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Isolated Splenic Metastasis From Colorectal Carcinoma : A Case Report

Isolated splenic metastasis arising from colorectal carcinoma is very rare and there has been only 6 cases reported in the English literature. A new case is presented, and its possible pathogenesis was considered with previously reported cases. A 65-year-old male patient had received a right hemicolectomy for ascending colon cancer 36 months earlier. He was followed up regularly with serial measurement of serum carcinoembryonic antigen (CEA). Rising serum CEA was discovered from 33 months postoperatively and CT revealed an isolated splenic metastasis. He therefore underwent splenectomy, which was proven to be a metastatic adenocarcinoma with similar histological feature to the original tumor. As all reported cases showed elevated serum CEA at the time of metastasis, isolated splenic metastasis might be associated with CEA in regard to its biological functions of immunosuppression and adhesion.

Key Words: *Colorectal Neoplasms; Spleen; Neoplasm Metastasis; Carcinoembryonic Antigen*

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INTRODUCTION

Isolated splenic metastasis is an uncommon occurrence except for secondary involvement by lymphoma (1). Its rareness has been hypothetically explained by several characteristics of the spleen, e.g., anatomical, histological and functional (2). There are only 6 cases of isolated splenic metastasis arising from colorectal carcinoma in the English literature (3-8). A common biological preponderance may exist in the isolated splenic metastasis that can endure such an infertile soil for metastasis. In our case, rising serum carcinoembryonic antigen (CEA) was found like in all the cases excluding one in the earliest report in which CEA measurement was probably not available. The mechanism of isolated splenic metastasis was considered in regard to the biological functions of CEA.

CASE REPORT

A 65-year-old man had had a right hemicolectomy for an adenocarcinoma of the ascending colon in December 1994. Serum CEA level immediately before operation was 12.4 ng/mL (normal, <6 ng/mL). Histologic examination showed a moderately differentiated adenocarcinoma confined to the colonic wall. Two metastatic lymph nodes were found among 29 examined. He was followed up every 3 to 6 months with complete blood count, liver function test, serum CEA and chest radiography. Abdominal CT and colonofiberscopy were also included every year postoperatively. Adjuvant chemotherapy was given with a 6-cycle regimen of 5-fluorouracil (400 mg/m^2) and leucovorin (20 mg/m^2) for 6 months. He felt well except for a ureter stone, which was treated by extra-corporeal shock wave lithotripsy. His serum CEA level had risen to 10.9 ng/mL in October 1997 and abdominal CT demonstrated a low-attenuation area in the upper pole of the spleen (Fig. 1). As he strongly wanted the lesion observed for several months, laparotomy was given 3 months later when serum CEA level reached 14.9 ng/mL.

At laparotomy, the spleen contained a yellowish, well-demarcated nodule measuring 5×5 cm in its upper pole that was adherent to the diaphragm. There was no evidence of other recurrent disease either in the previous operation site or in the other intraabdominal viscera, including the liver. A splenectomy was performed en bloc with adjacent omentum and adherent diaphragmatic peritoneum. On histologic review including original tumor, the splenic nodule was consistent with metastatic adenocarcinoma similar to original colonic adenocarci-

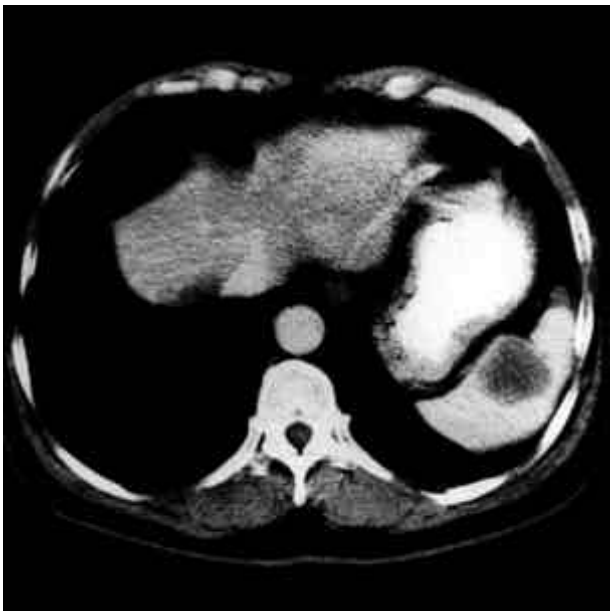

Fig. 1. CT demonstrates a low-attenuation area in the superior splenic area (right lower corner).

noma. An immunohistochemistry of both splenic and original tumors was made using anti-CEA monoclonal antibody (T84.66, ATCC, Rockville, MD, U.S.A.) to find out staining intensity and distribution patterns of CEA. Dark staining of apicoluminal with a few diffuse-cytoplasmic distribution was demonstrated in colonic adenocarcinoma, whereas that of diffuse-cytoplasmic one in splenic metastasis (Fig. 2). He showed no evidence of recurrence at 18 months postoperatively.

DISCUSSION

Careful autopsy examinations revealed microscopic splenic metastases upto 7-34% in cancer subjects (1). These cases of high incidence of splenic micrometastases contradicts Paget's concept of the spleen as poor soil for metastasis. A study based on the relative frequency of metastasis between the spleen and kidney also concluded that the spleen had no anti-neoplastic property and subsequent studies shared similar conclusions (9, 10). Although the incidence of splenic micrometastases arising from colorectal carcinoma is reported as high as 4.4% in 1,019 colorectal tumors (1), only 6 cases of isolated splenic metastasis from colorectal carcinoma are found in the English literature (3-8). This difference proposes the existence of a certain mechanism prohibiting tumor cell proliferation in the spleen.

Anatomical and immunological characteristics were suggested as reasons for the rarity of isolated splenic metastasis (2). In the anatomical basis, the sharp angle of the splenic artery with the celiac axis and rhythmic contraction by the sinusoidal splenic architecture were speculated as limiting factors of metastasis. As the spleen is the second largest organ of the reticuloendothelial system with profuse monocytes, immunoglobulin synthesis, and opsonin production, immune surveillance appears to potently inhibit tumor cell proliferation. The antigenic response to inoculated tumor cells in mice spleen was identified as inhibitory T cells preventing splenic metastasis (11). Other experimental evidence suggests that intense destruction of malignant cells in the

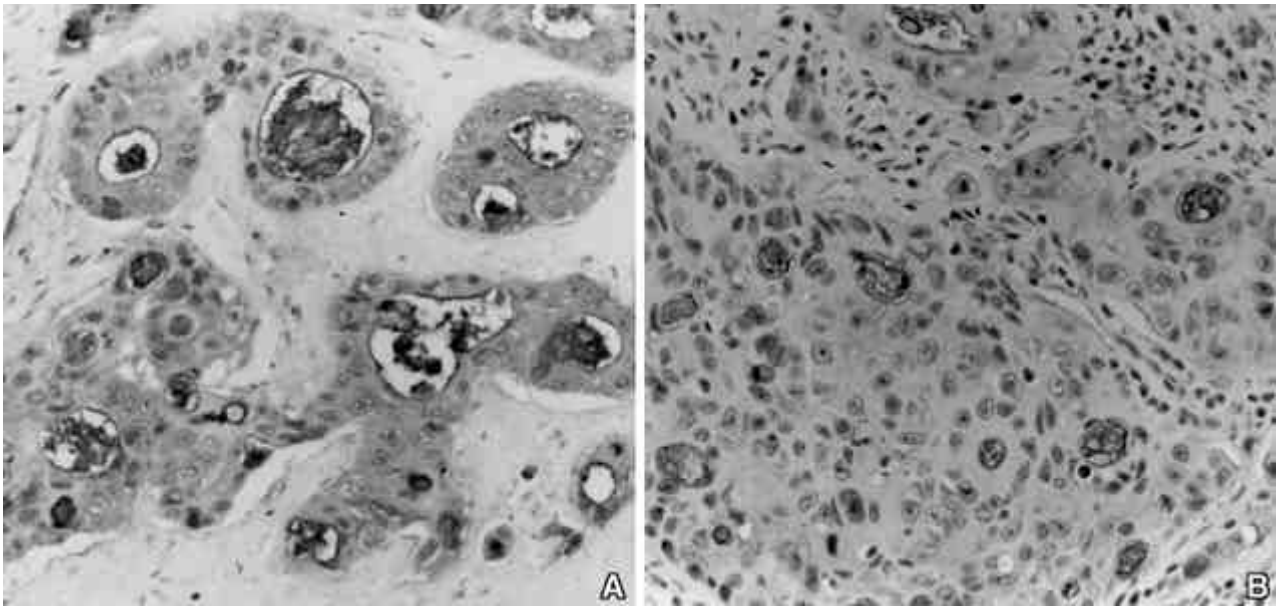

Fig. 2. **A:** Dark staining of CEA along the luminal border of tumor cells shows apicoluminal distribution with a few cells of diffuse-cytoplasmic one (×200). **B:** Metastatic tumors with diffuse-cytoplasmic distribution of CEA infiltrating splenic pulp (×200).

Table 1. A Summary of reported cases with isolated splenic metastasis from colorectal carcinoma

Author, Reported year (Reference No.)	Sex/ Age (yr)	Original tumor		1st Pop. s-CEA, ng/mL	2nd Pop. s-CEA, ng/mL	1st DFI, years	2nd DFI, years
		Location	Stage				
Dunbar, 1969 (3)	M/69	Rectum	III	n.a.	n.a.	3.8	0.5<
Waller, 1982 (4)	M/72	SC	n.a.	n.a.	8.1	4	0.5
Slavin, 1985 (5)	F/81	CE	III	n.a.	7.5	2.5	1<
Capizzi, 1992 (6)	F/51	Rectum	II	1.6	13.5	5<	1.2<
Thomas, 1993 (7)	F/72	TC or DC	II	n.a.	30.4	11	1<
Mainprize, 1997 (8)	F/62	TC or DC	III	n.a.	rised	3.5	n.a.
Present case	M/65	AC	III	12.4	12.1	2.7	1.3<

1st Pop., immediately before original tumor surgery; 2nd Pop., immediately before splenectomy; 1st DFI, disease-free interval between original tumor surgery and splenic metastasis; 2nd DFI, disease-free interval after splenectomy; CE, cecum; AC, ascending colon; TC, transverse colon; DC, descending colon; SC, sigmoid colon; n.a., not available

spleen limits the incidence of clinically apparent metastasis (12).

Two-thirds of the patients after curative resections for colorectal carcinoma develop recurrence within 2 years (13), whereas the median disease-free interval is 4 (2.5-11) years in all reported cases of isolated splenic metastasis (Table 1). Delayed recurrence in the spleen may be related with slow progression by the splenic function of immune surveillance. Old median age in these patients (69 years old) also reflects a weaker immunity. Around 30% of recurrent colorectal carcinoma are found to have normal serum CEA level (14). All reported cases and our case available for measurement showed rising serum CEA, possibly proposing a connection to CEA in the isolated splenic metastasis. Both colorectal and splenic tumor cells showed dark staining for CEA. Tumor cells with positive CEA staining presented more aggressive behavior than that with negative CEA staining (15, 16). Primary tumor cells showed mixed patterns of apicoluminal and diffuse-cytoplasmic distribution, while splenic tumor cells showed diffuse-cytoplasmic distributions. As tumor cells with diffuse-cytoplasmic staining are known to be a more aggressive than that of apicoluminal pattern, more malignant clones emerge in the splenic metastasis.

CEA as a metastatic potentiator has been proposed in regard to modulating immune responses, facilitating intercellular adhesion, and cellular migration (17, 18). Among these suggested functions, immune modulation can primarily protect the viability of tumor cells and enables other functions of intercellular adhesion and migration subsequently. CEA appears as an immunosuppressant involving humoral immune response, lymphocytes and NK cell activity (18). CEA can also act as an adhesion molecule between cancer cells and visceral macrophages (15). Thus, CEA may play an important role between tumor cells and numerous macrophages evading phagocytosis in the spleen.

All patients in previous case reports underwent splenectomy and their outcome could not be conclusively reached within the limited period of postoperative observation. CEA appears to be associated with isolated splenic metastasis in regard to its biological functions, e.g., immunosuppression and adhesion. All cases must be reported and followed up to reveal the pathogenesis and the outcome of this rare condition.

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