Familial adenomatous polyposis

Key facts

- Classic familial adenomatous polyposis (FAP) is a dominantly inherited cancer-susceptibility disorder.
- FAP occurs in about 3 in 100,000 people.
- People with FAP develop hundreds to thousands of pre-cancerous polyps (adenomas) in the colon from early adolescence. These polyps are highly prone to becoming cancerous.
- The mean age of diagnosis of colon cancer in untreated individuals is 39 years but can develop at younger ages than this.
- Diagnosis of FAP is usually made by observance of polyps by means of colonoscopy.
- Regular surveillance by colonoscopy and prophylactic surgery to remove the colon dramatically reduces the risk of developing colon cancer in high-risk family members.

Clinical features

- Classic FAP is defined as the development of more than 100 pre-cancerous polyps developing in the colorectal region. These may bleed, causing the presence of blood in the stool.
- In FAP, the presence of multiple polyps (termed polyposis) often appears as a 'carpet' of polyps in the bowel.
- 'Attenuated FAP' (AFAP) is a term given to the condition in which individuals develop fewer than 100 adenomas.
- Anaemia may occur owing to blood loss, gradually developing into iron deficiency.
- In the event of malignancy, an individual may experience weight loss, persistent unexplained fatigue, altered bowel movement and, if the tumours are not treated in time, cancer metastasis to areas such as the liver.
- Individuals can develop extracolonic features of FAP such as polyps in the stomach or small bowel, osteomas (harmless bone growths), CHRPEs (freckle-like spots on the retinal epithelium) and Desmoid tumours in the abdomen.

Diagnosis

- Colonoscopy reveals the presence of multiple pre-cancerous colorectal polyps.
- If a family history of FAP is known, pre-symptomatic testing is available.

Genetic basis

- Classic FAP is caused by an alteration in the *APC* gene on chromosome 5.
- *APC* gene products function in the Wnt signalling pathway, regulating the degradation of beta-catenin to control aspects of cell proliferation.
- *APC* also plays a role in microtubule stabilisation, meaning that elimination of this function can lead to chromosomal instability in cancer cells.

Clinical management

- Prophylactic surgery to remove the colon dramatically reduces the risk of developing colon cancer in high-risk family members.
- Regular surveillance by colonoscopy from early adolescence helps to guide the timing of colectomy. Usually colonoscopy is carried out annually until polyps number too many to monitor or remove individually.
- Non-steroidal anti-inflammatory drugs (NSAIDs) have been shown to reduce risk of colorectal cancer development in the general population, and of polyp (but not cancer) development in FAP individuals.

Genetic testing

- Laboratory analysis for *APC* mutation detection is used if inheritance of the condition is suspected. Blood from parents and other relatives may be useful for analysis.
- Linkage analysis is possible for families that do not have an identified *APC* genetic alteration (mutation).

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.