Cancer Prone Disease Section
Mini Review

MAP (MUTYH-Associated Polyposis)
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Identity

Other names: MYH associated polyposis
Note: MAP is a recently described condition predisposing to colorectal cancer, caused by germline mutations in the base excision repair (BER) gene MUTYH (MYH). The first description of an affected family was provided in 2002.
Inheritance: Autosomal recessive. Heterozygote frequency in the general population is currently estimated as 0.01-0.02.

Clinics

Phenotype and clinics
The phenotype is often undistinguishable from that of autosomal dominant familial adenomatous polyposis (FAP) caused by mutations in APC gene. The number of adenomas is often lower in MAP (from 5 to more than 100), and affected patients are often sporadic cases. Biallelic MUTYH mutations have also been detected in patients affected with early-onset colorectal cancer (CRC) without polyps and in one with more than 1000 polyps. Cancers are more frequently located in the proximal side of the colon compared to APC-related FAP. Generally, mean age at diagnosis of MAP is 48-56 years, later than in APC-related FAP. A number of extracolon manifestations have been observed, although their incidence is not yet well established. These include manifestations that are also associated with APC-related FAP, such as duodenal polyposis, duodenal cancer, osteomas, digital cysts and congenital hypertrophy of the retinal pigment epithelium. Breast cancer and thyroid cancer, and cutaneous tumors (pilomatricomas and sebaceous gland tumors) have also been reported.

Neoplastic risk
Penetrance of CRC is approximately 100% by age 65 years. Approximately 50% of patients present with CRC at the time of diagnosis. CRC risk in heterozygotes is not defined: some authors believe that monoallelic mutations may act as low penetrance alleles, increasing CRC risk, but larger studies with sufficient statistical power are necessary to accurately estimate the magnitude of such risk, if any.

Treatment
No specific screening guidelines have yet been established. Periodic colonoscopy of the entire colon should be offered to biallelic mutations carriers. Prophylactic colectomy should be considered when number, size and/or dysplasia of the polyps make continued surveillance unmanageable. Upper gastrointestinal surveillance is also indicated. Parents and children of individuals with biallelic mutations are obligate carriers of at least one MUTYH mutation. A baseline colonoscopy has been suggested for these carriers, and, if findings are negative, screening should be repeated every 3-5 years.

Genes involved and Proteins

MUTYH (human MutY homologue)
Location: 1p34.3-p32.1
Protein
MUTYH glycosylase.
Description: MUTYH is a DNA glycosylase that plays a key role in BER-mediated removal of 8-oxoG:A mismatches.
Mutations
Most reported mutations in this gene cause production
of a nonfunctional or low-functioning glycosylase enzyme. The two most common mutations in Caucasians, accounting for about 75%-80% of mutant alleles, are Y165C (or Tyr165Cys) and G382D (or Gly382Asp).

References


This article should be referenced as such: