Case Report

Isolated splenic metastasis of colon cancer: a case report and literature review

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ABSTRACT: Colorectal cancer (CRC) is a leading cause of death in the elderly and about 20% of these patients present metastasis at diagnosis, most often in the liver. Other common metastatic sites include: lung, bone and brain. Isolated splenic metastases are rare, and they are usually a sign of widespread disease. The authors report a case of the rare occurrence of synchronous isolated splenic metastasis, diagnosed by computed tomography in the preoperative staging of a patient with CRC.

Keywords: colorectal cancer; metastatic disease; splenic metastasis.

RESUMO: O câncer colorretal (CCR) é uma das principais causas de morte na população geriátrica, aproximadamente, 20% desses pacientes já apresentam, na altura do diagnóstico, metástase neoplásica, mais frequentemente hepática. Outros locais comuns de metastização incluem: pulmão, ossos e cérebro. As metástases esplênicas isoladas de CCR são raras, sendo habitualmente sinal de doença generalizada. Os autores relatam um caso clínico da ocorrência rara de metástases esplênicas isoladas síncronas, diagnosticadas através da tomografia computadorizada durante o estadiamento pré-operatório de um doente com CCR.

Palavras-chave: câncer colorretal; metástase neoplásica; metástases esplênicas.

INTRODUCTION

CRC (CRC) is the third most common neoplasm and the fourth cause of death from neoplasm worldwide[1,2]. In Western countries, it is the second cause of death from an oncologic disease[3].

CRC is a disease that mostly affects the elderly, as only 5% of the cases are diagnosed in patients under 40 years of age[1] and, despite the improvements observed in the last decades either in surgical or new chemotherapy treatments, the CRC mortality remains high, with liver metastasis in around 50% of the patients[3]. At diagnosis, around 20% of the patients already present metastasis, most often in the liver. Other common metastatic sites include: lung, bone and brain[4,5].

The spleen is the main mass of lymphoid tissue in the body, but it is not a typical site of neoplastic metastasis in patients diagnosed with colon cancer[4,6-14]. In theory, all cancers can involve the spleen[15], but most cases observed usually involve other organs, with infrequent isolated splenic metastasis[4,6,8-12,14-18].

Neoplasms that frequently involve the spleen are tumors usually with a high metastatic potential, e.g., breast, lung, ovarian and uterine cancers[8-10].

Although there is no conclusive explanation for the low occurrence of splenic metastasis, the literature reports several hypotheses based on anatomical, pathological and immunological characteristics[4,6-12,18,19].

These patients are usually asymptomatic, and the diagnosis is performed by imaging exams for CRC staging[5,8,10], or in the follow-up period of patients that submitted to surgical treatments[7,9,11,13,14].

Most cases of splenic metastasis described in the literature related to CRC report metachronous

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metastasis identified in the follow-up period, with rare occurrences of synchronous isolated splenic metastasis[14].

The authors report the clinical case of a patient with synchronous isolated splenic metastasis from colon cancer of the splenic flexure submitted to left colectomy and splenectomy.

CLINICAL CASE

A 74-year-old male patient, with pathological history of medicated arterial hypertension and cerebral vascular accident, without unknown history of gastrointestinal tract pathology or abdominal surgery.

At the initial evaluation, the patient reported the clinical condition for around two months, characterized by hematochezia and anorexia, as well as weight loss – around 10 kg in 2 weeks – and episodes of sporadic blood flowing out of the anus, with 2-year progress, and whose severity was not aggravated during the period.

At the clinical examination, the patient presented good state in general, without significant alterations at the physical examination.

At the laboratory exam, the patient presented normochromic-normocytic anemia and hemoglobin was 10.9 mg/dL, with elevated tumor markers: carcinoembryonic antigen (CEA) was 242.47 ng/mL and carbohydrate antigen 19-9 (CA 19-9) was 76.0 U/mL (reference values: 0–10 and below 37, respectively), without other analytical alterations.

A lower digestive endoscopy indicated: "At 50 cm of the anal margin, in the proximal descending colon, neoformation originating stenosis that does not allow the endoscope insertion. The aspect may be due to inflammatory stenosis associated with the diverticula. Acute diverticulosis in the descending and sigmoid colon". The histological result of the biopsy was adenocarcinoma.

The patient was then taken for surgery preparation, with preoperative staging. The abdominopelvic computed tomography showed "[…] Liver with parenchyma of homogeneous texture, without lesions occupying space […] At the splenic flexure, an accentuated wall thickening is observed, extending to the transverse colon, forming a mass of around 8 to 10 cm of transversal diameter (corresponding to colon neoplasm). It shows adenomegalies in the splenic hilum, as well as splenomegaly and multiples cold nodules measuring between 7.5 and 8.5 cm, suggestive of metastasis. Diverticulosis in the sigmoid colon". The rest of the imaging exam did not show alteration (Figures 1A and B).

The case was later analyzed by a multidisciplinary team (General Surgery/Oncology) that decided to perform a left colectomy and splenectomy with posteriorly oriented for adjuvant chemotherapy.

The patient was submitted to laparotomy, and it was preoperatively confirmed that it was a neoplasm

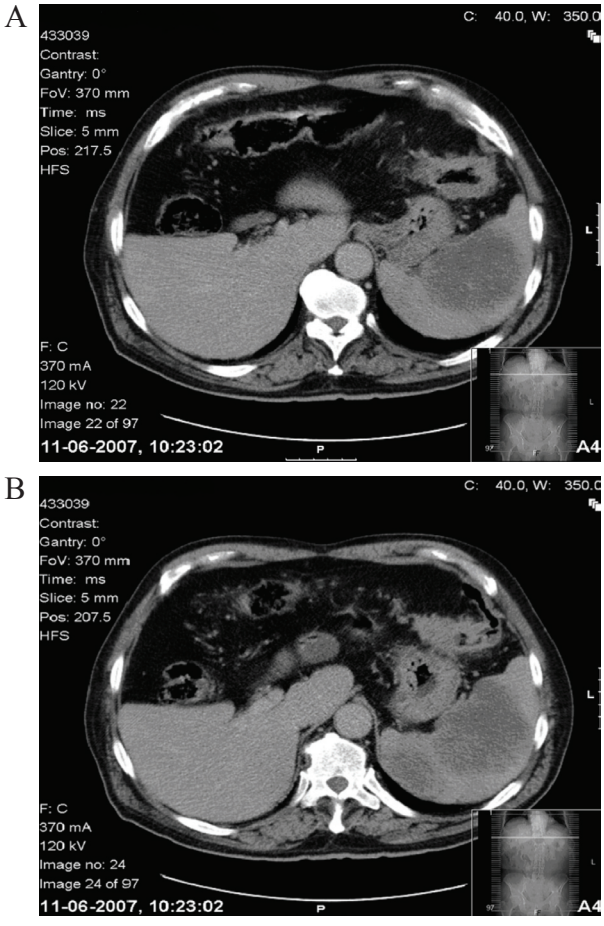

Figure 1. *(A and B) Abdominopelvic computed tomography showing "[…]At the splenic flexure, an accentuated wall thickening is observed […] (corresponding to colon neoplasm). Presence of adjacent fat densification and several grafts [...] It shows splenomegaly and multiples cold nodules measuring between 7.5 and 8.5 cm are evident, suggestive of metastasis […]".*

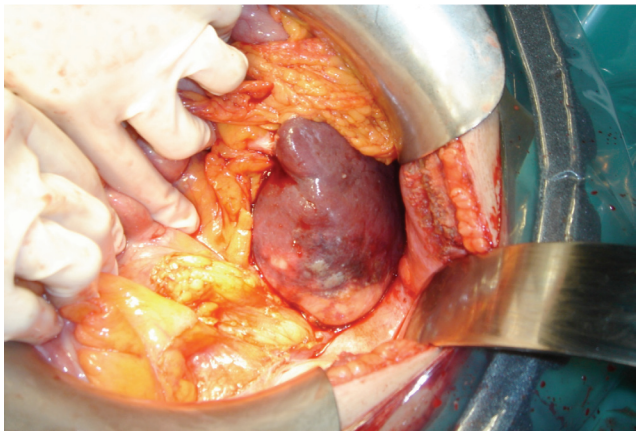

Figure 2. *Laparotomy showing splenomegaly and eventual splenic metastasis.*

in the splenic flexure, evidencing splenic lesion with characteristics of probable synchronous metastasis (Figure 2). Enlarged left colectomy and splenectomy were performed (Figures 3A, B and C).

In the postoperative period, the patient developed an intra-abdominal abscess and from the operatory wound, resolved with instituted antibiotherapy, and the patient was discharged from the hospital 12 days after the surgery.

The histological exam of the surgical specimen showed "[…] annular, infiltrative and ulcerovegetating neoplasm, of 5 cm max. longitudinal extension, 5 cm from the nearest surgical top, the histological exam shows moderately differentiated invasive adenocarcinoma. In depth view, the neoplasm has infiltrative growth, invading the entire colonic wall thickness and massively infiltrating into the pericolonic tissues. The images show lymphatic and venous neoplastic invasion. Seven lymphatic ganglia were taken from the pericolonic tissues, six of which with metastasis from the neoplasm described above". The histological exam of the specimen used in the splenectomy identified "[...] multiple yellowish-white well limited nodules, with several necrotic areas, the largest nodule with 8 cm max. diameter… splenic metastasis of adenocarcinoma, compatible with primary colon cancer. In the splenic hilum region, the images also showed lymphatic, perineural and venous neoplastic invasion".

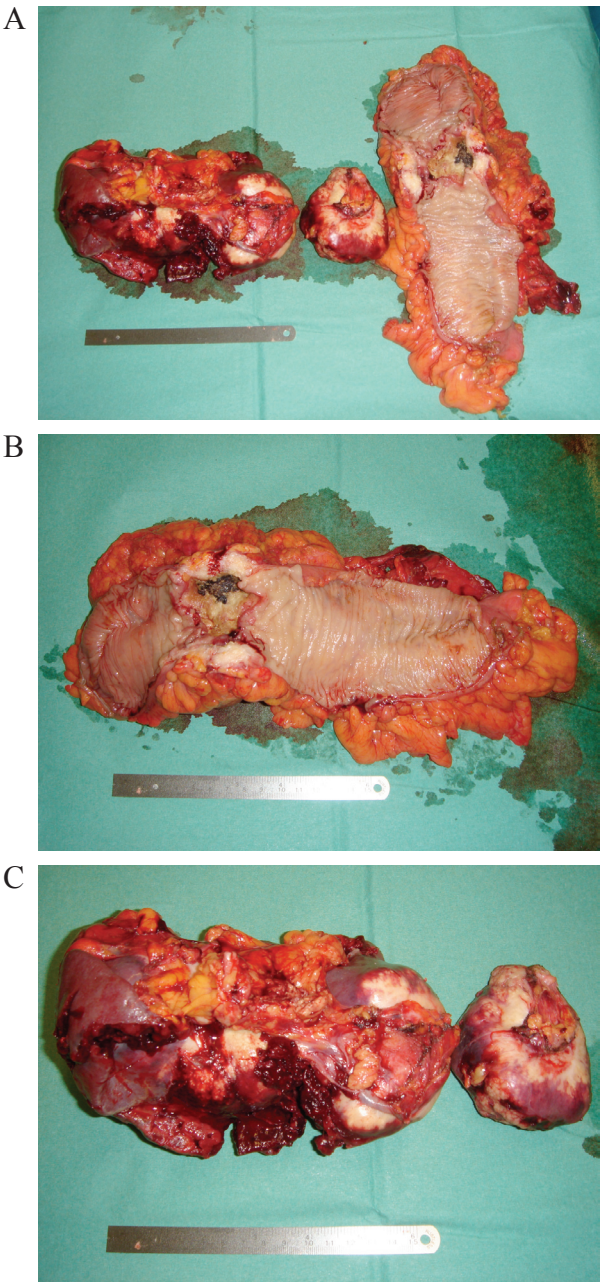

Figure 3. *(A, B and C) Macroscopic images of the surgical specimens (enlarged left colectomy and splenectomy).*

The pathological TNM (tumor, lymph nodes, distant metastasis) staging found was: pT4 G2 N2 M1, Dukes' C stage.

After discharged from the hospital, the patient was again evaluated by a multidisciplinary team that opted for secondary chemotherapy.

DISCUSSION

The spleen is not a typical site of colorectal adenocarcinoma metastasis and, if any is observed, it is rarely a single and isolated metastasis, with evidence of widespread disease[4,6,8-12,14-18]. Then, the spleen is rarely affected by isolated metastases, with around 20% of these patients with secondary liver lesions at the diagnosis[4,5,12]. Other common metastatic sites include: lung, bone and brain[4,5].

According to data from necropsies, the spleen is the metastatic site in around 7% of the autopsies performed in patients with neoplastic disease. In theory, all cancers can involve the spleen[15], but neoplasms that frequently involve the spleen are tumors usually with a high metastatic potential, e.g., breast, lung, ovarian and uterine cancers[6,8-10,17]. Analyses of necropsies identified the following as the primary non-lymphomatous origin of splenic metastases: melanoma (34%), breast (12%), ovarian (12%) and lung (9%) cancers[8,10].

As mentioned above, isolated splenic metastasis is extremely rare, with around 50 cases described today in the literature, including metachronous and synchronous lesions[10,13,20]. Around 60% of these cases of isolated splenic metastasis are due to malignant gynecological neoplasm, with colorectal carcinoma as the primary location representing about 11% of the reported cases[9]. Another factor is related to the histological type of the primary lesion, as most cases involve adenocarcinomas[9,21].

The first cases in the literature about the prevalence of splenic metastasis were reported by Dunbar et al.[22] who, in 1969, published the first article on metachronous splenic metastasis associated with colonic neoplasm[12,14,22].

Berge, in 1974, reported the incidence of splenic metastasis of 7.1% in 7,165 autopsies of patients with several neoplasms and the incidence of around 4.4% in 1,019 autopsies of patients diagnosed with colon or rectal adenocarcinoma[8,11]; and no isolated splenic metastasis was reported in this publication[4,7,8]. Berge also demonstrated that the main etiologies of non-lymphoproliferative origin identified as the cause of splenic metastasis are: melanoma (34%), breast (12%), ovarian (12%) and lung (9%) cancers[8,10].

In the literature, most cases of splenic metastasis related to CRC report metachronous metastasis identified in the follow-up period, with rare synchronous isolated splenic metastasis[14]. Okuyama et al., in 2001, reported only 20 cases of isolated splenic metastasis associated with CRC in the Japanese literature and only 8 cases in the English literature[11]. In 1993, Thomas et al. reported the fourth case in the English literature[18], Indudhara et al., in 1997, reported the fifth[23], in 1999, Weathers et al. reported the sixth[24] and, in 2000, Kim et al. reported the seventh case of isolated splenic metastasis[19] in the English literature. More recently, in 2001, Avesani et al. described the first case of isolated and synchronous splenic metastasis described in the literature[25].

Recent data, described in the literature in 2007 by Pisanu et al., document only three cases of isolated and synchronous splenic metastasis associated with CRC and 39 cases of metachronous lesions[12].

As mentioned before, there is no plausible explanation for the low occurrence of splenic metastasis, but several hypotheses have been suggested[4,6-12,18,19]. These hypotheses[4,6,18] include the evident acute angulation at the emergence level of the splenic artery at its origin in the celiac trunk[4,26], which can act as an anatomical obstruction of the tumor emboli to the spleen, and the rhythmic contractions of the spleen[4,27] that force the blood flow from the sinusoids to the splenic veins, which, in case of constant blood flow, could prevent tumor fixation. Another hypothesis[5,26] refers to the fact that the spleen has an immunological capability, through the reticuloendothelial system, that can prevent tumor cells[4,9] and the lack of afferent lymphatic vessels in the splenic parenchyma. Other assumptions include the phagocytic capability of the splenic cells and the anti-carcinogenic substances produced by the spleen[11].

Both lymphatic and hematogenous ways have been proposed as the dissemination method. Anatomically, the splenic lymphatic vessels in the capsular and subcapsular regions can cause subcapsular splenic metastases[4,28]; however, according to most authors in the literature, many of these cases of metastases occur via hematogenous spread, as these

secondary lesions are usually limited to the splenic parenchyma[4,9,11], and the splenic hilum adenopathies usually have no metastasis.

The literature also reports that the left colon is the predominant site of tumoral lesion in patients with CRC and concomitant splenic metastasis, either synchronous (as in our clinical case) or metachronous[4,12], which can be explained by the possible retrograde blood flow from the inferior mesenteric vein to the splenic vein, and from there, to the spleen[4,23]. In this clinical case, the pathological anatomy shows images of lymphatic and venous invasion, suggesting a dual method of neoplasm fixation, via hematogenous and lymphatic ways.

The splenic metastasis is usually asymptomatic, but it can be associated with nonspecific symptoms, e.g., splenomegaly, weight loss, epigastric pain or pain in the left hypochondrium, hypersplenism and the possibility of spontaneous splenic rupture[4,8,13].

Most situations of asymptomatic isolated splenic metastasis diagnosed today are essentially the result of complementary diagnostic exams performed in the follow-up period. Then, the secondary lesions are usually diagnosed through echography and/or computed tomography performed during the CRC staging[4,12,14] or during the follow-up of patients submitted to surgery, with the determination and monitoring of the CEA values[7,9,11,13,14]. According to Imada et al.[29] in 1991, these lesions usually appear as low-density masses at the computed tomography, while echography shows images of hypoechoic or hyperechoic patterns[6,29]. On the other hand, in 1997, Ishida et al.[30] published a study in which they identified by echography the presence of four cases of splenic metastasis of primary colon cancer, then suggesting the importance of special attention to the spleen of a patient diagnosed with CRC, either in staging or follow-up[6,30].

In the follow-up period, increasing CEA values may suggest tumor recurrence, requiring a complementary investigation to identify the possible metachronous metastatic focus. Today, the CEA value determination in the postoperative period of patients submitted to CRC surgery is strongly highlighted in the literature.

According to the literatura, the survival of patients submitted to splenectomy due to metachronous splenic metastases varies from 6 months to 7 years[4,11,12,24], with average survival of 66.6 months[4,13]; then, most authors defend the use of splenectomy in the presence of metachronous and isolated metastatic lesion in patients with primary colon cancer, followed or not by chemotherapy[4,9,11,12,14,17,20,23,24].

However, although the literature reports the use of splenectomy in synchronous isolated splenic metastases associated with CRC[4,12,25], one of the described patients died of peritoneal carcinomatosis one year later and another patient developed secondary liver lesions after the splenectomy. Thus, the role of splenectomy in these situations has not been properly clarified, as these are rare diseases. However, with the increasing frequency of this pathology, it will be possible to conduct randomized studies that provide better risk/benefit evaluations of splenectomy[4]. It is not relatively applicable to the resection of secondary liver lesions in patients with known CRC, which, according to the literature, can benefit the patients[5].

However, the use of splenectomy, either in synchronous or metachronous lesions, is important for the curative or palliative treatments, with chemotherapy having an essential role in the treatment of these patients with isolated splenic metastasis associated with CRC[12].

The prognosis of synchronous splenic metastasis, although described in few cases in the literature, seems to depend proportionally on the disease staging at the diagnosis[12].

In conclusion, the presence of an isolated splenic mass is usually suggestive of primary splenic lesion, such as lymphoma, hemangioma, among others. However, although a rare disease, splenic metastasis should not be disregarded by the coloproctologist, especially when treating patients with history of malignant neoplasm, in the presence of signs of recurrence or when the main sites of secondary lesion are isolated.

Our clinical case reports a patient with isolated and synchronous splenic metastasis, which is a rare disease, associated with colon cancer in the splenic flexure, in agreement with the literature, which identifies the left colon as the predominant site in these situations. The histological exam showed moderately differentiated invasive adenocarcinoma, also in agreement with the literature.

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