Case Report

Fibrogenesis and carcinoid tumor – a case report

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ABSTRACT: Carcinoid tumors are rare. They may appear in the entire gastrointestinal and respiratory tracts, with single or multiple occurrences. Prognosis is dependent on the size and location. Symptoms may appear in carcinoid syndrome, related to active substances, especially serotonin. One important aspect associated with these tumors and usually ignored is fibrogenesis. This is a case report of a patient with carcinoid tumor of the terminal ileum, treated by laparoscopy, associated with fat and fibrosis infiltration.

Keywords: carcinoid tumor; colectomy; laparoscopy.

RESUMO: Tumores carcinoides são pouco frequentes, podem surgir em todo o trato gastrointestinal e respiratório, podem ser únicos ou múltiplos. O prognóstico depende do tamanho e da localização do tumor. Podem ocorrer sintomas relacionados à síndrome carcinoide, decorrente da produção de substâncias ativas, em especial serotonina. Um aspecto comumente ignorado associado a estes tumores é a estimulação da fibrogênese. Relatamos um caso de tumor carcinoide de íleo, tratado por videolaparoscopia, associado à infiltração fibroadiposa.

Palavras-chave: tumor carcinoide; colectomia; laparoscopia.

INTRODUCTION

Carcinoid tumors are infrequent neuroendocrine neoplasms that may occur in the entire gastrointestinal, and outside it as well[1]. They may be single or multiple tumors and are associated with secretion of several active substances that can lead to many specific or nonspecific symptoms, particularly related to carcinoid syndrome. The presentation, although frequent but not always remembered, is the fibrous reaction that the tumor may cause. The purpose of this study was to report a case of carcinoid tumor of the terminal ileum, treated by videolaparoscopy, associated with fat and fibrosis infiltration of the abdominal cavity and the cecum.

CASE REPORT

A 68-year-old female patient, asymptomatic, was submitted to routine ileocolonoscopy for colorectal neoplasm screening four years ago, which showed submucosal tumor in the ileum of around 1 cm and two sessile polyps of 0.5 cm in the rectum, and polypectomy of rectal polyps (tubular adenomas) was performed. The patient remained without supervision for four years. A new ileocolonoscopy was performed (Figures 1 and 2), which showed ileocecal valve bulge and submucosal tumor of the terminal ileum of around 2 cm, involving 50% of the lumen. The abdominal computed tomography (CT) showed no anomalies and imaging and laboratorial exams showed no alterations.

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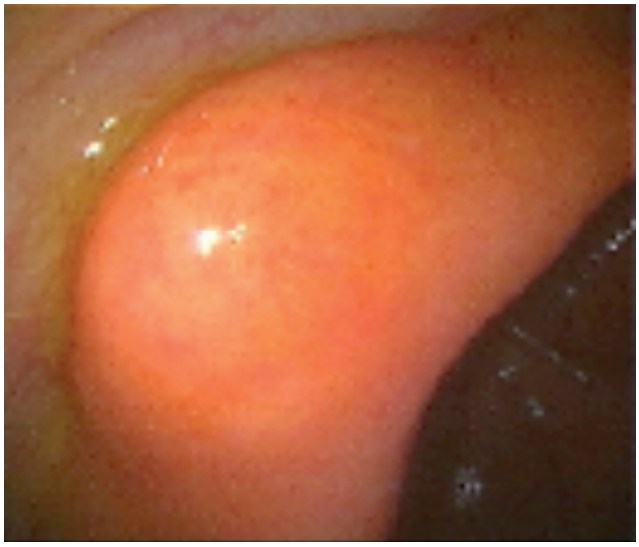

Figure 1. *Colonoscopy: ileocecal valve bulge.*

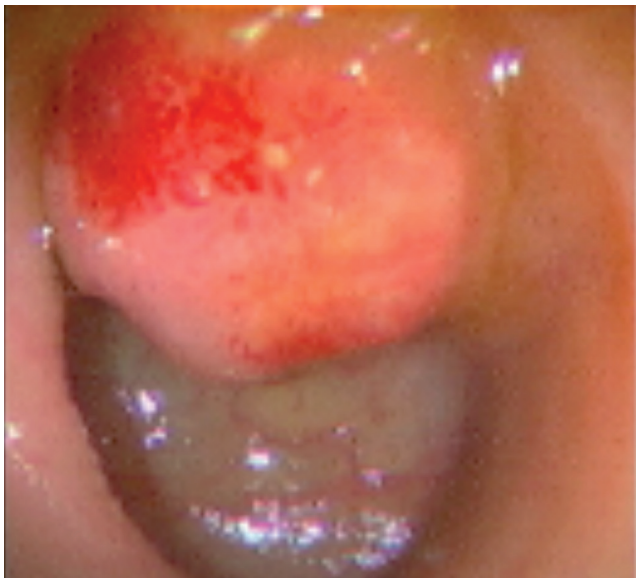

Figure 2. *Ileoscopy showing a 2-cm tumor of the ileum.*

Considering the future risk of obstruction, impossibility of endoscopic treatment and involvement of malignancy, the surgical intervention was the adopted therapy. At the surgical inventory, performed by laparoscopy, a high amount of fibrous adherence in the abdominal cavity was observed, with no evidence of metastases. Adhesiolysis and laparoscopic right hemicolectomy were performed, with laterolateral ileotransverse lymphadenectomy and extracorporeal mechanical anastomosis (Figure 3). The patient was discharged from the hospital on the third postoperative day.

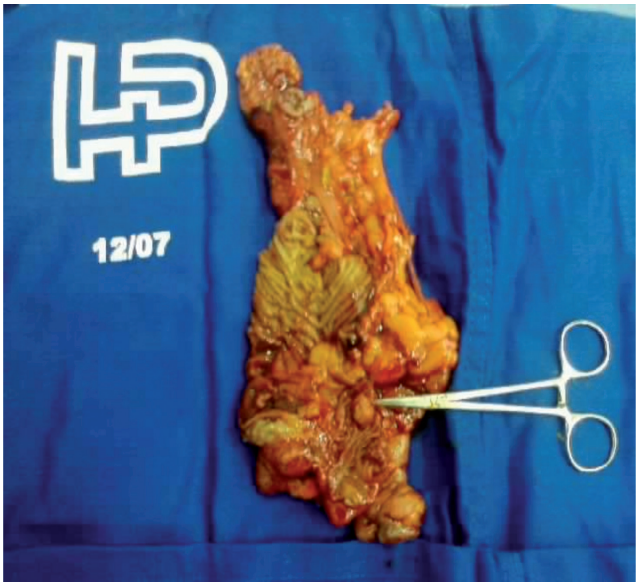

Figure 3. *Surgical specimen; product of laparoscopic right hemicolectomy: ileum, cecum, ascending colon and mesocolon, pointing to a tumor in the ileum.*

At the pathological anatomy, a carcinoid tumor of 2 cm was observed in the ileum, limited to the muscularis propria, and 23 neoplasm-free lymph nodes, as well as lipomatosis of the ileocecal valve and fat and fibrosis infiltration of the cecal appendix. The patient was taken to the service of oncology, which did not prescribe any adjuvant treatment.

DISCUSSION

The term *karzinoid tumor* was first used in 1907, by Oberndorfer, to describe tumors less aggressive than adenocarcinomas[2]. Carcinoid tumors derive from enterochromaffin cells, which are part of the diffuse endocrine system (*amine precursor uptake and decarboxylation* – APUD); although usually occurring in the form of subepithelial lesions, they are histologically considered epithelial tumors[3].

According to their embryological origin, carcinoid tumors can be classified as: *foregut (*thymus, respiratory system, stomach, duodenum, pancreas and ovaries), *midgut (*jejunum, ileum, appendix and proximal colon); *hindgut* (distal colon and rectum)[2]. The most frequently affected structures are: appendix, ileum, rectum and bronchi[1-5].

In a clinical perspective, they can be classified as functioning or non-functioning, depending on the production of substances, such as amines (serotonin and histamine), proteins (hormones and kinins) and prostaglandins. The first type causes carcinoid syndrome associated with vasomotor symptoms: hot flashes, alterations to systemic arterial pressure, bronchospasm and diarrhea[6,7]. The syndrome invariably occurs associated with liver metastases or tumors outside the hepatic portal system[1]. Metastases are more common in tumors in the jejunum and ileum. Tumors smaller than 1 cm rarely cause metastases, while around 10% of the tumors up to 2 cm and 70% of tumors over 2 cm are associated with metastases.

Insulin-like growth factor (IGRF) and vascular endothelial growth factor (VEGF) are related to pulmonary and intestinal carcinoid tumors, and the increased expression of these factors is associated with tumor growth due to increased angiogenesis, which seems to be related to metastases and reduced survival[1].

Another aspect related to the production of substances by the tumor, especially serotonin and the transforming growth factor-beta 1 (TGF-β1), is the occurrence of fibrogenesis, mainly in tumors of the ileum and jejunum, which many times leads to bowel obstruction[3,4]. Fibrosis usually occurs in the mesentery, called desmoplastic reaction. Fibrosis occurs less frequently in the retroperitoneum, pleura, skin and endocardium, leading to heart valve lesions, particularly in the right side.

Serotonin regulates the production of TGF–β, which, in turn, promotes the collagen synthesis by stimulating fibroblasts in the extracellular matrix. Tachykinins promote the DNA synthesis in fibroblasts and neurokinins are involved in heart valve fibrosis[4,8].

Studies show that high serum levels of serotonin bound with platelets and high urinary levels of 5-hydroxy-indole-acetic acid (5-HIAA – the serotonin metabolite produced in the kidneys) are commonly associated with liver metastases; whereas the peritoneal mass associated with fibrosis is only related to high levels of serotonin bound with platelets[1].

The preoperative diagnosis is not always possible. The urinary excretion of 5-HIAA above 8 mg/24 h presents sensitivity and specificity of 73% and 100%, respectively[2]. *Hindgut* and *foregut* tumors are not associated with high urinary levels of 5-HIAA, neither with serum serotonin, but the serum level of platelet serotonin is more sensitive in the detection of these tumors. Imaging exams are more useful when associated with methods that detect metabolites secreted by the tumor, such as: scintillography and positron emission tomography (PET). Fibrous tumors smaller than 1.5 cm are identified in tomography in 50 to 75% of midgut tumors[2].

The treatment is surgical, depending on the tumor location and size. Tumors of the appendix smaller than 1 cm can be treated through appendicectomy and tumors over 2 cm, with right hemicolectomy. Tumors of intermediate size should be individualized. Small bowel tumors are treated with resections of both primary and secondary lesions. Colon tumors should be resected depending on their location. Rectal tumors smaller than 1 cm can be treated with local resections, for 1 to 2 cm, the treatment is individualized, over 2 cm, with rectosigmoidectomy, if possible, or rectal amputation[6].

The drug treatment I used to relieve the symptoms related to carcinoid syndrome, such as octeocride, lanreotide, H_2 blockers, phenothiazine, corticosteroids, serotonin blockers[2]. Chemotherapy is ineffective in advanced stages of the diseases. Substances that inhibit angiogenesis and tumor growth, such as endostatin, sunitinib, sorafenib and bevacizumab, seem to bring promising results[1]. Prognosis is dependent on both tumor staging and location, and tumors of the ileum and jejunum present the worst prognosis.

CONCLUSION

A high level of suspicion for carcinoid tumors should be taken into account, especially in the presence of systemic symptoms and signs of local or distant fibrosis.

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