Brooke-Spiegler syndrome

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Identity

Other names
Ancell-Spiegler cylindromas, Familial cylindromatosis, Turban tumor syndrome, Brooke-Fordyce trichoepitheliomas, Multiple familial trichoepitheliomas

Note
Familial cylindromatosis/Turban tumor syndrome and multiple familial trichoepitheliomas were considered as separate diseases; it is now known that they are allelic diseases and represent two ends of the Brooke-Spiegler syndrome spectrum (Welch et al., 1968; Young et al., 2006). Familial cylindromatosis/Turban tumor syndrome is characterized by cylindromas and multiple familial trichoepitheliomas by trichoepitheliomas as the only tumor type.

Inheritance
Autosomal dominant disease, with high penetrance, and penetrance increasing with age, and variable expressivity. Female predominance (8M/13F).

Clinics

Phenotype and clinics
Brooke-Spiegler syndrome is a skin appendage tumors syndrome, with development of cylindromas, spiradenomas, and/or trichoepitheliomas, from late childhood, and gradually increase in size and numbers. Cylindromas are dermal papules and nodules. They grow slowly. They classically occur on the scalp and occasionally on the face, trunk or extremities. Scalp cylindromas can become numerous and may eventually cover the entire scalp ("turban tumors"). They present as multinodular, well circumscribed nest of undifferentiated basaloid cells in a characteristic "jigsaw puzzle" pattern.

Spiradenomas are usually located on the face, the trunk and extremities. A frequent symptom is pain. They present as bluish nodules of basaloid cells in the dermis, with presence of numerous lymphocytes, in contrast to what is found in cylindromas. There are hybrid forms between cylindromas and spiradenomas. Trichoepitheliomas typically occur on the face, predominantly on the nose, the nasolabial folds, and the lips. Trichoepitheliomas derive from the trichoblast (i.e. the folliculo-sebaceous-apocrine germ). They are small skin-colored papules or nodules, with nests of basaloid cells forming cysts containing horn cells (with keratin) (Lee et al., 2005; Kim et al., 2007; Blake and Toro, 2009).

Neoplastic risk
Apart from cylindromas, spiradenomas, and trichoepitheliomas, patients with Brooke-Spiegler syndrome are also at risk of basal cell carcinomas and syringomas. Cylindromas may transform into cylindrocarcinomas, which are locally aggressive and metastasize. Spiradenomas may transform into spiradenocarcinomas or show sarcomatous differentiation. An increased risk of developing tumors of the salivary glands has also been described (basal-cell adenomas and adenocarcinomas of the parotid glands and minor salivary glands) (Lee et al., 2005; Kim et al., 2007; Blake and Toro, 2009).

Treatment
Removal by surgery. Salicylic acid is efficient in only a small proportion of tumours.

Genes involved and proteins

Note
Although most cases of Brooke-Spiegler syndrome have been described with a mutation in CYLD (Bignell et al., 2000; 68 unique CYLD mutations have been
identified so far), some cases do not have mutations or loss of heterozygosity in CYLD gene (Ponti et al., 2011).

Transcriptome of the tumors: cylindroma and spiradenoma tumours showed similar profile, with LOH at 16q found in the majority of the tumours, and upregulation of TRKB, TRKC, NT3/NT4, and BDNF, and ERK and BCL2 as well, while the transcriptome of trichoepitheliomas was different (Rajan et al., 2011).

**CYLD**

**Location**
16q12.1

**Protein**

**Description**
Member of the deubiquitinase family. Cleaves Lys-63-linked polyubiquitin chains. Negative regulator of NF-kappaB and JNK signalings. Binds NEMO, TRAF2 and TRAF6 and deubiquitinates them. Participates in antimicrobial defense and inflammation (Review in Courtois, 2010).

**Mutations**

**Germinal**
Most of the mutations produce large deletions of the protein.

**Somatic**
Different types of somatic mutations in benign and malignant tumors (Kazakov et al., 2010).

**References**


This article should be referenced as such: