FAMILIAL ADENOMATOUS POLYPOSIS; 30-YEAR OBSERVATION OF A FEMALE PATIENT – CASE REPORT

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Familial adenomatous polyposis (FAP) is a colorectal cancer syndrome caused by a mutation inherited in an autosomal-dominant pattern with a 100% penetrance. Our detailed case report presents a history of a 55-year-old FAP female patient who had been under constant clinical observation for 30 years. The disease was diagnosed at the age of 22. The patient underwent restorative proctocolectomy with ileal pouch-anal anastomosis (PRC-IPAA). During our follow-up extra-colonic manifestations occurred such as a desmoid tumour, fundic gland polyps in the stomach and duodenal polyps also in the periampullary region. Apart from disease-related symptoms the patient manifested other complications such as small bowel adhesive obstruction, benign breast tumours, uterine myomas, cholelithiasis and thyroid nodules.

Our analysis of the above case presents advantages of a long-term medical observation of a FAP patient carried out by a specialist surgical medical centre. Key words: familial adenomatous polyposis, complications, clinical follow-up

Familial adenomatous polyposis (FAP) is a colorectal cancer syndrome caused by a mutation in a suppressor gene. FAP is also associated with the occurrence of other diseases which can develop throughout a patient’s life.

The aim of the study was to conduct a detailed analysis of a FAP female patient who had been under clinical observation for 30 years.

CASE REPORT

A 22-year-old female (R.Z.) presented to a Gastroenterological Clinic in Wroclaw in 1984, complaining of an abdominal pain that had been present for a few years, chronic diarrhoea that had been present for a few months, with recurrent bloody and mucous stools. The patient had been complaining of symptoms’ exacerbation since two months. Laboratory tests done in the Gastroenterological Clinic revealed anaemia. Gastroscopy showed no abnormalities, colorectal contrast examination showed segmental loss of haustrations in the transverse colon with rigid, rough contour and segmental constrictions in descending and sigmoid colon.

Rectoscopy showed numerous polyps in the rectum. Collected polyps underwent histopathologic examination, which confirmed adenomatous polyposis of the large intestine. Once a new history had been taken, it was established that both colorectal polyposis and colorectal cancers did not run in the patient’s family. Genetic tests confirmed typical mutation of the APC gene. The patient was admitted to a Surgical Ward in Wroclaw, where a non-invasive treatment consisting of packed red blood cells and Salazopyrin was introduced. The treatment resulted in a decreased number of bowel movements and improved general condition of the patient. Subsequently, the
patient was transferred to the Department of General and Gastroenterological Surgery on a planned manner on 13 May 1986 in order to undergo a surgical treatment. A colectomy (fig. 1) with mucosectomy of the rectal stump according to Utsunomiya’s method (1) was performed, with creation of the intestinal J-pouch connected with rectum just above the anal sphincter, together with temporary ileostomy. Postsurgical hospitalisation was uncomplicated.

On 2 August 1986, the patient was admitted again to the Department of General and Gastroenterological Surgery in Poznań in order to remove ileostomy. On 18 May 1988, the patient was transferred to the Department again, with symptoms suggesting bowel obstruction – immediate surgery was performed. The obstruction was caused by numerous adhesions in the peritoneal cavity. In March 1990, the patient underwent surgery again, because of an enormous abdominal tumour, which invaded the left kidney, spleen, pancreas and the left side of the diaphragm. The tumour was removed during the surgery (fig. 2), together with the left kidney, part of the tail of the pancreas and left side of the diaphragm. Histopathologic examination of the tumour showed features of a desmoid tumour. The patient stayed under strict control of a hospital out-patient clinic.

In 1994, a follow-up gastroscopy showed numerous squat hyperplastic polyps below the cardia of the stomach, measuring 2–3 mm. In 1997, during the next abdominal ultrasound, the patient was diagnosed with cholelithiasis – the gallbladder, with signs of chronic inflammation, was removed laparoscopically. In 1998, abdominal ultrasound showed a cyst of the right ovary, measuring 8x6x6 cm, numerous uterine myomas, up to 3 cm, and paracervical cysts. In 2002, a follow-up gastroscopy, apart from numerous polyps in the stomach and in the extrabulbar part of the duodenum, showed a tumour being a tubular adenoma (fig. 3). In 2004, the patient was diagnosed with bilateral ovarian cysts and was qualified for a surgery. The procedure consisted of the hysterectomy, adnexectomy and liberation of numerous adhesions. Histopathologic examination ruled out the presence of malignant lesions. In 2005, mammography showed a cyst of the left breast, which was then confirmed in the ultrasound and measured 22x15 mm. Cyst’s biopsy revealed fibroadenomatosis. In 2008, magnetic resonance showed a lesion being a two-chamber cyst behind the posterior wall of the bladder, measuring 36x25 mm
DISCUSSION

Familial adenomatous polyposis (FAP) is a colorectal cancer syndrome caused by a germline mutation inherited in an autosomal-dominant pattern with 100% penetrance. Mild form of FAP is inherited in a recessive pattern. FAP constitutes approximately 1% of all colorectal cancers. According to available literature, the prevalence of “de novo” disease is 1 per 8,000–10,000 persons. The symptoms of FAP usually develop in the second decade of life. However, the occurrence of the disease in 3- to 5-year-old children was reported as well.

FAP syndromes can be characterised by the presence of a large number (>100) of polyps in the large intestine. FAP is associated with mutations in the APC suppressor gene located on chromosome 5 (5q21), which is involved in the control of cells’proliferation. Mild form of FAP (MAP) is caused by homozygotic mutations in the MUTYH gene, which is located on chromosome 1 (1p34.3–1p32.1) and is responsible for the repair of oxidative DNA damage. The number of polyps in the large intestine is lower than in classical FAP (<100) (2-5).

Almost all people suffering from FAP will develop colorectal cancer before reaching 35 years of age, thus surgical treatment should be performed directly after making a diagnosis, in the second or third decade of life, preferably before cancer cells are found in the polyps. The most common surgery in familial adenomatous polyposis is, deployed since 1976 (6), prophylactic complete resection of the large intestine, with creation of a pouch from the ileum, which is connected with the anus (TPC IPAA – total proctocolectomy with ileal pouch – anal anastomosis). The surgery, which involves creation of an intestinal pouch, helps to keep a natural way of defecation, which considerably increases the comfort of life of patients undergoing prophylactic proctocolectomy (7).

Postsurgical intraabdominal adhesions can develop in almost all patients after serious surgeries within the abdominal cavity. It is due to postsurgical biochemical and cellular repair processes of damaged peritoneum. Adhesive obstruction of the small intestine after proctocolectomy with the creation of an intestinal pouch (IPAA) occurs, according to different authors, in 13–35% of patients. There were no statistically significant differences between the creation of intraabdominal adhesions after IPAA in FAP patients and patients with ulcerative colitis (8).

Desmoid tumours in FAP patients are more common in women (by 9–18%). They constitute, together with duodenal cancer, the most common cause of death after prophylactic proctocolectomy (9). They are formed most often in the small intestinal mesentery as an uncontrolled, locally malignant fibroblasts infiltration of the abdominal organs. Desmoid tumours have a diverse, uncontrolled growth dynamics and, by infiltrating nearby organs, they lead to complications such as digestive tract obstruction, ureteral obstruction, small intestine loop ischaemia (10). There are no clear standards of therapeutic management in the case of a desmoid tumour after proctocolectomy in FAP patients. The most common form of desmoid tumours treatment is radiotherapy as well as the therapy with antiestrogens and NSAIDs. In the case of surgical treatment, many authors recommend surgery only for tumours with clinical symptoms, because of a relatively high rate of postsurgical death and the risk of tumour recurrence (11), which can be up to 88% (according to available data).
The risk of thyroid cancer in FAP patients is 1–2%. It is usually a papillary thyroid cancer. The incidence rate for women is a few times higher than for men. The incidence risk for women with FAP is 100–160 times higher than for healthy women. According to the literature, it is advised to perform thyroid ultrasound and fine-needle aspiration biopsy for nodules over 1 cm or, according to some authors, fine-needle aspiration biopsy regardless of the thyroid nodule size. Follow-up thyroid ultrasound should be repeated every 12 months (12).

Familial adenomatous polyposis predisposes to duodenal and stomach polyps. According to available data, 50% to over 90% of FAP patients have duodenal polyps. 3–5% of patients with duodenal polyps will develop duodenal cancer. There is no evidence in the literature if screening tests and early treatment of duodenal adenomas will result in a better prognosis in FAP patients. Nonetheless, authors suggest performing a follow-up gastroduodenoscopy every 2–3 years, with concurrent biopsy of the suspected polyps and/or endoscopic ultrasound (13).

The prevalence of uterine myomas, cholelithiasis and breast cysts is not directly associated with FAP. First two of the abovementioned diseases were treated surgically. That is why their presence had a negative impact on the further treatment of the underlying disease and the possibility of long-term complications has increased.

CONCLUSIONS

Familial adenomatous polyposis is a relatively rare disease with genetic background. In many cases standard surgical treatment – proctocolectomy with the creation of the intestinal pouch – in a young person fully protects against large intestine cancers (14). However, we should also remember about all diseases that coexist with FAP and about complications resulting from previous surgeries. It seems that presented case of a FAP female patient during an almost 30-year observation shows the major part of possible complications described in the literature and FAP comorbidities.

That is why a long-term observation of a patient and their family by a one specialist treatment centre with the highest referral level seems to be significant. It makes it possible to carefully monitor the treatment, possible complications and disease progression. What is more, it enables to gain an important experience by the team of doctors being in charge of FAP patients. Without doubt, it is of great advantage for the patient if they are treated in a single specialist centre. A patient stays under supervision of one team of doctors all the time, which for sure builds strong relations and increases patient’s confidence. Lack of patient’s anonymity during subsequent hospitalisations seems to be an important aspect, which can be not satisfied when treatment centres are frequently changed.

Creation of registers and databases of FAP patients or families containing data about types of genetic mutations as well as detailed clinical information on the course of treatment also seems to be important. Observed patient is of course treated in accordance with the Familial Adenomatous Polyposis of the Large Intestine Register and strictly cooperates with the authors of this paper.

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