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CASE REPORT

Isolated Metachronous Splenic Metastasis from Colon Cancer: Possible Explanations for This Rare Entity

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Introduction

The incidence of splenic metastases secondary to colorectal cancer is very low; these lesions have been more frequently reported as secondary to breast, lung, and ovarian cancer. Splenic metastases are particularly common in melanoma; their incidence has been reported as being as high as 34% at autopsy [1]. Most cases of secondary splenic metastases have been described in patients with tumors of the left colon while only few cases being reported as originating from right colon tumors (Table 1). The finding of a splenic mass in the absence of a history of malignancy suggests a primary lesion (lymphoma, hematoma, etc.), while a history of oncological disease raises the possibility of a secondary lesion [2].

Case Description

We report the case of a 76-year-old woman with a family history positive for breast carcinoma (sister and daughter). The patient underwent a left breast quadrantectomy in March 2006 for ductal infiltrating carcinoma (pT1a pN0 pMx, C-erb B2: 3+, ER 80%, 80% PgR, MIB <10%) followed by regional radiation and hormone therapy with letrozole for 5 years. She then went through standard follow-up.

In 2013, she underwent a colonoscopy and a CT scan of the abdomen which showed a 3-cm thickening and enhancement of the wall of the descending colon, complicated by lumen substenosis. The liver and the spleen were free of focal lesions. The CT also showed the presence of a saccular aneurysm of the splenic artery with a maximum transverse diameter of 1.6 cm and partial calcified thrombosis of the vessel wall. Some lymph nodes in the portacaval region were increased in volume. The patient underwent a left hemicolectomy in March 2013. Histological examination of the surgical specimen revealed an adenocarcinoma with a medium degree of differentiation, infiltrating the wall up to the subserosal layer with angiolymphatic but no perineural invasion. Two out of the ten perirectal lymph nodes showed metastatic involvement. The resection margins were free of tumor. The staging was pT3 pN1b pMx—G2. The patient began adjuvant chemotherapy in August 2013 following the CAPOX protocol: oxaliplatin 130 mg/mq g1q21, capecitabine 1000 mg/mq g1-14q21 for six cycles (not eight cycles for liver toxicity) until December 2013.

A follow-up chest abdomen CT scan performed at the beginning of July 2015 showed the presence of a 1-cm-diameter focal lesion in the lower third of the spleen in the subcapsular region associated with mild capsular retraction. A subsequent PET scan identified a 9-mm area of increased accumulation of radium localized at the same intrasplenic location and suggestive of secondary lesions. A splenectomy was performed in September 2015 and the lesion appeared on gross examination as a whitish nodule with a diameter of 1.6 × 1.5 × 1 cm, compact in appearance and well circumscribed by the surrounding parenchyma (Fig. 1). The lesion was found to be an

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Table 1 Literature review of isolated metachronous splenic metastasis from colorectal carcinoma

Case *n*	Year	Pathology	Primary tumor	Stage	Interval[a]	CEA level
1	1969	Adeno	Rectum	III	48	Not specified
2	1982	Adeno	Sigmoid	III	48	A
3	1986	Adeno	Cecum	III	30	A
4	1992	Adeno	Rectum	II	60	A
5	1993	Adeno	Left colon	II	144	A
6	1997	Adeno	Splenic flexure	III	42	A
7	1997	Adeno	Sigmoid	II	24	A
8	1999	Adeno	Rectum	Not specified	12	
9	1999	Adeno	Sigmoid	III	3	A
10	1999		Left colon			
11	2000	Adeno	Right colon	III	36	A
12	2000	Adeno	Not specified	Not specified	108	A
13	2001	Adeno	Sigmoid	III	72	A
14	2001	Adeno	Left colon	IV	52	A
15	2001		Left colon			
16	2001	Adeno	Sigmoid	III	23	A
17	2003	Adeno	Left colon		72	
18	2004	Adeno	Sigmoid	III	21	N
19	2004	Adeno	Left colon			
20	2006	Adeno	Sigmoid colon			
21	2006	Adeno	Descending	III	17	A
22	2008	Adeno	Splenic flexure	IV	36	A
23	2008	Adeno	Traverse colon	III	9	A
24	2008	Adeno	Rectum	III	18	A
25	2008	Adeno	Sigmoid	II	24	A
26	2009	Adeno	Hepatic flexure	III	60	A
27	2010	Adeno	Splenic flexure	III	24	A
28	2010	Adeno	Ascending	III	15	A
29	2011	Adeno	Rectum	III	15	N
30	2015	Adeno	Cecum	I	16	A
31	2016	Adeno	Descending	III	28	N

[a] *DFI* disease-free interval between treatment of primary tumor and diagnosis of the spleen metastasis

adenocarcinoma with immunophenotypic profile compatible with a secondary lesion from the digestive tract (Fig. 2a, b). The pretreatment CT scan performed in October 2015 again demonstrated the thrombosed saccular dilatation of the distal third of the splenic artery. The patient began adjuvant chemotherapy with capecitabine in November 2015; to date, 21 months after splenectomy, she is in complete remission.

Discussion

The most common sites of metastases from colorectal cancer are the regional lymph nodes, the liver, the lungs, and the peritoneum. Splenic metastases are much rarer. Berge demonstrated that the incidence of splenic metastases is approximately 7.1% in 7165 autopsies performed on subjects who died with various cancer histotypes. The secondary lesions arising from the colon are 4.4% while those that originate from the rectum are 1.6% [3]. In most cases, the individual splenic metastases from colorectal carcinoma are asymptomatic. Sometimes, they can be responsible for non-specific symptoms such as malaise, weight loss, heartburn, pain in the left abdominal upper quadrant, splenomegaly, and hypersplenism. Rarely, it is possible to have spontaneous splenic rupture or splenic abscess formation [4]. The diagnosis is made by imaging studies during follow-up or during disease staging. Possible explanations of the rarity of such splenic lesions [5] are due both to anatomical and immunological

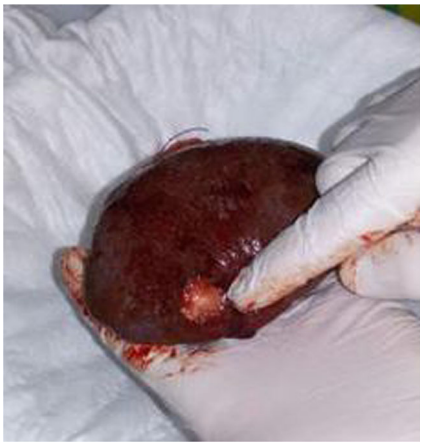

Fig. 1 Macroscopic view of the splenectomy specimen with colon cancer metastasis

characteristics. As regards the anatomical characteristics, the sharp angle of splenic artery with the celiac axis, the rhythmic contraction of splenic sinusoids, the absence of afferent lymphatic vessels within the splenic parenchyma, and the presence of a capsule which acts as a barrier for cell tumor could reduce the probability that tumor emboli can be implanted in the spleen. While, as regards the immunological characteristics that could reduce the probability of metastatic embolization in the spleen, these could be the production of an inhibitory factor that reduces the implantation and neoplastic cells growth, as well as the particular microenvironment rich in splenic monocytes, Kupffer cells, and Ig.

For these reasons, the exact etiopathogenetic mechanism is uncertain but several hypotheses have been made. Idhuara [6] argues that the metastatic spread occurs probably because of blood reflux from the inferior mesenteric vein in the splenic vein and from there to the spleen. This is in relation to the fact that the localization of primary carcinoma in these patients is mostly at the level of the left hemicolon. The literature suggests that high levels of serum CEA are associated with isolated splenic metastases from colorectal cancer. This is probably related to its biological functions: modulating the immune response by reducing the humoral, lymphocytic, and NK cell activity and facilitating the tumor cells adhesion to visceral macrophages in the spleen [7].

We found only 30 cases of isolated splenic metastases secondary to colorectal tumors from the first reported cases in 1969 up to 2016 (Table 1); none of these had further metastatic localizations at the time of the diagnosis. Most of the patients were asymptomatic, and the diagnosis was made by radiological examinations during follow-up. An increase in CEA level was detected in most cases. From these studies, it is clear that isolated splenic metastases from colorectal cancer are for the most part metachronous with a free survival period varying between 3 months and 11 years with an average of 4 years [8] and a disease-free survival ranging from 6 months to 7 years following splenectomy for metachronous lesions with colorectal cancer [9]. Five of the 30 cases reported in literature had a progression of the disease characterized by the onset of liver, peritoneal and lymph-node metastasis over a period between 6 and 24 months.

Such slow disease progression could be a direct consequence of immunological surveillance that makes it difficult for the engraftment and growth of tumor cells in the spleen [10, 11].

In addition, in our case, primary tumor was in the left colon as described more frequently in the literature. It was a stage III adenocarcinoma and the single splenic metastasis discovered after 28 months after surgery but without an increase in the serum CEA level. Our patient also showed a saccular dilatation of splenic which might have favored, by slowing the blood flow, the seeding of tumor cells in the splenic parenchyma. We can conclude that, in the absence of further lesions, splenectomy was indicated.

Because of the small number of cases reported in the literature and the absence of long-term follow-up data, a standard systemic treatment for splenic metastasis from individual colorectal cancer cannot be established.

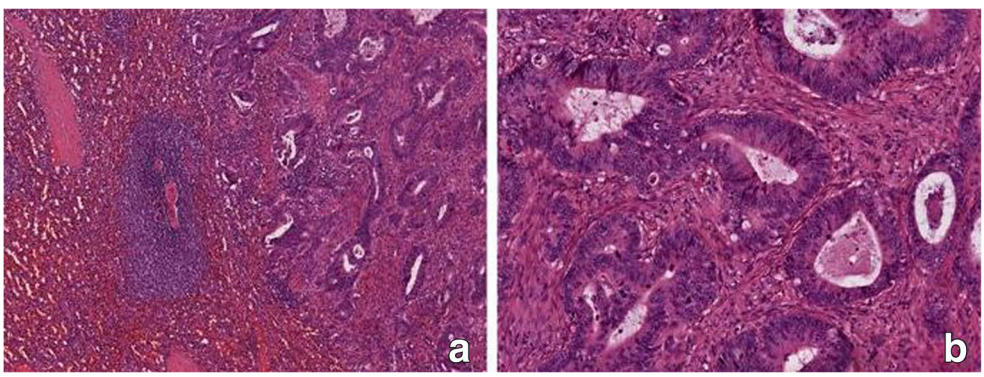

Fig. 2 Histological section of splenic parenchyma (**a**) infiltrated by a neoplastic glandular proliferation consistent with metastatic adenocarcinoma (**b**) (original magnification ×40; hematoxylin-eosin)

Compliance with Ethical Standards

Informed Consent Informed consent was obtained from the individual described in this report.

Conflict of Interest The authors declare that they have no competing interests.

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