A case of leptomeningeal carcinomatosis in advanced gastric adenocarcinoma with controlled peritoneal dissemination

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Abstract

A 48-year-old man with unresectable gastric cancer and widespread peritoneal dissemination received concentrated ascites reinfusion therapy, followed by systemic chemotherapy. However, leptomeningeal carcinomatosis (LMC) was diagnosed 1 year later. Spinal drainage and ventriculoperitoneal shunting improved the patient's neurological functions for approximately 2 weeks. The patient died 2 months after LMC diagnosis, but these treatments temporarily improved the quality of life during end-of-life care.

Keywords Advanced gastric cancer · Leptomeningeal carcinomatosis · Ventriculoperitoneal shunting

Introduction

Peritoneal dissemination with malignant ascites often occurs in patients with advanced gastric cancer (GC) and is considered incurable [1]. Leptomeningeal carcinomatosis (LMC), defined as the dissemination and growth of cancer cells within the leptomeningeal space, is rare in GC [2]. Although LMC has devastating neurological complications and high mortality rates, its methods of diagnosis, treatment outcomes, and prognosis remain unclear. As the duration of survival is several weeks, the intent of treatment is essentially palliative. Herein, we present a case of LMC in a patient with unresectable GC after controlled peritoneal dissemination and illustrate the quality of life (QoL) benefits of ventriculoperitoneal (VP) shunting for this rare form of central nervous system metastasis.

Case report

A 48-year-old man was admitted to our hospital with abdominal distension and constipation. Although carcinoembryonic antigen (CEA, 1.2 ng/mL) and carbohydrate antigen 19-9 (CA19-9, 1.3 U/mL) levels were normal (normal ranges, 0–5 ng/mL and 0–37 U/mL, respectively), a gastric tumor with lymph node metastases and ascites was detected via abdominal computed tomography (CT) (Fig. 1a). Upper gastrointestinal endoscopy revealed hypertrophy of the mucosal folds and diffuse wall thickening at the gastric corpus; these findings were consistent with those of a type 4 tumor (Fig. 1b). Pathological examination of the biopsy specimen revealed poorly differentiated adenocarcinoma, and ¹⁸F-fluorodeoxyglucose positron emission tomography (FDG-PET) showed multiple lymph node metastases.

The ascites rapidly increased during preparation for chemotherapy (Fig. 2a). Cytological examination showed malignant cells in the ascites fluid. Concentrated ascites reinfusion therapy was administered to palliate abdominal distention, and 8000 mL of ascitic fluid was drained. Two days later, the patient received DCS chemotherapy (docetaxel, 75 mg/m² on day 1; cisplatin, 75 mg/m² on day 1; and tegafur/gimeracil/oteracil [S-1], 120 mg/body per day on days 1–14). After three cycles of chemotherapy, ascites was no longer apparent (Fig. 2b), and the abdominal symptoms disappeared. After seven cycles, chemotherapy was continued for approximately 12 months using docetaxel and S-1 without cisplatin, owing to its clinical benefits. CT and

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Fig. 1 **a** Computed tomography scan showing a gastric tumor with lymph node metastasis and peritoneal metastasis. **b** Upper gastrointestinal endoscopy revealed hypertrophy of the mucosal folds and diffuse wall thickening at the gastric corpus; these findings were consistent with that of a type 4 tumor

Fig. 2 **a** While in the preparatory interval of chemotherapy, rapidly increasing ascites was observed. **b** After three cycles of chemotherapy, ascites was no longer observed

FDG-PET at 12 months did not show tumor progression, and adenocarcinoma was not detected on endoscopic biopsy. Tumor marker (CEA and CA19-9) levels were not elevated at any point during the treatments.

Three days after the last and thirteenth cycle of chemotherapy, the patient complained of dizziness. The CT scan of the head showed no evidence of recurrence. However, the dizziness was followed by nausea, and LMC was suspected based on the symptoms. Furthermore, magnetic resonance imaging (MRI) scans of the brain revealed leptomeningeal gadolinium enhancement (Fig. 3). Examination of the cerebrospinal fluid (CSF) showed supranormal protein (149.0 mg/dL) and subnormal glucose (21.0 mg/dL) levels; cytology testing revealed the presence of malignant cells. As these findings were consistent with LMC, the patient received systemic steroids, antiepileptic medications, and two intrathecal (IT) treatments with 15 mg of methotrexate and 40 mg of cytarabine.

The patient experienced a sudden generalized tonic-clonic seizure, and his CSF pressure was found to be elevated (47 cm H₂O), despite the treatments. The Eastern Cooperative Oncology Group performance status (ECOG-PS) score was four, and continuous assistance and observation were needed. A spinal drainage catheter

Fig. 3 A magnetic resonance imaging scan of the brain shows a pia-subarachnoid pattern

was placed at the level of the lumbar vertebrae to reduce CSF pressure. The convulsions disappeared promptly after drainage, thereby improving his everyday life. VP shunting was performed 7 days later, and he was discharged from our hospital after a week. No multifocal neurologic impairments including headache, nausea, dizziness, decreased consciousness level, or convulsions were observed during the first week after discharge. His psychological discomfort and anxiety were also resolved. He had an ECOG-PS score of 1 with almost no hindrance to his everyday life and was well enough to be able to go on a short trip with his family. However, he died 8 weeks after the diagnosis of LMC owing to the subsequent appearance and rapid aggravation of convulsions (Fig. 4). The patient survived for 14 months following the diagnosis of advanced GC.

Discussion

In our experience, a few GC patients with widespread peritoneal dissemination or massive ascites had developed LMC, which is mostly associated with leukemia, lymphoma, malignant melanoma, breast cancer, and lung cancer. LMC is extremely rare in GC, occurring in only 0.16–0.69% of GC cases [2]. Most of these cases also showed multiple metastases in regions other than the nervous system, including the liver, lungs, and bones [3].

Tumor cells may gain access to the leptomeninges directly from bone metastases or by spreading through the perineural or perivascular spaces and lymph nodes [4]. LMC causes multifocal neurologic deficits including headache, nausea or vomiting, dizziness, seizures, and motor weakness [5]. LMC

has a worse prognosis in patients with GC than in those with other solid cancers, with a reported overall median survival time of 4–7 weeks [6].

MRI is typically considered superior to measurement of tumor marker levels and CT for rapid diagnosis of LMC [7]. In our patient, the latter two procedures were not useful for rapid diagnosis, whereas cranial MRI showed leptomeningeal gadolinium enhancement. However, CSF sampling, which showed the presence of malignant cells in the CSF, provided the definitive diagnosis. In a previous study, repeated CSF sampling had a diagnostic sensitivity of up to 91% [3].

There is no established standard treatment for LMC. Most chemotherapeutic agents do not penetrate the blood–brain barrier and are administered intrathecally. IT chemotherapy with methotrexate and cytarabine, a conventional and popular regimen, was administered with the hope of achieving some response and prolonging survival. However, a previous study reported no improvements in survival or neurological responses after IT chemotherapy [8]. Determining the benefits of IT chemotherapy is still an important challenge for oncologists. Moreover, palliative radiotherapy has been selectively administered to LMC patients with a high-tumor burden, having severe neurologic dysfunctions or mass lesions. A recent study showed a more favorable outcome with combined IT chemotherapy, whole-brain irradiation (WBI), and VP shunting than with symptomatic treatments using steroid and mannitol [7].

Our patient had initially received IT chemotherapy. However, the IT pressure was subsequently elevated, and convulsions were observed. As his symptoms were intense and urgent palliation was needed, spinal drainage and VP

Fig. 4 The process of leptomeningeal carcinomatosis. *ECOG-PS* Eastern Cooperative Oncology Group performance status, *CT* computed tomography, *MRI* magnetic resonance imaging, *CSF* cerebrospinal fluid, *IT* intrathecal, *VP* ventriculoperitoneal

shunting were performed. WBI is not administered in patients with risks of seizures, owing to concerns about worsening QoL due to bodily restraints and prolonged hospitalization. All neurological symptoms in our patient regressed following VP shunting, and he could perform normal daily activities for 8 weeks thereafter.

There are some studies on VP shunting for LMC. In one study, 37 patients with LMC required VP shunting for management of intracranial hypertension [7]. The median overall survival time was 2 months (range 2 days–3.6 years) after VP shunt placement, with improvement in 27 (77%) patients [9]. One patient with LMC from a gastric tumor survived for 532 days after VP shunting.

There are some challenges associated with spinal drainage and VP shunting. Spinal drainage at the level of the lumbar vertebrae is relatively simple. However, VP shunting may be difficult to perform without a specialist in the hospital setting. Furthermore, these procedures are associated with a risk of obstruction of the drainage tube, requiring appropriate preventive measures.

In conclusion, the present case of unresectable GC was complicated with LMC. LMC is a rare entity, with a catastrophic outcome. The poor prognosis of LMC necessitates early diagnosis and treatment to maintain a satisfactory QoL. In suspected cases of LMC, it is necessary to perform CSF sampling at an early stage in addition to MRI. Furthermore, spinal drainage and VP shunting may better improve neurological function than best supportive care. Although the survival period may be relatively short after a diagnosis of LMC, better QoL may be achieved. Nevertheless, additional clinical studies are necessary to establish appropriate treatment strategies for GC with LMC, and to improve the QoL in end-of-life care in these patients.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical standards All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions.

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