



Isolated Splenic Metastasis from Colon Cancer: Case Report

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Abstract

Spleen metastases are rare and when present, are usually associated with disseminated disease. A single splenic mass is more suggestive of a primary splenic lesion than a metastasis. Any primary malignancy can metastasize to the spleen, however, the most common tumors to metastasize are melanoma, breast, ovarian and lung carcinomas. Colorectal carcinoma rarely metastasizes to the spleen.

The authors present a case of a 41-year-old woman, with a previous history of ascendant colon adenocarcinoma, treated with right hemicolectomy and adjuvant chemotherapy. On follow up, blood tests revealed an increase in tumor markers and Computed Tomography (CT) showed a single splenic mass. A percutaneous biopsy was performed and confirmed the presence of a splenic metastasis, and thus a splenectomy was performed.

Because these lesions are rare and patients are usually asymptomatic, the degree of suspicion must be high. Surgery is frequently the treatment of choice and can be curative in the absence of other disease.

Introduction

The spleen is an infrequent site for metastatic deposits and when present, they are usually indicative of a widely disseminated disease [1-9]. A solitary splenic mass is usually suggestive of a primary splenic lesion (lymphoma, hemangioma, abscess or infarction). However, although rare, splenic metastases can occur and should be hypothesized, particularly in patients with a previous history of malignancy [8,10].

The spleen can in fact be the site of metastatic disease, and according to literature may be present in 0- 6% to 7% of autopsies of cancer patients [1,3,9,11,12]. In one large series, isolated splenic lesions were seen in 5.2% of 92 patients with splenic metastases [13].

Splenic metastases may arise from metastatic melanoma (32%), breast (12%), ovarian (12%) and lung (9%) carcinomas as well as, rarely, in pancreatic, colon, and stomach carcinomas [5,6,8,9,11,14]. Any primary malignancy, however, can metastasize to the spleen [5,11].

Case Presentation

We present a case of a 41-years-old woman with a previous history of colorectal adenocarcinoma (ascendant colon), who underwent a laparoscopic right hemicolectomy and adjuvant chemotherapy two years before. The anatomopathological results revealed a metastasis of colorectal adenocarcinoma. As a result, a genetic study was performed, revealing a RAS variant (variant c.35G>A p.(Gly12Asp) in exon 2 of the KRAS gene was detected. Two years later, on the oncology follow-up, an increase in CEA and CA 19.9 serum levels was identified (5.5 ng/mL and 141 U/mL, respectively). A CT scan was performed and revealed a new, single and solid lesion in the splenic parenchyma with 60 mm, hypodense, with Bossel contours, adjacent to the splenic hilum, probably related to a secondary disease of colorectal cancer, without other signs of disseminated disease (Figures A-G). The patient has previously performed three CTs, and neither, including the last one performed, 11 months before didn't show any lesion.

The case was discussed multidisciplinary and a decision was made to restart treatments with chemotherapy and to perform a percutaneous biopsy (Figures H-K). This procedure was complicated with hemorrhage and hemoperitoneum, and was managed with selective angioembolization of a branch of the splenic artery, with good results (Figures L-Y). The biopsy's histology revealed an adenocarcinoma metastasis whose morphology and immunohistochemical profile (CK20 and

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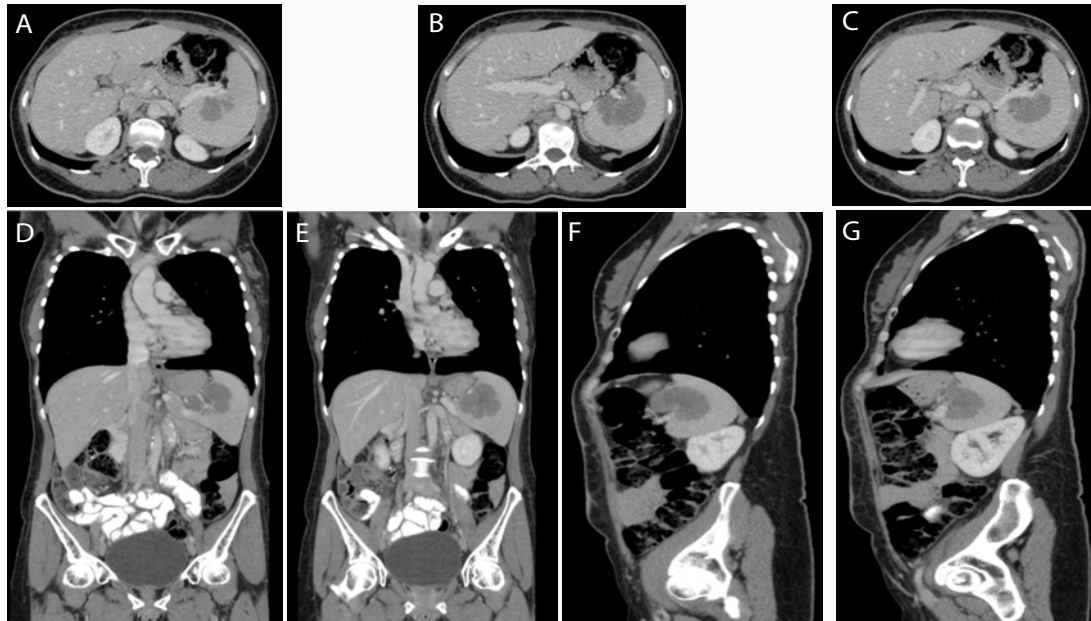


Figure A-G: CT scan: Single and solid lesion in the splenic parenchyma with 60 mm, hypodense, with Bossel contours, adjacent to the splenic hilum - probably related to a secondary disease of colorectal cancer.

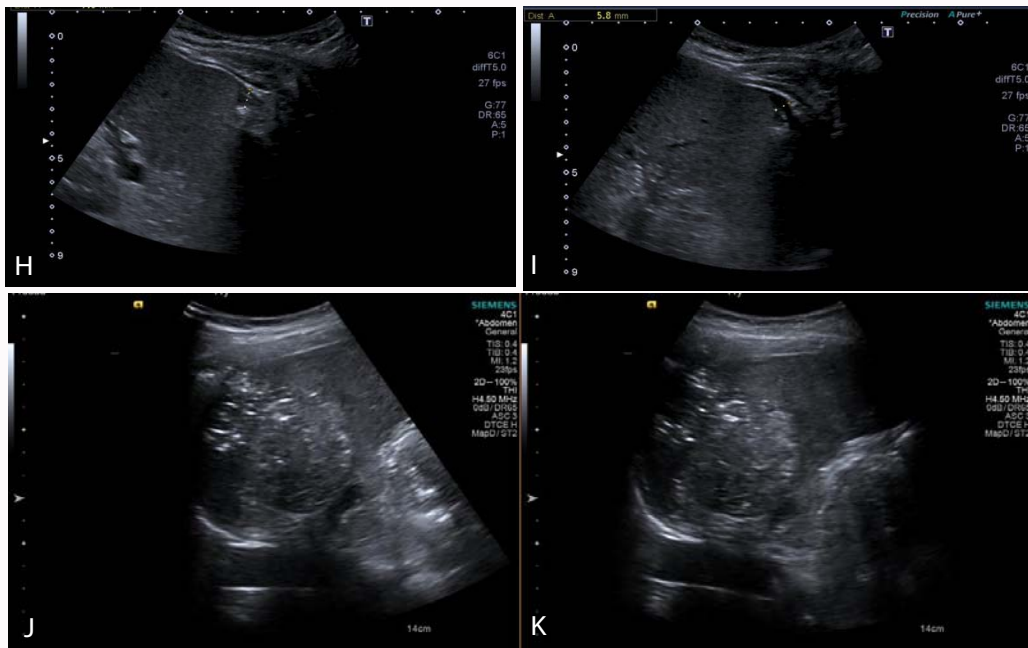


Figure H-K: Percutaneous biopsy of lesion.

CDX2 positive and CK7 negative) were compatible with colorectal origin.

Three months later we performed an open splenectomy, which occurred without complications (Figures 1-3). The anatomopathological results confirmed a splenic metastasis of colon adenocarcinoma.

The patient was seen in an outpatient clinic and did not present any evidence of surgical complications, signs of other metastatic sites and the values of tumor markers had reduced to within the reference values. After discussion in a multidisciplinary meeting, the patient was referred for follow-up in an oncology consultation, with no

indication for QT, maintaining only surveillance.

Discussion

Both primary and metastatic tumors of the spleen are exceedingly rare because this organ consists of a mass of lymphoid tissue [10]. Splenic metastasis must be distinguished from primary splenic lesion [10,15].

There is no conclusive explanation for the low occurrence of splenic metastases [5,7]. Tumor metastasis is a complex process, which is influenced by anatomical structures, mechanical factors, the immunological tissue microenvironment, and the intrinsic

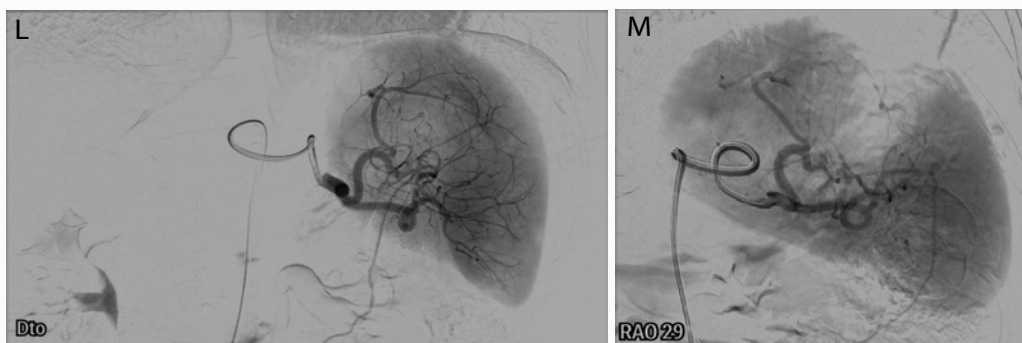


Figure L-M: Selective angioembolization of a branch of the splenic artery.

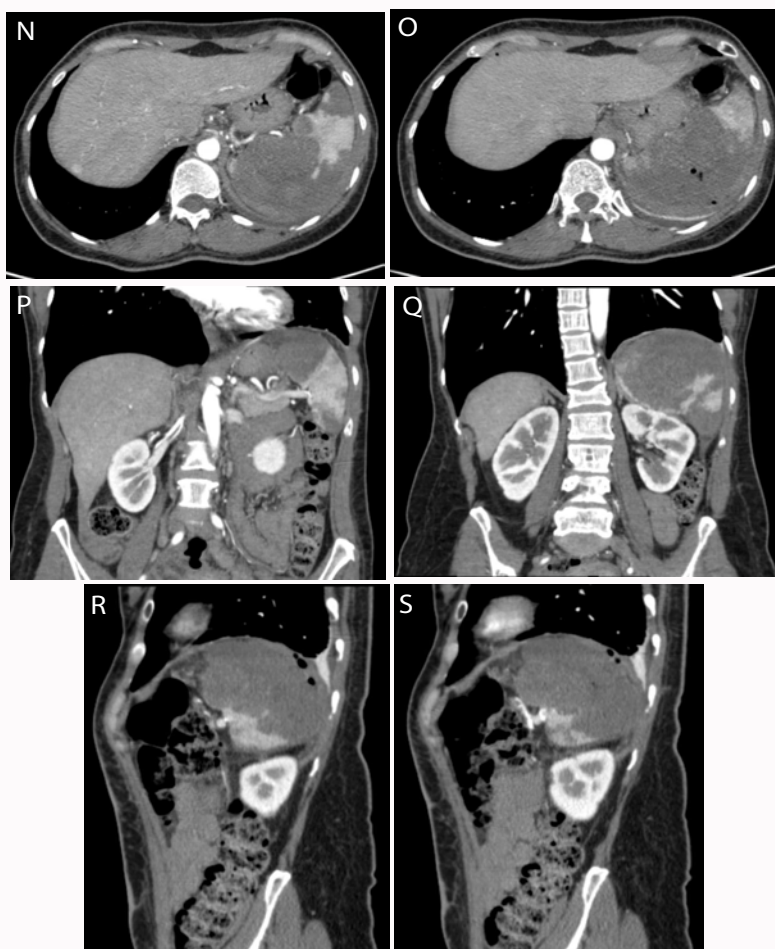


Figure N-S: CT scan after selective angioembolization of a branch of the splenic artery.

characteristics of tumor cells. The spleen is usually considered an infertile soil for metastases [2,3,6,8,10,12,15]. Explanations proposed for the relative scarcity of splenic metastases have included the sharp angle made by the splenic artery which makes it difficult for tumor emboli to enter the spleen, the absence of afferent lymphatics bringing metastatic cells to the spleen, the rhythmic contracture of the spleen which “squeezes” out the tumor emboli and prevents seeding in the spleen and lastly the antitumor activity due to the high concentration of lymphoid tissue in the spleen [16]. Our thoughts in this case are that the origin for this metastasis may be the result of the lack of afferent lymphatics, high antitumor activity of splenic lymphoid tissue and sharp angle of splenic vessels [14]. Splenic

metastasis is theorized to occur *via* hematogenous routes rather than lymphatic spread [17]. Many authors believe that the vascular route is the major pathway, supporting this in one hypothesis of retrograde hematogenous spread to the spleen *via* the inferior mesenteric vein, because these metastases are usually limited to splenic parenchyma [8,18]. The spleen lacks afferent lymphatic vessels. Splenic lymphatic vessels may lead to subcapsular metastases; however, most splenic metastases occur in the parenchyma [18].

Based on the formation time of metastases, splenic metastases can be divided into synchronous and metachronous metastasis. Synchronous metastasis means that the splenic lesion is discovered

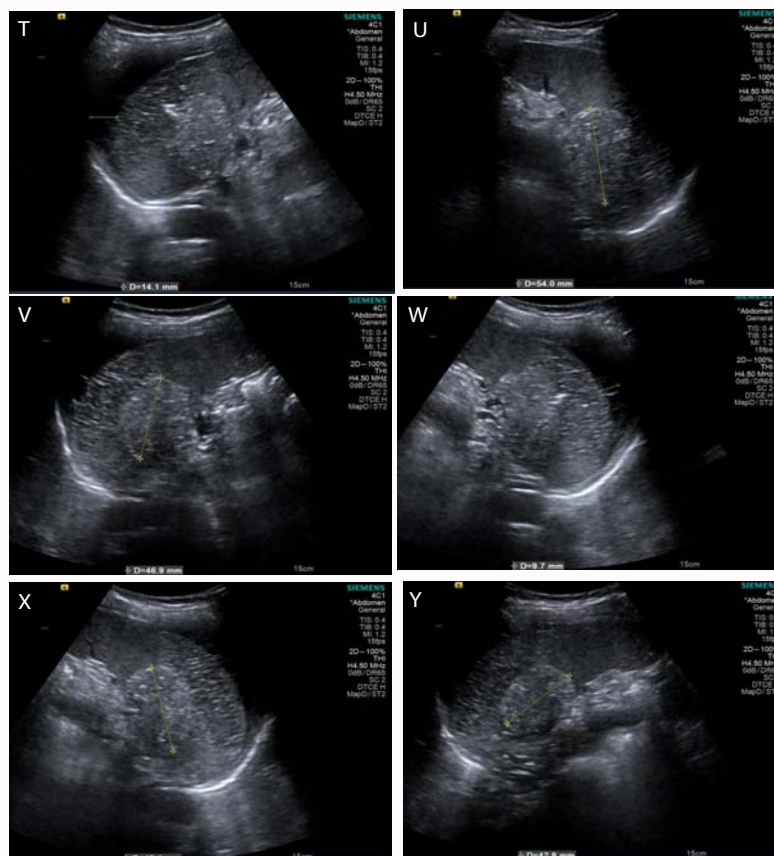


Figure T-Y: US images after angioembolization, revealing a small reduction in the size of lesion.

by imaging studies together with the primary tumor. Differently, the diagnosis of metachronous metastasis is usually made during the follow-up of patients in the postsurgical period [10]. Many authors believe that metachronous splenic metastases are more prevalent than synchronous [8].

The first cases in literature about the prevalence of splenic metastases were reported by Dunbar et al. who, in 1969, published the first article on metachronous splenic metastasis associated with colonic neoplasm [5,9]. Berge, in 1974, reported the incidence of splenic metastasis in 7.1% in 7,165 autopsies in patients with several neoplasms and the incidence of around 4.4% of 1,019 autopsies of patients diagnosed with colon or rectal adenocarcinoma; no single splenic metastases were reported in this publication [8,9,5,19].

Isolated metastasis to spleen is an infrequent event, with around 50 cases described today in literature, including metachronous and synchronous lesions [5,8]. About 60% of these cases of isolated splenic metastasis are due to malignant gynecological neoplasm, with colorectal carcinoma as the primary location representing just 11% of the reported cases. Another factor to be taken in account is related to the histological type of the primary lesion, as most cases involve adenocarcinomas [5].

Colorectal Cancer (CRC) is the third most common cancer world-wide and the fourth leading cause of death [10]. Colorectal cancer is a common malignancy and approximately 20% of patients have metastatic disease at their clinical presentation [20]. The liver is the most common site of distant metastasis. Other common sites include regional lymph nodes, lungs and peritoneum; fewer common

sites include the spleen, brain and axial skeleton [6,8,9,20]. The spleen is an exceptional site of colorectal cancer metastasis and it is usually discovered as a part of a of multivisceral metastatic disease [9].

Literature also reports that the left colon and rectum are the predominant sites of tumoral lesion origin in patients with colorectal cancer and concomitant splenic metastasis, either synchronous (as in our clinical case) or metachronous, 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 [5,6]. There are very few cases of colorectal carcinoma seen in literature presenting with solitary splenic involvement [8]. Overall, isolated splenic metastases are relatively easy to diagnose [2].

Metastases to the spleen are seen as solitary or multiple masses and vary in number and size from a few millimeters to several centimeters. Diffuse infiltration is a rare phenomenon [13,14].

Metastases are often asymptomatic or present themselves with minor symptoms [8,10,20] but symptoms such as weight loss, epigastric pain, left hypochondriac pain caused by an enlarged spleen, splenomegaly, hypersplenism and spontaneous rupture may be present. Splenic rupture that can occur indolently and quickly and evolve to a hemorrhagic diathesis and shock [10,11,14,20]. Left shoulder pain (Kehr's sign) or left-sided pleuritic chest pain may also occur as a result of diaphragmatic compression or subdiaphragmatic fluid collection or abscess [14].

Physical examination is usually nonspecific. Left hypochondrial pain, tenderness or signs of peritonitis, splenomegaly and frequently petechiae or purpura (as a result of thrombocytopenia) may be

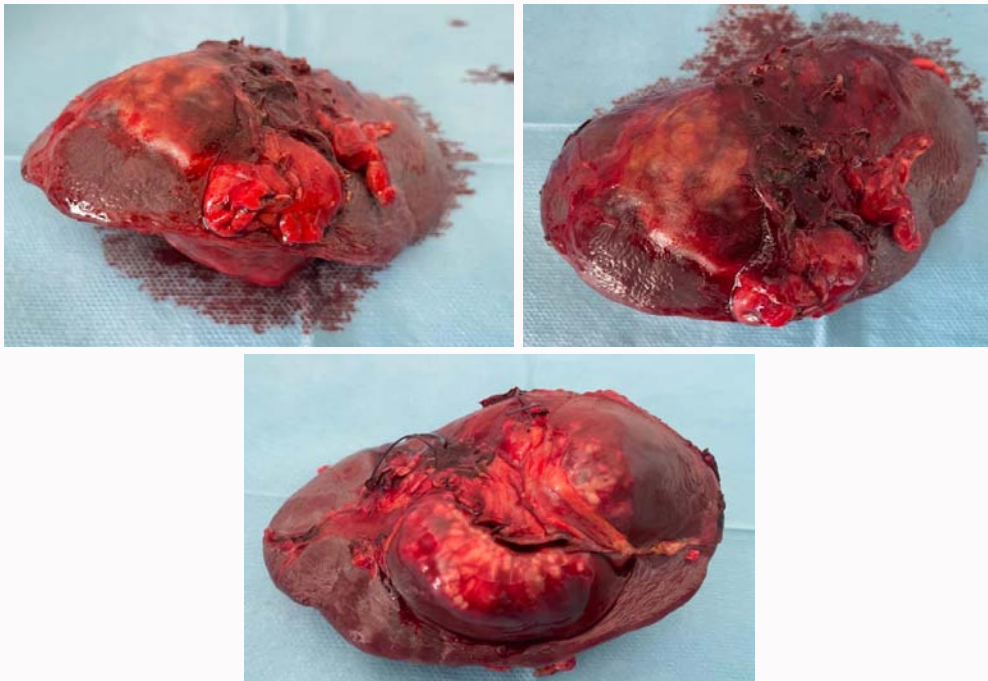


Figure 1-3: Splenic metastasis, after splenectomy surgery.

splenic specific [14].

The diagnosis of splenic metastases of colorectal cancer is usually made by imaging studies during the evaluation of a rising CEA level in the postoperative follow-up period of colorectal cancer patients [2,3].

On the follow-up, increasing CEA values may suggest tumor recurrence, thus requiring a complementary investigation to identify the possibility of a metachronous metastatic tumor [5]. CEA levels are elevated in more than 80% of such cases, from 4.6 ng/mL to 223 ng/mL [2].

Radiologic imaging is variable and often finds cystic and necrotic lesions [14]. Calcification in a splenic metastatic disease is rare unless the primary tumor is a mucinous adenocarcinoma [14]. Implants on the serosa surface of the spleen are seen in patients with peritoneal carcinomatosis, commonly from an ovarian or Gastrointestinal (GI) primary lesion [14]. Direct tumor invasion of the spleen is uncommon but may be seen in tumors originating in nearby structures, such as the kidney, retroperitoneum, colon, stomach, and distal pancreas [14].

Most of the splenic abnormalities have unique imaging patterns and biopsy or an invasive procedure rarely are needed before treatment decision [14]. Abdominal Ultrasound (US), CT scan, or Magnetic Resonance Imaging (MRI) are the gold standard for diagnosis, and contrast administration is recommended for differential diagnosis of hemorrhage or parenchymal abnormalities [14]. On ultrasound, a splenic metastasis predominantly appears as small hypoechoic and, occasionally mixed or hyperechoic or may be well defined as either cystic or solid masses [13,21]. Cystic alterations are seen when necrosis occurs or due to the mucinous nature of the primary tumor (e.g., ovarian carcinoma) [21]. A cystic or necrotic mass may show contrast enhancement at periphery and within the lesion's septa on CT and MRI [13]. On CT, splenic metastases appear

as well-delineated, low-attenuated cystic or solid masses. Calcification is unusual, unless the primary tumor is a mucinous adenocarcinoma. Most lesions show peripheral or septal enhancement. Peritoneal metastases cause scalloping of the splenic surface [21]. MRI imaging shows moderate hyperintensity on T2-WI and isointensity on T1-WI, comparing to the splenic parenchyma. The presence of blood products or other paramagnetic substances, such as melanin, in metastatic melanoma, may result in high signal intensity on T1-WI [21]. Positron Emission Tomography (PET) scan can be helpful as it provides a better detection of metastatic deposits, especially when they are too small to be shown in other radiological studies [3]. In addition, PET-CT fusion may specifically suggest that the mass seen on the CT is tumoral in nature. On the other hand, a solitary metastasis can be demonstrated and predicted preoperatively by PET-CT fusion scanning [3,9]. PET scan or pulled White Blood Cell (WBC) scintigraphy can demonstrate splenic infections as well, such as splenic abscess, one of the complications of spleen metastasis [14].

When needed the diagnosis can be confirmed by fine-needle aspiration or percutaneous biopsy instead of splenectomy [9]. Historically the technique of percutaneous splenic biopsy was not widely performed due to the perceived high complication rates mostly involving hemorrhage. With the advent of improved imaging modalities, splenic biopsies are now performed relatively safely using either ultrasound or CT guided techniques. Ultrasound is currently favored over CT due to the real time images projected [6].

Metastatic colorectal cancer may be treated with surgery, chemotherapy, and/or radiotherapy [10]. In an isolated splenic metastasis, in the absence of systemic recurrence, surgery is the primary modality of treatment and probably the only chance for radical cure, with low operative morbidity and may provide potential for long-term survival [1,2,5,9]. It can be followed by chemotherapy with or without radiotherapy in a metastasis of colorectal carcinoma origin [6,8]. In colorectal cancer, splenectomy is usually performed

in the setting of a rising CEA level and radiological suggestive. Splenectomy seems to be the favored therapy for splenic metastasis. If left untreated, splenic metastases may lead to splenic rupture [9].

Splenectomy is appropriate for diagnosis, treatment, and/or palliation of these conditions [11]. The surgical procedure is the same for primary tumors or for metastases [9].

This procedure can be performed by both the traditional open technique and more recently laparoscopically [1,6]. The principles of splenectomy technique are the same as for the primary splenic cancers. They include a good exposure, the removal of an intact spleen without rupture of the capsule, the removal of adjacent structures when necessary, and an adequate hemostasis. If possible, hilar lymph nodes should be removed [9].

There is a place for laparoscopic splenectomy in isolated splenic metastasis. It is generally indicated for benign hematological diseases, but its use for splenic malignancies remains controversial, due to the risk of peritoneal dissemination [2,9]. However, some studies have demonstrated that laparoscopic surgery used in colorectal and gynecological cancer were not associated with a greater risk of intraperitoneal dissemination of cancer than the conventional technique [9]. Moreover, this technique is easy and safe, and yields outcomes superior to those of open surgery, allowing earlier discharge and adjuvant therapy initiation. It also enables us to make a diagnosis of peritoneal carcinomatosis, avoiding a laparotomy [2,9].

Some authors suggest that splenectomy may lead to long-term survival in patients with isolated splenic metastasis, despite the fact that this splenic metastasis is a form of distant metastasis [2,4,9,19]. Long-term survival rate following splenectomy in patients with solitary splenic metastasis from colorectal cancer is still unknown. However, the limited data extracted from case reports indicate that these patients may survive up to 7 years [2,3,5,8,19,20]. The prognosis of synchronous splenic metastasis, although described in few cases in literature, seems to depend proportionally with the disease staging at the diagnosis [5,20].

Therefore, the importance of early suspicion of metastases and assessment with appropriate imaging techniques cannot be overemphasized [19]. The prognosis of isolated splenic colorectal metastasis is more favorable, even though these cases show distant metastatic spread [8]. Nevertheless, the growing frequency of colorectal carcinoma justifies further studies on the risks and benefits of splenectomy in cases of isolated metastases [20].

A Multidisciplinary Treatment (MDT) approach is important in colorectal cancer, especially in patients with synchronous metastasis [2]. An MDT approach may not only reduce the risk of perioperative morbidity and mortality but also improve long-term survival [2].

Conclusion

The presence of an isolated splenic mass is usually suggestive of primary splenic lesion, however, although a rare disease, splenic metastasis should not be disregarded, especially when regarding treating patients with history of malignant neoplasm, in the presence of signs of recurrence such as the increase of CEA serum levels.

These lesions are usually asymptomatic so the degree of suspicion must be high. Therefore, a careful follow-up and a high degree of suspicion are fundamental for the early identification of signs of recurrence or disseminated disease. Splenectomy is the gold standard

for the treatment of isolated splenic metastasis in colorectal cancer, and it is related to an improvement in long-term survival.

A multidisciplinary treatment approach is fundamental for improving treatment and prognosis of these patients.

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