broad range regarding somatic mutations.[1] These neoplasms emerge in “childhood and early adolescence,” increase in size and count over time.[1] Despite their typically benign nature, these tumors can lead to disfigurement, and there exists a risk of malignant transformation in “pre-existing neoplasms in 5 to 10 percent of the patients”.[1,4]

A review was conducted of 55 cases and found that age only is thought to be a predictor for malignant transformation,[1,5] since most malignancy was documented after 40 years of age.[1] When a case of multiple skin tumors occurring from childhood along with a family history of these tumors is documented, BRSS can be diagnosed.[1] The family history may indicate an "autosomal dominant pattern of inheritance," which is a part of BRSS's definition.[1] We are presenting this case due to the exceptional rarity of BRSS, emphasizing the significance of documenting and sharing insights about this infrequently encountered genetic disorder.[1]

CASE PRESENTATION

A 53-year-old female presented with complaints of palpitations on 08/14/23 for a cardiac consultation. She stated that she had seen a cardiologist three years ago. She complained of experiencing worsening episodes of palpitations, occurring intermittently, for the past several weeks. She denied alcohol intake and has never smoked. Her physical exam noted no motor or sensory defects and she exhibited normal reflexes and tone. There was no cyanosis, clubbing, or edema. Acne and scarring was noted at periorbital area, perioral area, and around nasal area. Figure 1,2 In the musculoskeletal part of the physical exam, multiple lesions surrounding the vermilion border of the lip bilaterally were noted, as well as other tumorous lesions of skin of scalp and neck. (Figure 1,2)

She is a known patient of end stage kidney disease with renal failure and is on hemodialysis (HD) for the past 16 years. She has had a kidney transplant in 2016. There was an arteriovenous (AV) fistula for HD in the left upper arm. She also has sleep apnea, hyperlipidemia, hypertension, cardiomegaly, diastolic dysfunction, hypovitaminosis D, and obesity, as well as an anxiety disorder. She is on long term (current) immunosuppressive medication of mycophenolate mofetil. She has a history of BRSS, with a record of a shave and punch (S/P) biopsy of the left periorbital area, after which a possible cancer had been ruled out. The neoplasms began forming when she was about 27 years old. She denies any family history of BRSS. She applies Tretinoin (0.05 mg QD) and reports beneficial effects.

She had a stroke in 2014. Her surgical history includes a thyroidectomy. Her family history includes her mother having hypertension. Her current medications include Amlodipine (5 mg, PO QD), aspirin (81 mg, PO QD), Atorvastatin (40 mg, PO QHS), and Tacrolimus. She is also taking Vitamin D3 and Vitamin C supplements.

Her EKG was done on this date (08/14/23), and sinus rhythm was within normal range. Her echocardiogram done on 10/23/23 was a technically difficult study due to the patient's obesity. The left ventricle appeared normal in size and function. The results indicated an ejection fraction (EF) of 55-

60%, E-A reversal, mild left ventricular hypertrophy (LVH), moderate left atrial enlargement, mitral annular calcification (MAC), mild mitral regurgitation (MR), and mild tricuspid regurgitation (TR). The 24-hr Holter done on 10/23/23 showed sinus rhythm with a heart rate ranging from 56 bpm to 132 bpm, with an average rate of 73 bpm. No arrhythmias were seen. On a later followup, an adenosine cardiolite stress test was recommended to assess for angina and coronary artery disease (CAD).

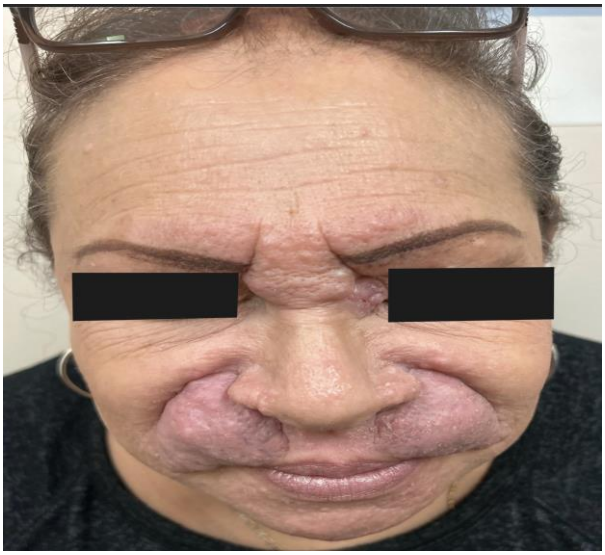

Figure 1: Multiple pinkish-colored lesions affecting nasal area and center of forehead are visible.

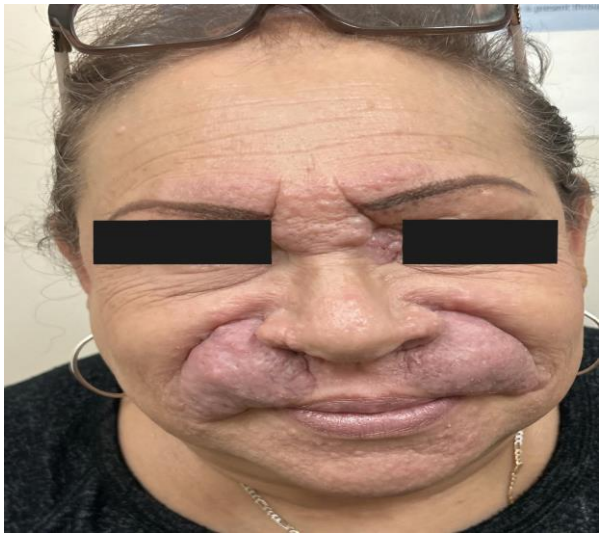

Figure 2: Multiple pinkish-colored lesions affecting nasal area and center of forehead are visible.

DISCUSSION

While specific histologic features may be more common in some patients, these tumors are found spaced together in patients with this diagnosis.[1,6,7] Spiradenomas associated with BRSS are purplish nodules that tend to concentrate on the face and scalp and may be found near cylindromas.[1] These neoplasms can cause pain and grow to be several centimeters.1 For patients diagnosed with the variant MFT1, numerous trichoepitheliomas are visible as “skin-colored papules,” primarily around the nasal area.[1,2,8]

Cylindromas, characterized by a slow rate of growth, manifest as “red, pink, or bluish papules” that have variable sizes under a few centimeters and are seen on the head/neck region and form “turban tumors”.[1,4,9] They typically emerge before or during the time of puberty, multiplying throughout life, and may cause pain as nerves are compressed with increased tumor size.[1] Malignant change, though uncommon and “reported in 5 to 10% of cases,” is indicated by increased growth rate, bleeding, or the formation of ulcers.[1,4,5,10,11] As such, it is advisable that patients with BRSS receive consistent monitoring throughout their lives and that their families also receive genetic counseling.[1] The characteristic and diagnostic histopathology of cylindromas reveals lesions in which epithelial cells make up “islands" that present in a “jigsaw puzzle” organization with basaloid cells around the edges.[1,3,5]

BRSS is an uncommon disease, and its incidence has not been quantified, as well as its prevalence.[1] It has been documented across all ethnicities and impacts men and women at the same rates.[1] Interestingly, patients presenting with only cylindromas are more likely to be female, with a ratio ranging from “6:1 to 9:1”.[1] BRSS patients have been occasionally found to present with membranous basal cell adenoma, a condition where tumors grow within the parotid gland, as well as the “minor salivary glands”.[1,2,12] Histological assessment of tumor biopsies is essential for determining the exact variety of tumor.[1,6] In individuals with BRSS, biopsies of tissues find a coexistence of several neoplasm types.[1,6]

BRSS is conclusively diagnosed upon confirmation of a mutation relating to the CYLD gene in “chromosome 16q12-q13,” which normally functions as a “tumor suppressor gene”.[1,3,13] It is expressed through “a deubiquitinating enzyme” that downregulates a pathway called the “nuclear factor kappa B (NF-kB) signaling pathway”.[1,14] In BRSS, inappropriate levels of transcription of this pathway results in the growth of cylindromas, spiradenomas, trichoepithelioma, and other related tumors.[1,15]

Therefore, some anti-inflammatory treatment options are being considered that inhibit this pathway, including salicylate[1,16] and prostaglandin A1.[2] Nonsurgical options such as “curettage, cryosurgery,

electric cautery, and laser resurfacing" are available, but surgically addressing neoplasms is highly recommended for BRSS cases to reduce risk and symptoms.[1]

The rarity of Brooke-Spiegler Syndrome underscores the significance of this case report, as the scarcity of documented cases makes each new insight valuable for enhancing our understanding of this rare genetic disorder.[3] Given the unknown exact incidence and prevalence, this case report contributes essential data to the medical literature, offering insights into the clinical manifestations of this infrequently encountered syndrome.[3] We believe that this report and further documentations of BSS are necessary for bridging knowledge gaps surrounding the disorder, offering clinicians, researchers, and geneticists valuable information to better diagnose and manage the complexities of BSS, whose rarity demands careful documentation and analysis.

CONCLUSION

Brooke-Spiegler syndrome, a highly uncommon disorder due to a mutation in a tumor suppressor gene, presents with dermatological neoplasms. A 53-year-old female diagnosed with BSS sought cardiac consultation due to complaints of palpitations. Multiple lesions surrounding the vermilion border of the lip bilaterally were observed, along with other tumorous lesions of the skin of the scalp and neck. The rarity of Brooke-Spiegler Syndrome highlights the significance of this case report, as the limited number of documented cases adds value to each new insight, contributing to an enhanced understanding of this rare genetic disorder.

DECLARATIONS

Funding: None to Declare

Conflict of Interest: None to Declare

Data Availability Statement: The data that support the findings for this study are available from the corresponding author upon reasonable request.

Ethics Statement: This case report was concluded with the consent of the patient.

Author Contributions: All authors contributed in gathering data, writing the case report, researching relevant literature, and finalizing the report.

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