Cancer Prone Disease Section
Mini Review

Hereditary non polyposis colorectal carcinoma (HNPCC Syndrome)

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Identity

Alias: Lynch syndrome
Inheritance
Autosomal dominant; frequency is about 1 to 2/1000 inhabitants; founder effect has been found in finnish population.

Clinics

Phenotype and clinics
Hereditary non polyposis colorectal carcinoma is an autosomal dominantly inherited predisposition to develop colorectal cancer, endometrial carcinoma and ovary carcinoma, urinary tract carcinomas, stomach, small bowel and biliary tract carcinoma, and brain tumors. Colorectal carcinoma is characterized by early age at onset, predominantly right sided with an excess of synchronous and metachronous tumors.

Neoplastic risk
The risk of colorectal cancer in HNPCC patients is estimates up to 75% by age 75. The average age of diagnosis is 45 years for colorectal cancer. It is interesting to note that the risk of colorectal cancer for women was less that observed for men and average age of diagnosis was delayed. The risk of uterine cancer in HNPCC female is estimated up to 40% and the risk of ovarian cancer is less than 10%. The risk of metachronous colorectal cancer, when limited resection of colon was performed, is estimated to 30%.

Treatment
Full coloscopy to the caecum is recommended every two years beginning at age 25 years or 5 years before the first cancer. Annual screening for uterine cancer is recommended beginning at the age 35 years. The method of screening include transvaginal ultrasound and hysteroscopy.

Prognosis
Coloscopy screening at 3 year intervals more than halves the risk of colorectal cancer, prevents colorectal cancer deaths, and decreases overall mortality by about 65% in HNPCC families.

Genes involved and proteins

Note
Different genes can be responsible for Lynch syndrome:
- hMSH2 (mutS (E. coli) homolog 2 (colon cancer, nonpolyposis type 1)) located in 2p22-p21.
- hMLH1 (mutL (E. coli) homolog 1 (colon cancer, nonpolyposis type 2)) located in 3p21.3.
- hMSH6 (mutS (E. coli) homolog 6) located in 2p16
- PMS2 (postmeiotic segregation increased (S. cerevisiae) 2) located in 7p22.
- PMS1 (postmeiotic segregation increased (S. cerevisiae) 1) located in 2q31.1.
- TGFβR2 (transforming growth factor, beta receptor II (70-80kD)) located in 3p22.

Protein
Localisation: Nuclear.
Function: These protein works on DNA mismatch repair pathways. hMSH21 et hMLH1 are similar to MutS and MutL in Echerichia Coli. These two proteins participated to the recognition of DNA mismatch during DNA replication. They formed complex with hMSH3, hMSH6 and PMS2 allowing the mismatch repair.

Mutations
Germline: Yes; no mutations hot spot.
Somatic: Yes; extinction of hMLH1 by promoter hypermethylation.
References


This article should be referenced as such: