SkIndia Quiz 27

Rhinophyma and numerous facial papule and nodules in a 39-year-old woman

Vikram K. Mahajan, Anju Lath Sharma, Pushpinder S. Chauhan, Karaninder S. Mehta, Saurabh Sharma[1]

Departments of Dermatology, Venereology, Leprosy and [1]Pathology, Dr. R.P. Government Medical College, Kangra, Tanda, Himachal Pradesh, India

A 39-year-old female presented with numerous papulonodular lesions over face appearing since the age of 7 years. These had been asymptomatic and relatively stable in size and number until 3-4 years back when she noticed a coalescence of lesions over her mid face/nasal bridge and progressive enlargement of her nose. Her medical history was unremarkable. Her 23-year-old daughter had also beginning to develop similar lesions over the face since the age of 17 years. Her parents, one male sibling, two sons, and another daughter were reportedly healthy. Physical examination showed rhinophyma-like enlarged nose and innumerable, 2-10 mm sized, skin-colored, smooth surfaced, papules, and nodules involving the whole face [Figure 1]. The glabella, periocular, nasal bridge, alae nasi, nasolabial folds, perilabial and chin were involved predominately. Her daughter also had few lesions of similar morphology over the nose and nasolabial folds. The findings of hematoxylin and eosin stained histology sections of a nodular lesion are shown in Figures 2 and 3.

WHAT IS YOUR DIAGNOSIS?

Access this article online

Website: www.idoj.in

DOI: 10.4103/2229-5178.182404

Quick Response Code:

Address for correspondence:
Dr. Vikram K. Mahajan, Department of Dermatology, Venereology and Leprosy, Dr. R.P. Government Medical College, Kangra, Tanda - 176 001, Himachal Pradesh, India.
E-mail: vkm1@rediffmail.com

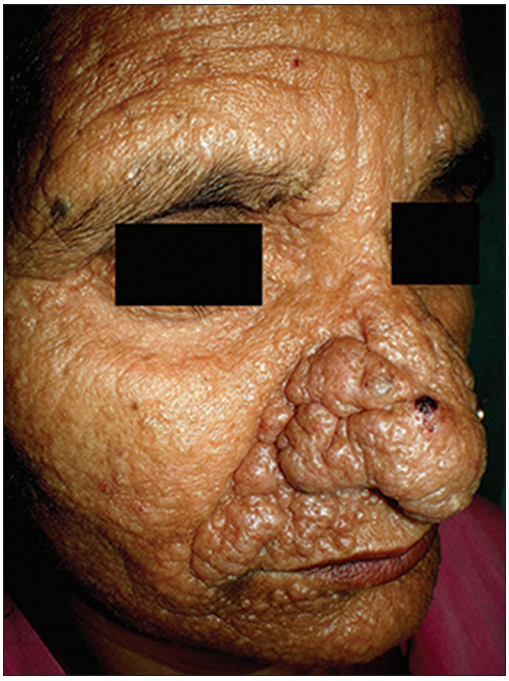

Figure 1: Rhinophyma and innumerable skin-colored, smooth surfaced, papulo-nodular lesions over the whole face, predominately involving the nasal bridge, alae nasi, and nasolabial folds

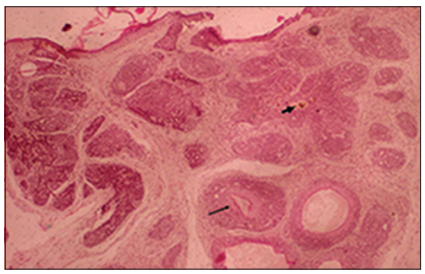

Figure 2: Multiple, well-circumscribed nests, lobules and cords separated by fibrous stroma. Calcification of cystic material (thick arrow), and primitive hair shaft-like structures (thin arrow) are seen (H and E, ×10)

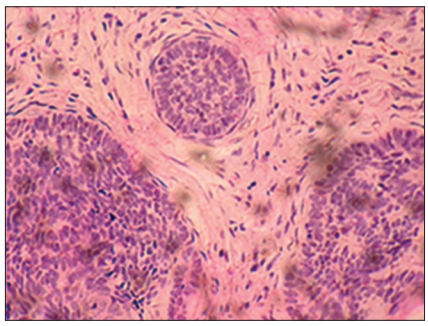

Figure 3: Well-circumscribed nests of palisading basaloid cells, without pleomorphism, cellular atypia or mitosis are seen and suggest well-differentiated trichoepitheliomas (H and E, ×40)

ANSWER

Diagnosis: Brooke–Spiegler syndrome: Multiple familial trichoepithelioma

Microscopic findings

Histopathology shows multiple circumscribed lobules and cords of palisading basaloid cells separated by fibrous stroma [Figures 2 and 3]. There is no pleomorphism, cellular atypia or mitosis. Presence of calcified cystic material and primitive hair shaft-like structures suggests well differentiated trichoepitheliomas.

DISCUSSION

Brooke–Spiegler syndrome (familial cylindromatosis, multiple familial trichoepithelioma, turban tumor syndrome), an autosomal dominant condition, is characterized by multiple trichepitheliomas, spiradenomas, or cylindromas with or without overlapping features. There is no racial or gender predilection and its exact prevalence remains unknown. Once considered separate entities both multiple familial trichoepithelioma and Brooke-Spiegler syndrome have the same gene mutations and are now considered phenotypic variants. The mutations in the *CYLD* gene (cylindromatosis oncogene, mapped to 16q12-q13), the product of which functions as a deubiquitinating enzyme, negatively regulates the nuclear factor kappa B (NFκ-B) that is responsible for the development of epidermal appendages and oncogensis.[1] On the other hand, the genetic mutation for multiple familial trichoepithelioma is mapped to a locus on chromosome 9p21, while genetic mutations in sporadic trichoepitheliomas have been mapped to PTCH, which is also involved in nevoid basal cell syndrome.[2,3] It is possible that mutations in the genes regulating proliferation and differentiation of putative stem cells of the pilosebaceous-apocrine unit lead to different combinations of adenexal tumors or neoplasms with features of pilosebaceous differentiation (trichoepithelioma, basal cell carcinomas [BCCs]) or apocrine differentiation (spiroadenoma, spiroadenocylindroma).[4] In addition, involvement of a defective tumor suppressive gene located on chromosome 16q too has been suggested. However, other yet to be identified genes may also be responsible for phenotypes not associated with *CYLD* or PTCH mutations as no firm genotype-phenotype correlations could be demonstrated in a few cases.[3,5]

Clinically, skin-colored, small, coalescing papules and nodules start appearing in childhood/puberty, and gradually increase in number and size for several years before stabilizing. Nearly 50% of the lesions occur over face typically concentrating around forehead, nasolabial folds and upper lip. Although rhinophyma is principally associated with end stage rosacea, significant cosmetic disfigurement, even to an extent of leonine facies, may occur in Brooke-Spiegler syndrome. Although concurrent occurrence of trichoepitheliomas, cylindromas and spiradenoms/spiradenocylindromas is not unusual, it has been considered sporadic occurrence and unrelated to Brooke–Spiegler syndrome.[6,7] Malignant transformation to BCC may happen decades later presenting with ulceration, inflammation, or necrosis and these patients are also at increased risk of adenomas and adenocarcinomas of the salivary glands warranting a long term follow up.[8]

Diagnosis is mainly clinicopathologic and BCC remains the major histologic differential. Primitive hair structures, cornified cysts, cribriform pattern, and stromal fibrosis are pathognomic of trichoepithelioma. In addition, fibroblastic stroma in trichoepithelioma will stain positive for CD34 and not in BCC, which may sometimes be difficult to differentiate histologically. Many other genetic syndromes presenting with multiple facial lesions; BCCs (Gorlin's syndrome), trichilemmomas (Cowden syndrome), and perifollicular fibroma (Brit–Hogg–Dube syndrome), sebaceous neoplasia and keratoacanthoma (Muir–Torre syndrome), or colloid milia, and syringomas require differentiation clinically and histologically. Solitary lesions can be excised and for others split skin graft, photodynamic therapy, flattening of the lesions by dermabrasion, electrodessication cryosurgery or LASER (argon, CO_2, erbium, ND: Yag plus, CO_2) therapy have been used with variable results. Recurrences are common and repeated procedure(s) may be necessary for cosmetic improvement. Partial response to topical imiquimod (5%) has been reported. Sodium salicylate and prostaglandin A1 that inhibit NFκ-B activity and restore growth control are experimental therapies for cylindromas.[9]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

REFERENCES

1. Rajan N, Langtry JA, Ashworth A, Roberts C, Chapman P, Burn J, *et al*. Tumor mapping in 2 large multigenerational families with CYLD mutations: Implications for disease management and tumor induction. Arch Dermatol 2009;145:1277-84.
2. Harada H, Hashimoto K, Ko MS. The gene for multiple familial trichoepithelioma maps to chromosome 9p21. J Invest Dermatol 1996;107:41-3.
3. Ponti G, Nasti S, Losi L, Pastorino L, Pollio A, Benassi L, *et al*. Brooke-Spiegler syndrome: Report of two cases not associated with a mutation in the CYLD and PTCH tumor-suppressor genes. J Cutan Pathol 2012;39:366-71.

4. Bozi E, Katoulis AC. Multiple familial trichoepitheliomas. Orphanet Encyclopedia, April 2004. Available from: http://www.orpha.net/data/patho/GB/uk-kindler.pdf. [Last accessed on 2013 Feb 28].
5. Grossmann P, Vanecek T, Steiner P, Kacerovska D, Spagnolo DV, Cribier B, *et al*. Novel and recurrent germline and somatic mutations in a cohort of 67 patients from 48 families with Brooke-Spiegler syndrome including the phenotypic variant of multiple familial trichoepitheliomas and correlation with the histopathologic findings in 379 biopsy specimens. Am J Dermatopathol 2013;35:34-44.
6. Trufant J, Robinson M, Patel R. Brooke-Spiegler syndrome. Dermatol Online J 2012;18:16.
7. Kacerovska D, Vanecek T, Spagnolo DV, Bisceglia M, Zelger B, Michal M, *et al*. A clinicopathologic and molecular biologic study of patients presenting with few adnexal tumors (two to four) from the morphological spectrum of Brooke-Spiegler syndrome. Am J Dermatopathol 2013;35:19-24.
8. Bowen S, Gill M, Lee DA, Fisher G, Geronemus RG, Vazquez ME, *et al*. Mutations in the CYLD gene in Brooke-Spiegler syndrome, familial cylindromatosis, and multiple familial trichoepithelioma: Lack of genotype-phenotype correlation. J Invest Dermatol 2005;124:919-20.
9. Brummelkamp TR, Nijman SM, Dirac AM, Bernards R. Loss of the cylindromatosis tumour suppressor inhibits apoptosis by activating NF-kappaB. Nature 2003;424:797-801.

Cite this article as: Mahajan VK, Sharma AL, Chauhan PS, Mehta KS, Sharma S. SkIndia Quiz 27: Rhinophyma and numerous facial papule and nodules in a 39-year-old woman. Indian Dermatol Online J 2016;7:350-2.

Source of Support: Nil, **Conflict of Interest:** None declared.