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Familial adenomatous polyposis: current status and case report

Poliposis adenomatosa familiar. Estado actual y reporte de caso

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ABSTRACT

Introduction: Familial adenomatous polyposis is a rare disorder and accounts for less than 1% of the causes of colorectal cancer. It is characterized by thousands of colorectal adenomas with high risk of developing cancer. **Case report:** A 48-year-old female patient with hematochezia and weight loss. Colonoscopy showed more than 100 polyps and a tumor in the sigmoid colon. She has a history of three direct relatives with colon cancer. **Conclusion:** It is necessary to perform an early assessment and family evaluation to prevent the appearance of cancer. Surgery is the basis of treatment.

RESUMEN

Introducción: *La poliposis adenomatosa familiar es un trastorno poco frecuente y significa menos de 1% de las causas de cáncer colorrectal. Se caracteriza por presentar miles de adenomas colorrectales con alto riesgo de desarrollar cáncer.* ***Caso clínico:*** *Paciente femenino de 48 años con hematoquecia y pérdida de peso. La colonoscopia muestra más de 100 pólipos y un tumor en colon sigmoides. Cuenta con antecedente de tres familiares directos con cáncer de colon.* ***Conclusión:*** *Es necesario realizar una valoración precoz y evaluación de familia directa para prevenir la aparición de cáncer. La cirugía es la base del tratamiento.*

INTRODUCTION

Colorectal cancer is the third leading cause of cancer and the fourth most common cause of cancer-related deaths in the world. Most occur sporadically in approximately 70 to 80% of cases, and 10 to 20% are familial.[1]

Familial adenomatous polyposis (FAP) is an autosomal dominant inherited disorder that occurs in approximately 1:10,000 live births and affects both genders equally and all races. It may be asymptomatic or present with bleeding, diarrhea, abdominal pain, or mucous discharge. It also presents with anemia, intestinal occlusion, or weight loss when large polyps are present or increase in number preceding the development of cancer. The main characteristic is the presence of hundreds to thousands of colorectal adenomas with areas of normal mucosa between each lesion. Mild polyposis is when 100 and 1,000 adenomas are identified. When fewer than 100 adenomas are found, it is diagnosed as attenuated polyposis. Nearly 100% of patients will develop cancer if they do not receive treatment.[2]

FAP is a multisystem disease that can present with numerous extracolonic manifestations. These include gastroduodenal adenomas and cancer, desmoid tumors, osteomas, epidermoid cysts, papillary thyroid cancer, small bowel polyps and cancer, congenital hyperplasia of the retinal pigment epithelium, and dental anomalies.

Gardner syndrome is a polyposis accompanied by desmoid tumors, osteomas, epidermoid cysts, or supernumerary teeth. Turcot syndrome is a FAP associated with

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malignant tumors of the central nervous system. Both syndromes are caused by mutations in the APC adenomatous polyposis coli (APG) gene.

GENETIC BASIS

FAP is caused by an inherited mutation in the APC gene located on chromosome 5q21,[2,3] Affected patients are born with only one functional copy of this "guardian" gene. Loss of the second allele leads to the rapid development of hundreds to thousands of colorectal adenomas. More than 850 different mutations have been described, in which there is abnormal development of the APC protein. About 25% of patients with FAP have a *de novo* mutation, with no family history.[4]

DIAGNOSIS

Familial adenomatous polyposis can be diagnosed genetically or clinically. Genetic testing reveals a mutation of the APC gene in approximately 80% of cases. Indications for referral to genetic counseling include family history of FAP, personal history of 10 or more adenomas, personal history of adenomas, and extracolonic manifestations of the disease. In at-risk patients with family members with known mutation, targeted testing for that mutation is performed. In approximately 20% of patients the mutation cannot be identified, but the clinical phenotype is present.[5]

RISK OF CANCER DEVELOPMENT

FAP presents a risk of developing colorectal cancer close to 100%. It represents only 0.5 to 1% of the causes of colorectal cancer and mean age of presentation is 39 years. The goal of treatment in these cases is to increase survival by decreasing the risk of death from colorectal cancer by performing colectomy or proctocolectomy before cancer occurs. The risk of cancer in attenuated FAP is approximately 70% and develops at an older age compared to classic disease.[5,6]

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EXTRACOLONIC MANIFESTATIONS OF FAMILIAL ADENOMATOUS POLYPOSIS

Approximately 90% of patients with FAP develop duodenal adenomas, but only 5-10% develop periampullary cancer. Up to 50% of patients also have polyps in the gastric fundus, which have minimal risk of malignancy.[5]

Desmoid disease affects approximately 5% of patients with polyposis. About half of the tumors originate in the mesentery and 40% develop in the abdominal wall. The remainder occur in the back, neck, or extremities. Desmoid tumors manifest as flat, fibrous lesions, or discrete masses. They are more frequently associated with female gender and family history of desmoid tumors. Most of these lesions develop five years after abdominal surgery possibly as part of the inflammatory response.[5]

The risk of developing thyroid cancer is only 2%; however, it corresponds to twice that of the general population. The incidence is 17 times higher in women than in men and develops on average at 27 years of age. The main histology is papillary carcinoma.[5]

Less frequent associated malignant lesions include pancreatic adenocarcinoma, hepatoblastoma, and medulloblastoma. There are also associated benign lesions that, although they do not require treatment, are useful for diagnosis. Congenital hypertrophy of the retinal pigment epithelium corresponds to dark gray or brown oval lesions seen in 60-85% of patients. Osteomas are dental abnormalities seen in 20% of cases. Some skin lesions such as dermoid cysts, lipomas or fibromas may be seen. Their presence on the face, neck, skull, or extremities usually suggests the diagnosis of FAP.[5,7]

SCREENING STUDIES FOR FAMILIAL ADENOMATOUS POLYPOSIS

Screening studies should be performed for both colonic disease and extracolonic manifestations to limit the risk of developing cancer by timely intervention and surgical referral. Screening should be done in everyone by genetic diagnosis or in first-degree relatives diagnosed with FAP. Even with only the clinical diagnosis, a complete study of family members should be done. Studies should begin at 12 years of age by flexible recto-sigmoidoscopy. If polyps are observed, a complete colonoscopy should be requested. If there are no polyps on initial examination, sigmoidoscopy should be repeated every one to two years or sooner if symptoms are present.[5]

The first upper endoscopy should be performed between 20 and 25 years of age and surveillance intervals are performed according to the findings. In the case of thyroid disease, physical examination and ultrasound should be performed every year in search of suspicious lesions. For desmoid tumors and other extracolonic lesions there is no specific screening system; however, special studies should be performed if there is high penetrance of a particular lesion in other family members.[7,8]

TREATMENT

The goals of treatment in familial adenomatous polyposis are to eliminate or limit the risk of cancer, to increase life span, and improve the patient's quality of life. Since the possibility of developing cancer is high, timely surgical treatment is the mainstay of treatment. The decision on the timing of surgery depends on the presence of symptoms, the age of the patient at the time of diagnosis and other special circumstances. When symptomatology is present, the patient should be offered surgery to treat the symptoms themselves and prophylactically for the potential risk of developing cancer. In asymptomatic children and adolescents, surgery is reasonably delayed until late adolescence or around the age of 20 years, when some physical and emotional maturity has been reached. Because the risk of cancer increases with age, surgical treatment is offered to patients from the third decade of life onwards at the time of diagnosis.[7]

For patients in whom there is no evidence of rectal cancer, colectomy with ileorectal anastomosis or proctocolectomy may be offered. The latter removes all the mucosa at

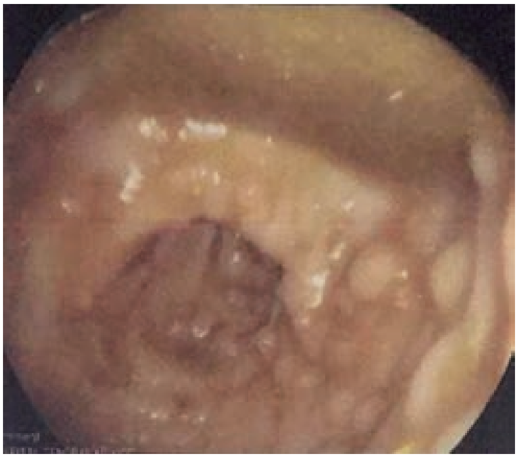

Figure 1: Multiple sessile polyps in rectal mucosa.

risk and the possibility of developing cancer in the future.[9] An ileo-anal pouch anastomosis or ileal reservoir (pouch) has higher bowel movements, higher risk of incontinence and the quality of life is affected compared to ileorectal anastomosis; however, the risk of developing cancer in the remaining rectal mucosa is 4-10%. The risk of developing cancer increases up to 12% 20 years after surgery; 42% of postoperative ileorectal anastomosis patients will require proctectomy in the future due to the presence of cancer or uncontrolled polyposis.[9]

When there is a colon cancer and distant metastasis the decision on the type of surgery is based on the possibility, even if low, that there is a metachronous cancer in the rectum if the rectum is respected. Patients with locally advanced tumors (or at risk of metastasis) with minimal polyps will benefit from open or laparoscopic colectomy on a case-by-case basis, with ileorectal anastomosis or proctocolectomy with end ileostomy. In patients with stage IV cancer with low life expectancy, proctectomy is recommended if there is no colon cancer or the presence of polyps is minimal. It should be considered that proctectomy is associated with an increased risk of urinary and sexual dysfunction, decreased fertility in women and a lower quality of life in general.[10]

A small percentage of patients develop cancer in the anal transition zone or in the

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ileal reservoir anastomosis zone. Mucosectomy has been proposed as an alternative, but if mucosectomy is not performed properly it may fail in its purpose. Up to 21% of patients undergoing mucosectomy have cancer seeding near the ileal pouches.[8]

Duodenal adenoma can rarely (up to 11%) progress to cancer and lesions can be treated by upper endoscopy.[7]

Desmoid tumors present from asymptomatic to severe pain, intestinal occlusion, or fistula. Treatment depends on the symptoms, location, size, and extent of the disease.

Thyroid nodules larger than 1 cm should be analyzed by fine needle puncture. Thyroid cancer is treated by total thyroidectomy and iodine ablation.

EVALUATION OF FAMILY MEMBERS AT RISK

All first-degree relatives have a 50% chance of developing FAP, so they should be initially evaluated by a genetic specialist. Potentially affected relatives should be screened at the time of diagnosis and in the case of children at 12 years of age. When an APC mutation is known in the family, DNA testing is recommended. At-risk family members who do not have a genetic diagnosis should begin surveillance at 12 years of age with flexible sigmoidoscopy or colonoscopy if screening is initiated in adulthood. Relatives who do not have polyps at 40 years of age will be managed according to the guidelines for the general population.[7]

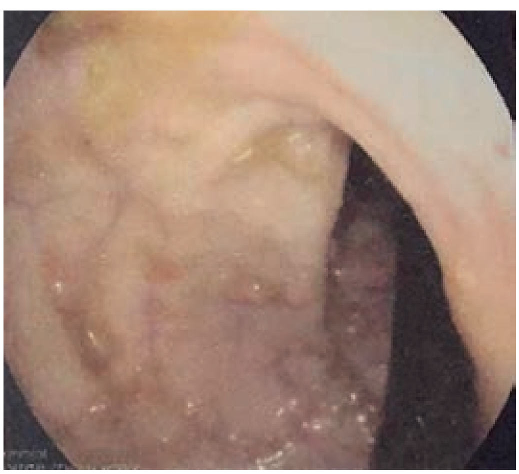

Figure 2: *Polyps in sigmoid colon mucosa.*

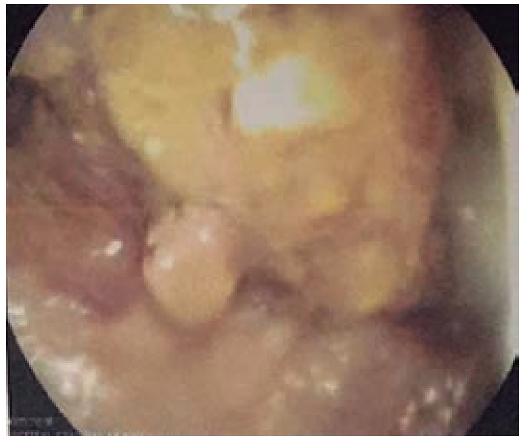

Figure 3: *Stenosing tumor at the level of the sigmoid colon seen by colonoscopy.*

CLINICAL CASE

The patient is a 48-year-old female patient who started with hematochezia approximately six months ago, loss of more than 10 kilograms of body weight and non-specific abdominal pain. She also presents a history of three first-degree relatives diagnosed with colon cancer and one second-degree relative diagnosed with polyposis. Colonoscopy was performed, finding more than 100 sessile polyps and a stenosing tumor 25 cm from the anal margin *(Figures 1 and 2)*. The patient underwent open proctocolectomy with terminal ileostomy, identifying a 3 × 2 cm tumor at the level of the sigmoid colon *(Figures 3 and 4)*. The histopathological study reported invasive moderately differentiated adenocarcinoma of the colon. It was classified as a T4a N1b M0, stage IIIB, for which he received adjuvant treatment with chemotherapy.

DISCUSSION

Familial adenomatous polyposis is a rare condition that requires a timely and accurate diagnosis to prevent the formation of colorectal

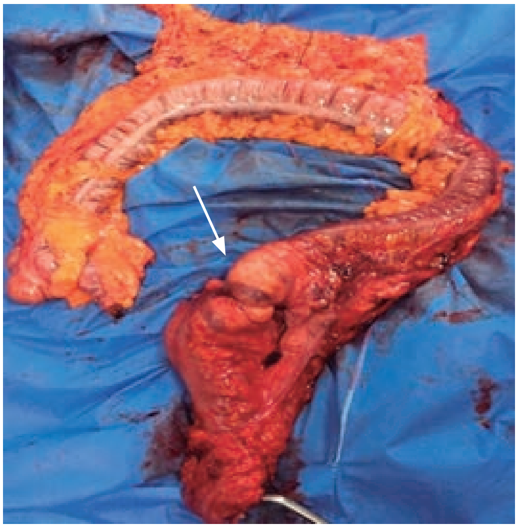

Figure 4: *Proctocolectomy product. The tumor can be seen at the sigmoid colon level (arrow).*

cancer in both the patient and first-degree relatives. Surgery remains the only preventive treatment at present; proctocolectomy, with or without restitution of intestinal transit, is the best procedure, as it removes the mucosa at risk of cancer formation.

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Ethical considerations and responsibility: The procedures in humans must comply with the principles established in the Declaration of Helsinki of the World Medical Association (WMA) and with the provisions of the General Health Law Title Five and the Regulations of the General Health Law on Research for Health, and NOM-012-SSA3-2012, which establishes the criteria for the execution of research projects for health in human beings, as well as with the rules of the Research Ethics Committee of the institution where they are carried out.

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