Familial Dermal Eccrine Cylindromatosis with Emphasis on Histology and Genetic Mapping

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Abstract

Familial cylindromatosis (FC) is an autosomal dominant disorder with apparently complete penetrance, but variable expression. There is an increasing evidence that FC is clinically, genetically, and histologically heterogeneous disorder as the simultaneous occurrence of cylindromas and other tumors of skin appendages within the affected individuals and families. The presence of multiple scalp cylindromas is often associated with autosomal dominant Brooke-Spiegler syndrome, a condition in which there are co-existent facial trichoepitheliomas and spiradenomas. We present here a case of multiple cylindromatosis in a family affecting many members successively.

Keywords: Adenexal, Cylindromatosis, Turban

Introduction

Cylindromas are benign skin adnexal tumor with ductal differentiation. It occurs mostly on the forehead and scalp. Lesions may cover the entire scalp like a turban (turban tumor). Less than 10% of cases may occur on trunk and limbs.[1] This is inherited in an autosomal dominant manner and presents as multiple, smooth, firm, pink to red, and pedunculated nodules of various size.

Clinically, cylindroma can present as: (i) A solitary type, occurring sporadically in patients who have no family history of similar lesions (ii) A variant of cutaneous cylindromas; the multiple type, occurring on the head and neck can also be seen on the trunk and the extremities. Solitary cylindromas are lesions that affect middle-aged and elderly persons. Multiple, inherited cylindromas usually begin in early adulthood and increase in size and number throughout the life.[2]

We are presenting here a case of familial cylindromatosis (FC), which was diagnosed cytologically and confirmed histopathologically along with genetic mapping study.
Histopathologically, the lesion consisted of well-circumscribed islands of epithelial cells surrounded by a dense membrane material, and focally containing hyaline globules. Islands of epithelial cells fit together like pieces of “jig-saw” puzzle. Two distinct cell populations were seen; smaller peripheral basoloid cells in palisade arrangement and larger central cells with vesicular chromatin [Figure 6].

**Discussion**

Term cylindroma was first introduced by Ancell in 1842.[3] Cylindromas occur as numerous papules, nodules or tumors of various sizes. Brooke-Spiegler syndrome (BSS) known as familial autosomal dominant cylindromatosis is a rare disorder characterized by various adnexal tumors including cylindromas, trichoepitheliomas, and spiradenomas.[4]

Cylindroma is a dermal tumor with no attachment to the epidermis. Tumor islands are composed of two cell types. Peripheral cells are small and highly basophilic. Larger, more pale-staining cells are seen centrally. The lesion is composed of numerous oval and polygonal nests molded into a jig-saw-like pattern. Masses of epithelial cells are surrounded and penetrated by a hyaline sheath closely resembling a basement membrane. This sheath separates the tumor from the dermal mesenchyme, yet does not interfere with tumor growth and proliferation.

Malignant cylindromas demonstrate islands of cells displaying marked anaplasia and pleomorphism of nuclei. Mitoses are increased and are abnormal. Besides invasion into surrounding tissue, loss of the delicate hyaline sheath occurs. Malignant transformation is rare. Death in such patients occurs via visceral metastasis or hemorrhage or meningitis due to transcranial invasion/erosion.[5]

FC is a condition involving multiple skin tumors that develop from structures associated with the skin (skin appendages), such as hair follicles and sweat glands. People with FC typically develop large numbers of tumors called cylindromas. Individuals with FC occasionally develop other types of tumors, including growths called spiradenomas and trichoepitheliomas.

Multiple cylindromas are usually seen as a component of BSS or as the only skin lesions of FC. Patients with BSS are predisposed to multiple skin appendage tumors such as cylindroma, trichoepithelioma, and spiradenoma. They are occasionally present in association with basal cell adenomas of the parotid glands, milia, organoid nevi, and basal cell carcinomas.[6,7]

BSS as well as sporadic cylindromas results from mutations leading to loss of both alleles of the cylindromatosis gene (CYLD1). The CYLD gene is located on the long (q) arm of chromosome 16 at position 12.1. CYLD1 is a tumor suppressor gene, which has been shown to inhibit tumor cell...
proliferation by blocking Bcl-3 dependent NF-κB signaling. Loss of CYLD1 function increases resistance to apoptosis.

People with FC are born with a mutation in one of the two copies of the CYLD gene in each cell. For tumors to develop, a second mutation or deletion of genetic material involving the other copy of the CYLD gene must occur in certain cells during a person’s lifetime. There is no curative therapy yet available for multiple cylindromas. Treatment modalities for cylindromas include excision, dermabrasion, electrodessication, Carbon dioxide laser, cryotherapy, and radiotherapy. Currently, surgical excision or laser ablation is the treatment of choice in multiple...
cylindromas multiple cylindromas usually require numerous tumor excisions or extensive plastic surgery with coverage by split thickness graft. Total scalp and forehead excision with coverage by skin grafts has been described in patients with turban tumors. Recently, a therapeutic attempt has been made to treat a single cylindroma in BSS with topically applied salicylic acid at varying concentrations. Salicylic acid acts by interfering with the NF-κB signaling pathway.\[10,11\]

Follow-up care of patients with multiple cylindromas is recommended because of the tendency for new lesions to develop. Follow-up care is also recommended because of the risk of malignant degeneration.

**Conclusion**

This is a rare case of FC affecting many family members in the pedigree without association with other tumors involved in BSS and incidence of this case occurring now in the youngest member of the family.

**References**


How to cite this article: Dhir G, Makkar M, Suri V, Dubey VK. Familial dermal eccrine cylindromatosis with emphasis on histology and genetic mapping. Ann Med Health Sci Res 2013;3:S3-6.

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