

Liver adenoma

Identity

Other names Hepatocellular adenoma
 Liver cell adenoma

Clinics and Pathology

Disease Hepatocellular adenomas (HA) are rare benign liver tumors, most frequently occurring in women using oral contraception. HA are single or more rarely multiple nodules; the presence of more than ten nodules in the liver indicates a specific nosological entity: liver adenomatosis

Etiology In 90% of the cases, adenomas are sporadic and only rare cases are developed in a familial context: ([Familial liver adenomatosis](#)). Patients with an inherited mutation in one allele of [TCF1/HNF1a](#) may develop maturity onset diabetes of the young type 3 (MODY3) and familial liver adenomatosis, when the second allele is inactivated in hepatocytes by somatic mutation or chromosome deletion.

Epidemiology Hepatocellular adenomas are usually related to oral contraceptive use. The other risk factors are : glycogen storage diseases and the androgen therapy. HA are rare tumours: their estimated incidence in France is approximately one case per 100,000 women. Over the past fifteen years, their incidence has seen a sustained decline in industrialised countries; this trend is probably linked to the reduction in ethinylestradiol doses in oral contraceptives.

Pathology These tumours result from a benign proliferation of hepatocytes which destroy the normal architecture of the liver. They are usually hyper-vascularised and typical adenoma corresponds to a proliferation of benign hepatocytes, intermingled with numerous thin-walled vessels, without portal tracts.

Treatment Surgery is usually proposed for lesion of more than 3 cm

Evolution Hepatocellular adenoma may bleed, or rarely, undergo malignant transformation.

Prognosis The molecular and pathological classification of hepatocellular adenomas permits the identification of strong genotype-phenotype correlations and suggests that adenomas with beta-catenin activation have a higher risk of malignant transformation.

Genetics

Note Germline TCF1/HNF1A mutation can predispose to familial liver

adenomatosis

Genes involved and Proteins

Note Half of the adenoma cases are mutated for TCF1 gene encoding HNF1a. These mutations are inactivating and both allele are mutated in tumors. Patients with an inherited mutation in one allele of HNF1a may develop maturity onset diabetes of the young type 3 (MODY3) and familial liver adenomatosis, when the second allele is inactivated in hepatocytes by somatic mutation or chromosome deletion. Mutations of [CTNNB1](#) activating the beta-catenin was also found in 15% of the HA cases. The molecular and pathological classification of hepatocellular adenomas permitted the identification of strong genotype-phenotype correlations and suggested that adenomas with beta-catenin activation have a higher risk of malignant transformation.

Gene Name [TCF1](#)

Location 12q24.31

Note Alias: HNF1A, hepatocyte nuclear factor 1 alpha, HNF1, LFB1, M57732, MODY3

More than 50 different HNF1a mutations have been identified in HA. These mutations are distributed mainly from exon 1 to 6. Point mutations, small deletions and insertions were identified. Gene deletions are less frequent.

Gene Name [CTNNB1](#)

Location 3p22.1

Note Description: catenin (cadherin-associated protein), beta 1

Activating mutations are amino-acid substitution in exon 3 or in-frame deletion including part or all exon 3.

Protein Beta-catenin is an adherens junction protein. Adherens junctions are critical for the establishment and maintenance of epithelial layers, cells adhesion, signal communication, anchorage of the actin cytoskeleton. CTNNB1 has important functions in the E-cadherin-mediated cell-cell adhesion system and also as a downstream signaling molecule in the Wnt pathway. Cytoplasmic accumulation of b catenin allows it to translocate to the nucleus to form complexes with transcription factors of the T cell factor-lymphoid enhancer factor (Tcf-Lef) family. b-catenin is assumed to transactivate mostly unknown target genes, which may stimulate cell proliferation (acts as an oncogene) or inhibit apoptosis. The b-catenin level in the cell is regulated by its association with the adenomatous polyposis coli ([APC](#)) tumor suppressor protein, [axin](#) and GSK-3b. Phosphorylation of b-catenin by the APC-axin-GSK-3b complex leads to its degradation by the ubiquitin-proteasome system.

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