Non-occlusive Mesenteric Ischemia after Splenic Metastasectomy for Small-Cell Lung Cancer

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Abstract

A 68-year-old man presented with severe abdominal pain. Seven months earlier, he had received systemic chemotherapy for small-cell lung cancer with solitary metastasis to the spleen, followed by splenectomy. Abdominal computed tomography and abdominal arterial angiography showed diffuse ischemia of the mesenteric artery without apparent occlusion. The patient also suffered from septicemia caused by *Enterococcus faecium*. Therefore, a diagnosis of non-occlusive mesenteric ischemia (NOMI) induced by septicemia was supposed. Although treatment with antibiotics and papaverine hydrochloride was administered and the necrotic tissue in the intestinal tract was resected, the patient died.

Physicians should be aware that patients undergoing splenectomy are likely to be affected by septicemia, which may subsequently induce NOMI.

Key words: non-occlusive mesenteric ischemia, septicemia, small-cell lung cancer, splenectomy

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Introduction

Non-occlusive mesenteric ischemia (NOMI) comprises all forms of mesenteric ischemia without occlusion of the mesenteric arteries. It is commonly caused by a decreased cardiac output resulting in splanchnic hypoperfusion, with a mortality rate of approximately 70% (1). NOMI generally affects elderly and weakened patients suffering from myocardial infarction, congestive heart failure, sepsis and renal or hepatic disease. This condition also accounts for 20-30% of all cases of acute mesenteric ischemia (1).

In patients with malignant tumors, splenic metastases are common components of multivisceral metastatic disease, while solitary splenic metastases are rare (2). Although lung cancer is one of the most common primary sources of splenic metastasis, solitary splenic metastasis is unusual, especially in cases of small-cell lung cancer (SCLC). To the best of our knowledge, no cases of SCLC have been previously reported in the literature, including Compérat’s report, which described 93 malignant tumors with solitary splenic metastases (2).

Splenectomy and/or fine-needle aspiration biopsies (FNABs) are recommended to confirm the stage of disease in cases of malignant tumors with solitary splenic metastasis (3, 4). In the past, splenectomy was thought to be a safe and easy procedure compared to image-guided FNAB; however, septicemia and septic shock have been reported as severe late-onset complications of splenectomy (5). We herein present a fatal case of NOMI in which the condition appeared to be a late complication of splenectomy in a patient with SCLC.
Case Report

A 68-year-old Japanese man was referred to our institution for the treatment of extensive disease SCLC. Chest and abdominal computed tomography (CT) revealed a tumor in the left upper lobe and mediastinal lymphadenopathy with a solitary splenic lesion. Fluorodeoxyglucose-positron emission tomography (FDG-PET) demonstrated the same findings with a high uptake of FDG (Fig. 1A), and the patient was diagnosed with SCLC (T2N2M1b, stage IV) based on a CT-guided biopsy of the primary lung tumor (Fig. 2A, B). He subsequently received four cycles of combination chemotherapy consisting of cisplatin and etoposide, and the primary tumor and mediastinal lymph nodes significantly decreased in size. However, the splenic lesion, which was thought to be a metastatic lesion did not adequately respond to the treatment (Fig. 1B, C). At that point, we wondered whether the splenic lesion was really metastatic. Therefore, we performed laparoscopic splenectomy (Fig. 2C), which confirmed the lesion to be derived from metastasis (Fig. 2D). The excised spleen was not enlarged. The patient then received thoracic irradiation (1.5 Gy per fraction twice daily, 30 fractions) for local control, as no other distant metastases were observed after the splenectomy procedure.

Around 7 in the morning, seven months later, the patient suddenly experienced a high fever of 40°C, with chills and general fatigue, although no abdominal symptoms were reported. He immediately took an antipyretic (loxoprofen) and antibiotic (levofloxacin), which had been previously prescribed for febrile neutropenia during the administration of chemotherapy, and subsequently visited a clinic at 3 PM that day due to general fatigue and abdominal discomfort. A blood test showed an increased white blood cell count (17,130/μL), and severe abdominal pain with hypotension was noted at 5 PM in the clinic. Therefore, he was referred to our hospital. Upon admission, abdominal CT revealed diffuse narrowing of the superior mesenteric vein compared to the superior mesenteric artery (SMA) as well as inflammation of the adipose tissue surrounding the right kidney (Fig. 3A); however, no portal venous gas was detected. Abdominal arterial angiography (AAA) showed diffuse narrowing of the SMA and inferior mesenteric artery (IMA) (Fig. 3B, C), and a blood culture revealed septicemia caused by Enterococcus faecium.

Since a diagnosis of NOMI due to septicemia was suspected, treatment with antibiotics, papaverine hydrochloride and heparin sodium was administered. Colonoscopy subsequently revealed diffuse ischemia of the colonic mucosa, with a small amount of bleeding and surrounding edema, consistent with the features of NOMI (Fig. 3D). Although surgical resection of the intestinal tract to remove the necrotic tissue was performed, the patient nevertheless died five days after hospitalization due to a progression of acidemia and multiple organ failure.
Discussion

We experienced a very rare case of NOMI induced by septicemia after splenectomy in a patient with SCLC. The clinicopathologic diagnostic criteria for NOMI include the absence of occlusion of the mesenteric artery or vein in the area of bowel necrosis and the presence of ischemic and necrotic spots and segments distributed over a wide area in a non-consecutive manner (6). The histopathological findings include hemorrhagic and necrotic changes without fibrin plugs (6). Since abdominal CT and AAA revealed diffuse ischemia of the SMA and IMA without arterial occlusion and colonoscopy showed diffuse ischemia with necrosis of the colonic mucosa in this case, the diagnosis of NOMI in our patient was obvious.

One may consider that the chemotherapy agents and/or the patient’s comorbidities caused the NOMI. If so, the cause of the septicemia could be the breakdown of the mucosal defense system as a result of NOMI. However, we believe that the NOMI was induced by septicemia, which was caused by a preceding urinary tract infection, for the following two reasons: 1) the high fever and chills, which are often observed in cases of septicemia, appeared approximately eight hours before the onset of abdominal symptoms; 2) inflammation of the adipose tissue surrounding the right kidney, which is indicative of pyelonephritis, was detected on CT (Fig. 3A). As to other possible causes of NOMI, excessive drinking of alcohol and/or the use of medical drugs, including interferon-alfa-2b, digitalis and diuretics, have been reported (1, 7). However, the current patient was not a heavy user of alcohol, and neither loxoprofen nor levofloxacin, which he took prior to the onset of abdominal pain, have been reported to induce NOMI. Furthermore, no chemotherapeutic drugs had been administered for nine months, and no other comorbidities were observed in this case. Hence, we suppose that the septicemia was the most likely cause of the NOMI.

Hypoperfusion of the mesenteric arteries, a major cause of morbidity in patients with NOMI, may be caused by different mechanisms. For example, various forms of shock, septicemia, dehydration and hypotension following dialysis and heart or major abdominal surgery have been reported (1). In the present case, the septicemia seemed to induce the NOMI. Asplenic individuals are vulnerable to developing bacterial sepsis, which is often fulminant with a high rate of mortality. Overwhelming post-splenectomy infection has been reported to occur in such cases at an estimated incidence of 0.23-0.42% per year, with a lifetime risk of 5% (8). The pathogenesis and risk of developing a fatal infection after splenectomy remain poorly defined (9), although the inhibition of immunologic and phagocytic host...
defenses is supposed (10). The spleen is the most efficient organ for clearing IgG-coated bacteria and plays a critical role in removing virulent encapsulated bacteria that are not opsonized by antibodies or complement (11).

The treatment approach for splenic lesions is a divisive problem. Lesions that are very likely to be metastases require further intervention. However, it is difficult to diagnose splenic lesions accurately using multimodality imaging techniques, including CT, ultrasound and magnetic resonance imaging (12). The lesion in the present case may have been infectious, such as an abscess or other malignancy, as it did not respond to chemotherapy compared with the intra-thoracic lesions. Splenectomy is relatively safe compared with FNAB and should be performed for both diagnosis and treatment (13). We therefore decided to perform splenectomy in this case.

Unfortunately, our choice to perform splenectomy may have brought about the onset of septicemia, followed by NOMI. However, to the best of our knowledge, there are no other reports describing the occurrence of NOMI after splenectomy in patients with SCLC. Based on the findings of previous reports and the present case, we believe that splenectomy may be used as a standard method for diagnosing and treating malignant tumors associated with solitary splenic lesions. Furthermore, physicians should be aware that patients undergoing splenectomy are likely to be affected by septicemia, which may induce the development of NOMI.

The authors state that they have no Conflict of Interest (COI).

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