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Deep Insight Section

Hereditary papillary renal cell carcinoma

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Identity

Note: Other (well known) classes of inherited renal cell carcinomas are:
- the Von Hippel-Lindau syndrome, and
- the Lynch syndrome II.

Inheritance: Some familly trees resemble autosomal recessive transmission (affected sibs with unaffected parents), other exhibit typical autosomal dominant trasmission with a vertical parent-to-child pattern; the situation is not that of (recessive) tumour suppressor genes as in the retinoblastoma, nor that of a recessive DNA replication/repair gene like in Bloom's, but the overexpression of the mutant allele through (acquired) chromosome imbalance (see below).

Clinics

Note
No phenotypic sign.

Neoplastic risk

Multiple and/or bilateral papillary renal cell carcinomas, with median age 45 years at diagnosis (range 18-79 years, most cases being between 35 and 55 years old), sex ratio 29M/12F, the presence of asymptomatic cases (mutations have also been detected in tumour-free individuals in these pedigrees pointing to a low expressivity), and still a median age at death of affected individuals at 52 years.

Cytogenetics

Note
Similar to what is found in sporadic papillary renal cell carcinoma, in particular trisomy 7 and 17.

Other findings

Note
No loss of heterozygosity at loci on 3p in the tumours; this contrasts with clear-cell renal cell carcinomas which are associated with deletions of 3p.

Genes involved and proteins

MET

Location
7q31

Protein
Expression: Wide.
Localisation: Membrane.
Function: Transmembrane tyrosine kinase receptor for the hepatocyte growth factor/scatter factor (HGF/SF).

Mutations
Germinal: Found mutated in half of the cases of hereditary papillary renal cell carcinoma so far studied; mutations were in exons 16-19 (tyrosine kinase domain); cases without a detected mutation may either have a mutation in non-tested parts of MET, or mutations in another gene.
Somatic: The mutant MET allele is duplicated (via the trisomy 7) in the tumours; might lead to a constitutive kinase activation.

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