Cowden disease

Michel Longy

Unite de Genetique Oncologique, Institut Bergonie, 180, rue de Saint-Genes, 33076 Bordeaux, France (ML)

Published in Atlas Database: June 2000
Online updated version: http://AtlasGeneticsOncology.org/Kprones/CowdenID10018.html
DOI: 10.4267/2042/37655
This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.
© 2000 Atlas of Genetics and Cytogenetics in Oncology and Haematology

Identity

Alias: Multiple hamartoma syndrome
Inheritance: Autosomal dominant; high penetrance (close to 100% by the age of 30 yrs); highly variable expressivity (between and within families).

Clinics

Phenotype and clinics
Clinical manifestations usually occur during the 2nd and 3rd decade; they are dystrophic, hamartomatous or tumoral lesions including the following to variable extend:
- mucocutaneous papillomatous lesions (facial papules, sometimes related to trichilemmoma; oral papillomatosis with cobblestone gingiva; acral keratoses);
- both dystrophic and adenomatous multinodular goiter;
- intestinal tract polyps with variable histologies;
- adenosis and fibrocystic disease of the breast;
- macrocephaly;
- lipomas;
- genito-urinary abnormalities.

Overlapping syndromes
Bannayan-Riley-Ruvalcaba syndrome including precocious stigmata of Cowden disease (macrocephaly, lipomas, genital pigmented macules, hamartomatous intestinal tract polyps) is considered as a pediatric form of Cowden disease.
Lhermitte-Duclos syndrome or dysplastic gangliocytoma of the cerebellum is a rare and complex hamartomatous condition of the cerebellum which can occur alone but also in association with Cowden disease.
Juvenile polyposis and Peutz Jeghers syndrome: Cowden disease, by its intestinal tract lesions can be linked to the scope of hereditary hamartomatous polyposis; molecular diagnosis can be useful in distinguishing juvenile polyposis, Peutz Jeghers syndrome or Cowden disease/Bannayan.

Neoplastic risk
The main neoplastic risks are thyroid carcinoma (follicular type) and breast carcinoma of various histological types which are reported in respectively 15% of the patients and 30% of the affected women. Other tumor types occur rarely but more frequently than expected in the general population: renal cell carcinoma, neuroendocrine cell carcinoma, germ cell tumor, malignant melanoma, endometrial carcinoma.

Genes involved and proteins

PTEN (or MMAC1 or TEP1)

Location
10q23

Protein
Expression: 403 amino-acids, phosphatase with tumor suppressive effects, negative regulator of the PI3K/Akt signal cell pathway by dephosphorylating PIP3.

Mutations
Germinal: To date, at least 110 mutations have been described; they are observed along the various exons of the gene except the 9th (never described) and the 1st (very few reports); a mutational hot spot is observed in exon 5 in relation with the catalytic core motif; in the great majority of cases, inactivating mutations are observed, either by protein truncation, or by misense mutation within the phosphatase domain.
Somatic: A lot of somatic mutations (more than 300) have been described in several tumor types but mainly in glioblastoma and in endometrial carcinoma; they lead to a biallelic inactivation of the gene more often by a combination of point mutation and large deletion of the second allele.
References


This article should be referenced as such: