Familial tylosis

Othman Saraj, Janusz A Jankowski

Digestive Disease Centre, University Hospitals of Leicester NHS Trust, Leicester, United Kingdom (OS, JAJ); Gastrointestinal Cancer Presentation Group, Oxford University, Oxford, United Kingdom (JAJ); GI Centre, Queen Mary's Hospital, University of London, London, United Kingdom (JAJ)

Published in Atlas Database: July 2009

Online updated version: http://AtlasGeneticsOncology.org/Kprones/FamTylosisID10100.html

DOI: 10.4267/2042/44788

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.

© 2010 Atlas of Genetics and Cytogenetics in Oncology and Haematology

Identity

Alias: Howell-Evans syndromes; Tylosis oesophageal cancer; Focal non epidermolytic palmoplantar keratoderma (NEPPK) with carcinoma of the oesophagus

Note: Synonyms include: (a) Tylosis oesophageal cancer or (b) Focal Non Epidermolytic Palmoplantar Keratoderma (NEPPK) with carcinoma of the oesophagus (Howel-Evans et al., 1958; Stevens et al., 1996).

Inheritance: Is a rare autosomal dominant condition with full penetrance of skin phenotype by puberty. No race prevalence has been noted (Howel-Evans et al., 1958).

Clinics

Phenotype and clinics

Tylosis is divided into two types: Type A with late onset of NEPPK between age of 5 to 15 years and Type B with early onset around the first year of age (Maiillefer and Greydanus, 1999; Nagai et al., 2000).

It usually involves the pressure areas mainly sole of feet and later mild involvement of palms (more obvious in manual workers). It can also affect frictional areas like elbows and knees. It regresses completely on bed rest (Howel-Evans et al., 1958; Stevens et al., 1996).

The affected skin has a thickened epidermis which sheds horny large flakes, usually in autumn, to leave a red tender surface which quickly get covered with another thick layer of epidermis (Howel-Evans et al., 1958).

Oral leukokeratosis (which are white “spongy” plaques) and follicular hyperkeratosis (which are pinkish-to-tan papules) on the body and flexure areas, are often seen in patients with tylosis and it could be a possible indication for developing oesophageal cancer (Tyldesley and Osborne-Hughes, 1973; Tyldesly, 1974).

See example of Tylosis on DermAtlas.

Neoplastic risk

Malignancy Risk: Type A has a higher risk of developing squamous oesophageal carcinoma up to 95% by age of 65 years, while Type B runs a benign course (Howel-Evans et al., 1958; Ellis et al., 1994; Stevens et al., 1996).

These malignancies are predominantly in the distal oesophagus whereas acquired squamous cell carcinomas are mostly mid-thoracic in location (Howel-Evans et al., 1958; Maiillefer and Greydanus, 1999). Increase risk has been noted with history of smoking (Stevens et al., 1996).

Histological findings: Thickening of the all skin layers especially epidermis, hypertrophy of sweat glands and their ducts which often occluded by hyperplastic epithelium (Howel-Evans et al., 1958).

Treatment

Monitoring: Annual endoscopic surveillance with biopsies taken should be offered to affected individuals in view of risk of oesophageal cancer (Robertson et al., 2008).

Prognosis

Prognosis of squamous cell cancer of oesophagus: In general is poor with 5 year survival of 75% in Stage 0 (intraepithelial cancer) to <5% in stage IV (Distant metastasis). Overall survival is about 20-25% (Mayer, 2001).
Cytogenetics

**Note**
The tylosis oesophageal cancer gene (TOC) is localized to a small region on band 17q25, a region frequently deleted in persons with sporadic squamous cell oesophageal tumours (Kelsell et al., 1996; Risk et al., 2002). This region contains 5'end of uncharacterized (FM8) gene, which is likely non coding RNA, a promoter of another gene and the whole cytoglobin gene (Langan et al., 2004). So far studies has failed to identify TOC specific mutations in any of the 3 genes above (Langan et al., 2004). However recent studies of the gene expression in the 42.5 kb TOC minimal region has shown down regulation of cytoglobin gene expression by 70% in tylotic patients which might contribute to TOC phenotype. This reduction exceeds the expected 50% effect from autosomal dominant conditions therefore rules out a simple haplo-insufficiency as a mechanism of the disease, instead a novel trans-allele interaction (ie the mutated allele causing suppression of the normal allele) has been suggested (McRonald et al., 2006).

Genes involved and proteins

**TOC**
**Location**
17q25
**Note**
TOC gene or tylosis with oesophageal cancer gene.

**DNA/RNA**
Note: Abnormality in this area has been noted in breast and ovarian cancer (Nagai et al., 2000; Harada et al., 2001).
Description: 42.5kb.
No mutations have been identified in the gene.

References


Langan JE, Cole CG, Huckle EJ, Byrne S, McDonald FE, Rowbottom L, Ellis A, Shaw JM, Leigh IM, Kelsell DP, Dunham I, Field JK, Risk JM. Novel microsatellite markers and single nucleotide polymorphisms refine the tylosis with oesophageal cancer (TOC) minimal region on 17q25 to 42.5 kb: sequencing does not identify the causative gene. Hum Genet. 2004 May;114(6):534-40


This article should be referenced as such: