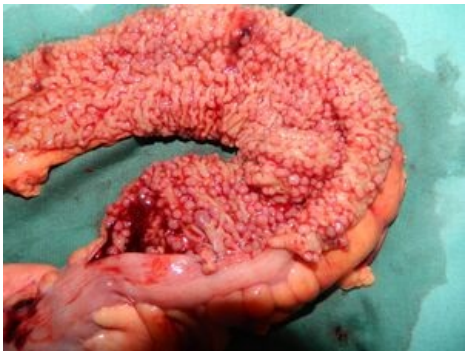
Familial adenomatous polyposis

Familial adenomatous polyposis (OMIM 175100), abbreviated as FAP or FAP1 , is an inherited disease with an autosomal dominant type of heredity, in which hundreds to thousands of colon polyps develop , and are almost certainly malignant within ten years without adequate therapy. In addition to polyps, a number of other extraintestinal manifestations are described. The molecular basis is a germline mutation in the APC gene. The incidence is estimated at around 1 / 10,000, the prevalence in the EU is estimated at 1 / 37,600 to 1 / 11,300. About 1% of colorectal cancers are based on FAP.



FAP preparation

Clinical picture

Clinical manifestations are uncommon in childhood and adolescence. The first manifestations are usually manifestations of colon polyposis, especially anemia caused by occult bleeding. Sometimes non-specific symptoms such as constipation, diarrhea, abdominal pain or palpable masses may appear first.

Large intestine

Colon involvement gave rise to the definition of the disease, in the fully developed form there are hundreds to thousands of adenomatous polyps in the colon. This picture is only rarely seen in countries with well-functioning healthcare.

Polyps begin to develop without significant symptoms as early as childhood as asymptomatic small nodules in the mucosa, more of them are in the rectosigmoid. The size and number of polyps increase with age. By the age of 15, polyps develop in about 15% of patients, and by the age of 35 in 95% of patients. Malignant reversal occurs within 10 years after the formation of polyps.

Stomach

About 90% of patients develop polyps of the fundus glands . Unlike their benign sporadic counterparts, these polyps have adenoma features and can rarely become malignant.

Duodenum

10 to 20 years after the diagnosis of colorectal polyps, virtually all patients develop adenomatous polyposis of the duodenum and periampullary area. It is estimated that about 5% of periampullary polyps in particular become malignant within 10 years. Acute pancreatitis can also be one of the manifestations of ampoule adenoma .

Small intestine

Adenomatous polyps of the small intestine can occur, apparently occurring in about half of patients.

Extraintestinal manifestations

Extraintestinal manifestations are rarely malignant. The following may appear:

- skin lesions: fibromas , lipomas , sebaceous cysts and epidermoid cysts ,
- nasopharyngeal angiofibromas,
- osteomas
- congenital hypertrophy of the retinal pigment,
- mesenteric desmoid tumor

Malignancies that may occur in association with FAP are:

- mucinous pancreatic adenocarcinoma,
- hepatoblastoma,
- brain tumors (medulloblastoma, rarely glioblastoma),
- thyroid tumors.

Disease variants

The disease can manifest in the following forms, all sharing the same mutation:

- **Attenuated FAP** is a clinically milder form of the disease with fewer polyps, older age at diagnosis, and later development of malignancies.
- **Gardner syndrome** is a variant in which the clinical picture is dominated by extraintestinal symptoms.

- **Turcot's syndrome** is a genetically heterogeneous group of syndromes of colon and brain tumors. One variant is caused by a germline mutation in the APC gene, the other is caused by one of the mutations responsible for Lynch syndrome .
- **Familial adenomatous polyposis type 2** (OMIM 608456) is an autosomal recessive disease associated with a mutation in the MUTYH gene .

Molecular biology

The molecular basis of the disease is a congenital mutation in the tumor suppressor gene APC, in 25–30% of patients it is a de novo mutation, in others it is a family occurrence.

APC is a classical tumor suppressor gene, playing a central role in the Wnt signaling cascade. Due to APC, β-catenin is degraded in proteasomes and signaling is interrupted. This is because β-catenin is a transcription factor that affects the expression of a number of genes, in this case especially c-myc. Loss of APC function leads to higher transcription of genes responsible for proliferation. Loss has been reported in both FAP and a large group of sporadic colorectal cancers.

FAP is caused by a number of point mutations in the APC gene, a common feature of which is that they lead to protein shortening. There is a correlation between the site of the mutation and the clinical manifestation, but the clinical picture of the same mutation may vary from case to case.

Diagnostics and management

Diagnosis is based on the clinical picture and family history, it should be verified by genetic testing, histopathological examination of polyps also contributes to the distinction from other colon polyposes. The first detection is often in the stage of colorectal cancer and requires comprehensive oncological therapy. Relatives of patients should be examined much earlier, before the age of 20. If the diagnosis is confirmed, a surgical solution is indicated, ie total coloproctectomy with pouche or ileorectal anastomosis.

Medical care

- **The lower GIT** requires follow-up even after surgery.
- **Duodenal polyps** in particular have an upper risk of malignancy, and their presence signals a high risk of polyps elsewhere in the small intestine.
- **Desmoid tumors** are the result of increased alertness of patients to excessive fibroproduction. Screening is difficult, desmoids are most often found intra-abdominally, in case of suspicion, a CT or MRI examination should be performed and the desmoid should be verified by biopsy.
- **The thyroid gland** should be monitored for a significantly higher risk of malignancy, palpation (by an experienced endocrinologist) or ultrasound is recommended.

The risk of malignancy of the pancreas and female genitals is slightly increased compared to the control population.

Chemoprophylaxis

COX-2 (celecoxib) inhibitors reduce the risk of recurrence of intestinal polyps and their progression to cancer, so their preventive administration after colon surgery is recommended.

Prognosis

Even after the colon has been removed, patients have risks of further complications. The most common potentially lethal complications are duodenal cancer and desmoid tumor. Because colon removal is a radical intervention in the physiology of digestion, patients have a high risk of vitamin and mineral imbalance.

Links

Related articles

- Lynch syndrome
- Colon polyps
- Tumors with familial occurrence

References

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