

CASE REPORT

Synchronous isolated splenic metastasis from colon carcinoma and concomitant splenic abscess: A case report and review of the literature

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Abstract

This study aimed to describe a case in which an isolated splenic metastasis was synchronous with the colonic primary and a concomitant splenic abscess was associated. A wide review of the literature was also performed. A 54-year-old woman with abdominal pain and fever was admitted to our department. Abdominal CT revealed two low-density areas in the spleen and wall-thickening of the left colonic flexure, which was indistinguishable from the spleen parenchyma. The patient underwent emergency celiotomy, with the presumptive diagnosis of obstructing colon carcinoma of the splenic flexure, and concomitant splenic abscess. Subtotal colectomy and splenectomy were performed. Pathological findings were consistent with mucinous colonic carcinoma, synchronous isolated splenic metastasis and concomitant splenic abscess. This paper is also a review of the existing literature on the association between colorectal cancer and splenic metastasis. Only 41 cases of isolated splenic metastasis from colon carcinoma have been reported in the literature. This report is the third described case of synchronous isolated splenic metastasis from colon carcinoma. Only one case with concomitant splenic abscess has been previously reported. When obstructing left-sided colorectal cancer is suspected, careful CT examination can allow early diagnosis of splenic involvement by the tumor. The literature review suggests that there might be a significant improvement in survival following splenectomy for a metachronous isolated splenic metastasis from colon carcinoma. Prognosis for synchronous splenic metastasis seems to be related to the advanced stage of the disease. Nevertheless, no definitive conclusions can be drawn because of the small number of cases.

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INTRODUCTION

Primary and metastatic tumors of the spleen are described as unusual^[1], excluding secondary involvement by lymphoma^[2]. Since metastatic carcinoma involving the spleen is usually a manifestation of widely disseminated disease, isolated splenic metastasis from colorectal carcinoma is not a common occurrence^[1-3]. Its rareness has been hypothetically explained by several characteristics of the spleen, such as anatomical, histological and immunological features^[4]. Most cases are asymptomatic and the diagnosis is usually made by imaging studies during the diagnostic work up for colon cancer^[5]. However, a few patients become exceptionally symptomatic following spontaneous rupture of the spleen, or the presence of an associated splenic abscess^[6,7].

We report the case of a synchronous isolated splenic metastasis from colonic carcinoma, with a concomitant splenic abscess, and we also review all cases of isolated splenic metastasis from colorectal cancer reported in the literature. To the best of our knowledge, only one case of splenic metastasis from colonic carcinoma associated with concomitant splenic abscess has been reported in the literature^[7], which is an extremely rare clinical entity.

CASE REPORT

In June 2006, a 54-year-old Caucasian woman was referred to our emergency department because of abdominal pain associated with intermittent fever over 40°C, shaking and chills. She also complained of general fatigue and loss of appetite. Otherwise, her previous medical history was unremarkable. On clinical examination, the patient was pale and shocked. Blood pressure and pulse rate were 90/60 mmHg and 98/min, respectively. The abdomen was distended, with tenderness in the left hypochondrium. There

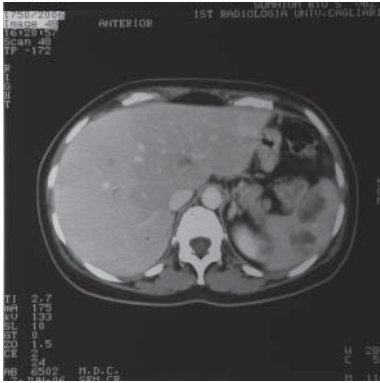


Figure 1 Two low density areas in the spleen (Axial CT-scan).

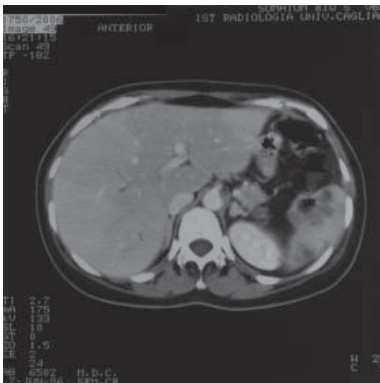


Figure 2 Wall thickening of the left flexure of the colon indistinguishable from the spleen parenchyma (Axial CT-scan).

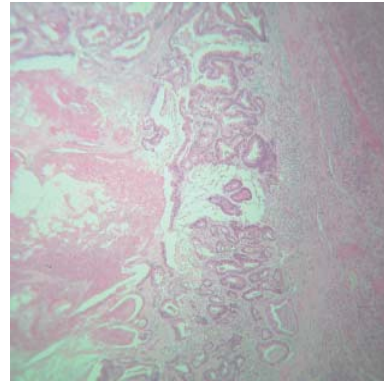


Figure 3 Splenic tumor showing glandular pattern consistent with metastasis from colonic mucinous carcinoma (HE, x 40).

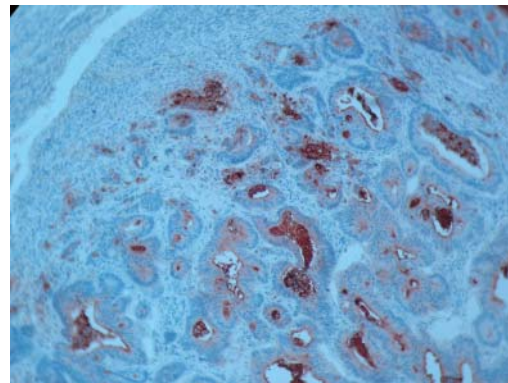


Figure 4 CEA along the luminal border of tumor cells infiltrating splenic pulp (anti-CEA monoclonal antibody staining, x 100).

was neither hepatosplenomegaly nor lymphadenopathy. Sepsis was identified both by a clear clinical picture which showed high fever and hemodynamic instability, and by positive blood culture which grew *Escherichia coli* and *Bacteroides fragilis*. Laboratory data on hospital admission were as follows: white blood cell count, $148 \times 10^9/L$; red blood cell count, $280 \times 10^{12}/\mu L$; hemoglobin, 67 g/L; thrombocyte count $383 \times 10^9/L$; fibrinogen, 5.17 g/L; albumin 23 $\mu g/L$; and carcinoembryonic antigen (CEA), 31.1 $\mu g/L$ (normal range $< 2.50 \mu g/L$).

Chest X-ray revealed a left pleural effusion. Abdominal plain radiography showed intestinal obstruction with typical air fluid levels in the bowel. Abdominal ultrasonography demonstrated a hypoechoic area with unclear margins in the lower pole of the spleen, with the features of a splenic abscess. Enhanced abdominal CT revealed two low-density areas in the spleen (Figure 1) and wall-thickening of the left colonic flexure, which was indistinguishable from the spleen parenchyma (Figure 2). Echocardiography was normal and detected no vegetations. The patient was treated with fluid, intensive antibiotics and blood transfusion as initial therapy, and then she underwent an emergency operation for a presumptive diagnosis of obstructing colonic carcinoma and septic shock from a concomitant splenic abscess. On explorative celiotomy, the splenic flexure of the colon presented a mass occluding the lumen, infiltrating the entire colonic wall, and invading the lower pole of the spleen. There were neither hepatic metastases nor peritoneal dissemination. Frozen section examination of the spleen was performed after splenectomy. Frozen section showed the presence of splenic metastasis from adenocarcinoma, with a concomitant splenic abscess.

A subtotal colectomy with side-to-side ileo-sigmoid anastomosis was then performed. The spleen weighed 160 g and measured 12 cm \times 7 cm \times 4.5 cm. On gross examination, the tumor originated from the left colonic flexure and invaded the spleen, in which it formed a fistula and an abscess in the metastatic tissue. The splenic metastasis measured 4.5 cm at its largest diameter and had a central abscess with a cavity of 2 cm. Histopathological findings were consistent with mucinous adenocarcinoma of the colon, synchronous isolated splenic metastasis from the primary colonic tumor (Figure 3), and concomitant splenic abscess, without metastatic lymph-node involvement (T4N0M1). Immunohistochemistry of both colonic carcinoma and splenic metastasis was performed using anti-CEA monoclonal antibody (Clone II-7, Dako Corporation, Carpinteria, CA, USA). Staining of CEA along the luminal border of tumor cells was demonstrated both in the colonic carcinoma and in the metastasis that infiltrated the splenic pulp (Figure 4). Left pleural effusion persisted for 10 d after the operation, and the patient was finally discharged on postoperative day 15.

After 1 mo, the CEA level dropped to 3.0 $\mu g/L$. The patient was treated with adjuvant chemotherapy. Six months after the operation, CEA level was 10.4 $\mu g/L$. Abdominal CT and positron emission tomography (PET) revealed a solitary liver metastasis of 2 cm, which was surgically removed. Exploration of the abdominal cavity revealed no further evidence of neoplastic disease. Afterward, the patient was once more subjected to adjuvant chemotherapy.

Table 1 Literature review of isolated splenic metastasis from colorectal carcinoma

Year	Author	Journal	Site of primary tumor	Synchronous metastasis	Metachronous metastasis	Concomitant splenic abscess
1969	Dunbar ^[10]	Mayo Clinic Proc	Rectum		1	
1982	Waller ^[25]	Clin Nucl Med	Sigmoid colon		1	
1986	Slavin ^[26]	Clin Nucl Med	Right colon		1	
1992	Capizzi ^[27]	South Med J	Rectum		1	
1993	Thomas ^[28]	Eur J Surg Oncol	Left colon		1	
1997	Mainprize ^[3]	Br J Surg	Splenic flexure		1	
1997	Indudhara ^[13]	South Med J	Sigmoid colon		1	
1999	Achuthan ^[6]	Ann R Coll Surg Engl	Rectum		1	
1999	Weathers ^[24]	Dis Colon Rectum ¹	Sigmoid colon		1	
1999	Vadala ^[29]	Minerva Chir	Left colon		1	
2000	Kim ^[4]	J Korean Med Sci	Right colon		1	
2000	Lee ^[30]	Am Surg	Not specified		1	
2001	Place ^[11]	Am Surg	Sigmoid colon		1	
2001	Avesani ^[11]	Am J Clin Oncol	Left colon	1		
2001	Paramelle ^[7]	J Radiol	Left colon	1		1
2001	Okuyama ^[20]	Jpn J Clin Oncol	Sigmoid colon		1	
2001	Quoted in Okuyama ^[20]	Jpn J Clin Oncol ²	Left colon		11	
			Left + right colon		1	
			Right colon		7	
			Rectum		1	
2003	Genna ^[17]	Minerva Chir	Left colon		1	
2004	Cavallaro ^[12]	J Exp Clin Cancer Res	Sigmoid colon		1	
2004	Pizzirusso ^[31]	Acta Chir Belg	Left colon		1	
2006	Cabanas ^[16]	Tumori	Sigmoid colon		1	
2006	Gencosmanoglu ^[5]	World J Surg Oncol	Sigmoid colon + splenic flexure		1	
2007	Pisanu	Present report	Splenic flexure	1		1
			Total	3	39	2

¹This metastasis occurred 3 mo after colonic operation; ²From the review of the Japanese literature.

DISCUSSION

Approximately 20% of colorectal carcinomas are metastatic at their clinical presentation^[8]. Metastases to other sites in the absence of liver, lung or axial skeleton involvement are very rare^[1,9]. Similar to the results of an autopsy study by Berge, microscopic splenic metastases were found in 7%-34% of cancer patients^[2]. The same author reported the incidence of splenic micrometastases arising from colorectal carcinoma to be as high as 2% in 1019 colorectal tumors, but all of these involved other organs as well^[2]. In 1969 Dunbar *et al*^[10] published the first case report of isolated splenic metastasis from colorectal carcinoma and to date, only 41 such cases have been reported in the literature (Table 1). All but two of previously described cases of solitary splenic metastases from colon carcinoma had a metachronous metastasis (Table 1). We have described the third reported case in which an isolated splenic lesion was synchronous with colonic carcinoma^[7,11]. The particularly interesting aspect of our case was also related to the simultaneous presence of a splenic abscess, because the only other reported case with similar clinical and pathological features is that by Paramelle *et al*^[7].

The rareness of splenic metastasis arising from colonic carcinoma suggests the existence of some mechanism that prohibits tumor cell proliferation in the spleen. Anatomical and immunological characteristics may be reasons for the rarity of isolated splenic metastasis^[4]. From an anatomical perspective, the sharp angle of the splenic artery with the celiac axis and rhythmic contraction by the sinusoidal

splenic architecture are limiting factors for metastasis^[4,12]. According to Indudhara *et al*^[13], neoplastic cells can reach the splenic vein and parenchyma by retrograde diffusion through the inferior mesenteric vein. The spleen parenchyma contains no afferent lymphatic vessels, but they are present in the capsular, subcapsular and trabecular regions^[12]. Tumor cells might also reach the spleen *via* the lymphatic system, which explains the typical subcapsular localization of isolated splenic metastases^[12]. As the spleen is the second largest organ of the reticuloendothelial system, immune surveillance appears to potently inhibit tumor cell proliferation^[14]. Moreover, experimental studies have shown that the growth rate of adenocarcinoma cells injected into the spleen is significantly lower than that of the same cells injected into the liver^[15].

Histopathological findings in our case were consistent with mucinous adenocarcinoma of the colon, as in three other cases of isolated splenic metastasis^[3,16,17]. Mucinous gastrointestinal malignancies are thought to cause perforation and infiltration of the full thickness of the bowel wall, which lead to extensive invasion of the pericolic fat^[3,16]. A new mechanism has been proposed in the case of contiguous splenic metastasis from mucinous colonic tumors. Cabanas *et al*^[16] have suggested that mucus-producing epithelial cells become trapped within the trabecula of the splenic capsule, in congenital clefts of the spleen, or in microfissures caused by trauma. The resistance of the splenic capsule or fibrous tissue surrounding the spleen causes the mucinous tumor to expand into the soft splenic parenchyma, rather than

the peritoneal cavity^[16]. Following the more aggressive behavior of mucinous colonic tumors, this mechanism may have explained the presence of the synchronous splenic metastasis in our case. Furthermore, since CEA appears as an immunosuppressant, and acts as an adhesion molecule between tumor cells and visceral macrophages, colonic tumor cells with positive CEA staining should display more aggressive behavior^[4,18]. In regard to these biological functions, CEA expression might be associated with the occurrence of isolated splenic metastasis^[4] (Figure 4).

The diagnosis of isolated splenic metastasis is generally made by imaging studies during the diagnostic work up for colonic cancer^[5]. Only a few patients with splenic metastasis become symptomatic because of the presence of an associated splenic abscess^[8] or spontaneous rupture of the spleen^[6,19], as in our case. Okuyama *et al*^[20] have pointed out that only six of 28 reported patients were symptomatic at the time of diagnosis. Our patient became symptomatic as a result of abdominal occlusion and sepsis originating from the splenic abscess, in which *E. coli* and *B. fragilis* grew, as in most cases of colonic abscess associated with colonic cancer^[21]. The association between splenic abscess and colonic cancer is a very rare clinical entity^[22], as is isolated splenic metastasis. Only a few cases have been reported in the literature, and sometimes the splenic abscess resulted from a direct fistula of descending colon carcinoma, without spleen metastasis^[23]. The most frequent complication of splenic abscess is its rupture into the peritoneal cavity, and untreated splenic abscesses have a high mortality rate^[23].

Most previously described patients with solitary splenic metastasis from colon carcinoma had a disease-free survival of 3-144 mo after the primary tumor^[11,17,24]. Long-term survival after splenectomy in patients with isolated metachronous splenic metastasis from colon carcinoma varied from 0.5 to 7 years^[11,20,24]. As a result, prognosis of isolated splenic metastasis after splenectomy appears to be rather optimistic, despite the fact that splenic metastasis is one form of distant metastasis^[20]. In our case of synchronous metastasis, intensive follow-up revealed a solitary liver metastasis 6 mo after operation, without further evidence of neoplastic disease in the abdominal cavity. However, the disease-free interval after splenectomy in the case of synchronous splenic metastasis reported by Avesani *et al*^[11] was 10 mo, and the patients died of diffuse carcinomatosis after 1 year.

The spleen is considered unfavorable to the development of metastases but the reason for this is not clearly understood. An isolated splenic metastasis from colon carcinoma is a rare clinical finding. On the basis of the present case, when an obstructing left-sided colorectal cancer is suspected in emergency setting, careful examination of the abdominal CT-scan can allow early diagnosis of a splenic involvement by the tumor. Clinicians must pay close attention to the spleen for the early diagnosis of isolated splenic metastasis when routinely evaluating abdominal CT-scan and abdominal ultrasonography following curative resection of primary colorectal cancer. Splenectomy is necessary in the presence of isolated metastases from colon carcinoma both

synchronous and metachronous. The occurrence of a splenic abscess makes emergency splenectomy mandatory as the most frequent complication is its rupture into the peritoneal cavity.

Splenectomy followed by chemotherapy seems to be the preferred treatment of isolated splenic metastases from colorectal carcinoma. There are few data available about recurrence after splenectomy for metastases of this type. Literature review suggests that there might be a significant improvement of long-term survival following splenectomy for metachronous splenic metastasis arising from colon carcinoma. Prognosis for synchronous splenic metastasis seems to be related to the advanced stage of the disease. Nevertheless, following the small number of cases reported in the literature, no definitive conclusions can be drawn.

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