Familial liver adenomatosis
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Identity
Other names: Familial hepatic adenomas
Note: Liver adenomatosis is a rare disease defined by the presence of multiple adenomas within an otherwise normal hepatic parenchyma. In 2002, frequent bi-allelic inactivation of TCF1/HNF-1alpha, was identified in hepatocellular adenomas. In 80% of the cases both mutations were of somatic origin. However, in the remaining cases, one heterozygous germline mutation has been found in patients revealing a relation between liver adenomatosis and maturity-onset diabetes of the young (MODY3). MODY3 is a rare dominantly inherited subtype of non-insulin-dependent diabetes mellitus characterized by early onset, usually before the age of 25, and a primary defect in insulin secretion. In 1996, heterozygous germline mutations of TCF1/HNF1a have been linked to the occurrence of MODY3 in humans.
Inheritance: autosomal dominant disorder with low penetrance.

Clinics
Phenotype and clinics
To date, all familial liver adenomatosis cases described are related to TCF1/HFN1a constitutional mutation. Genotype-phenotype correlation analysis showed that TCF1/HNF1a benign lesions were steatotic.
Neoplastic risk
Among MODY3 patients only a very small minority will develop liver adenomatosis. Cases of malignant transformation are uncommon.
Evolution
Patients presenting TCF1/HNF1a mutated adenomatosis are at risk of tumor hemorrhagic rupture.

Genes involved and Proteins
Note: HNF1α is a homeodomain containing transcription factor that is implicated in hepatocyte differentiation and is required for the liver-specific expression of several genes, including β-fibrinogen, albumin and α1-antitrypsin.

TCF1
Location: 12q24.31
DNA/RNA
Description: 10 coding exons.

Protein
Description: hepatocyte nuclear factor 1 alpha, HNF1A
Function: transcription factor.
Homology: Homeodomain, pou family.
Mutations
Germinial: at least 6 different mutations were found in familial adenomatosis: R229X, R272S, P291fs (2 cases), G55fs, IVS2 +1 G>T.
Somatic: inactivation of the second allele in adenoma tumors is by gene deletion or mutation.

References


This article should be referenced as such: