MYH-associated polyposis

Key facts

- MYH-associated polyposis (MAP), also known as MUTYH polyposis, is a bowel cancer predisposition syndrome.
- Individuals with MYH-associated polyposis develop moderate numbers of polyps in their bowel; often between 10 and a few hundred.
- The risk of a polyp progressing to cancer is high, giving a substantially increased risk of colorectal cancer.
- Regular colonoscopy allows the removal of polyps and consequently reduces the risk of later cancer. In more severe cases, if the number and density of polyps prohibits removal, colectomy may be considered.
- MYH-associated polyposis occurs when an individual carries alterations in both copies of the *MUTYH* gene.
- MYH-associated polyposis is inherited in an autosomal recessive manner. Therefore siblings of someone who has MYH-associated polyposis have a 1-in-4 (25%) chance of also having it. Children and parents are usually at low risk.

Clinical features

- The key clinical feature is the development of polyps in the bowel. Often individuals develop between 10 and a few hundred by the age of 50. These may include adenomas, hyperplastic polyps and serrated polyps.
- The condition is very variable. Some people develop few polyps; others have hundreds. A few individuals with MYH-associated polyposis have remained cancer free at age 60.
- There is a significant risk of transformation of an adenoma to cancer. Consequently, individuals with MYH-associated polyposis have a high risk of colorectal cancer (estimates lifetime risks range from 40% upwards).
- Duodenal and gastric polyps have been reported in some individuals, but the probability of developing these cancers remains small.

Diagnosis

- Suspicion of MYH-associated polyposis can be suggested through taking a detailed family history and obtaining pathology details of polyp type and number.
- MYH-associated polyposis is suspected in a family where:
  - an individual has developed multiple adenomas (between 1 and 10) below the age of 40;
  - an individual has developed 10-100s of polyps; particularly where Familial Adenomatous Polyposis (FAP) has been excluded; or
  - the family history is suggestive of a bowel cancer/polyposis condition inherited in an autosomal recessive way, eg the individuals with bowel cancer and/or polyps all belong to the same sibship, with little family history in other generations.
- Diagnosis is confirmed through genetic testing to identify that an individual carries two alterations in the *MUTYH* gene (bi-allelic mutations).

Genetic basis

- MYH-associated polyposis is caused by bi-allelic mutations in the *MUTYH* gene, ie an individual with MYH-associated polyposis has alterations in both their copies of the *MUTYH* gene. This occurs because an alteration is inherited from each parent, both of whom are usually carriers for MYH-associated polyposis (although occasionally one or both parents can be affected themselves).
- Two common alterations (mutations) (536A>G (p.Tyr179Cys) in exon 7 and c.1187G>A (p.Gly396Asp) in exon 13) account for around 70% of cases in northern European populations. A further mutation (p.Tyr104X) is common in Pakistani populations.
- The *MUTYH* gene is important in DNA repair pathways. Individuals with impaired DNA repair accumulate DNA damage, increasing the risk of cancer development.
- Genetic testing for siblings of an individual who has MYH-associated polyposis is particularly important as they have at least a 1-in-4 (25%) chance of also having the condition.
- Unless they have a family history of polyposis or are related in some way, it is unusual for the partner of someone with MYH-associated polyposis to also carry an alteration in the *MUTYH* gene (they have a 1%-2% chance of carrying an alteration). Therefore, the probability of a child of someone with MYH-associated polyposis also developing MYH-associated polyposis is usually low. However, genetic testing for the common alterations may be offered to concerned partners and offspring in some circumstances.

Clinical management

- Regular colonoscopy (usually twice a year) from age 18-20 onwards for those with MYH-associated polyposis enables cancers to be detected at an early stage and adenomas to be identified and removed.
- Continued surveillance of remaining bowel tissue is important for those who have developed colorectal cancer, as there is an increased risk of further cancers.
- In more severe cases, if the number and density of polyps prohibits removal, colectomy may be considered.

Genetic testing

- Laboratory analysis of the *MUTYH* gene is available. Testing for common alterations may be preferable initially.
- Testing should initially be offered to an affected individual, if possible, to confirm the diagnosis and to identify the causative alterations in the family.
- Once the diagnosis has been confirmed in an affected individual, relatives at risk can be offered testing. This is most appropriate for siblings of an individual with MYH-associated polyposis, who have the greatest risk.

This information is intended for educational use and was current in March 2015. For clinical management, it is recommended that local guidelines and protocols are used.