Meningitis Carcinomatosa Originating from an Alpha Fetoprotein-producing Gastric Cancer

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Abstract

Alpha fetoprotein (AFP)-producing gastric cancer is relatively rare and meningitis carcinomatosa is similarly a rare manifestation among the neoplastic diseases. There have been no previous reports of meningitis carcinomatosa originating from AFP-producing gastric cancer. A 68-year-old man with AFP-producing gastric cancer was treated with cisplatin and doxifluridine because of multiple liver metastases. Although the liver lesion was reduced to 30% of pretreatment size after 6 courses of chemotherapy, meningitis carcinomatosa subsequently occurred. Immunostaining of AFP and magnetic resonance imaging (MRI) were useful in the diagnosis of meningitis caused by AFP producing cancer cells.

Key words: MRI, chemotherapy, immunostaining

Introduction

Alpha fetoprotein (AFP)-producing gastric cancer is relatively rare (1), however it is known to metastasize easily to the liver even in the early stages (2). In neoplastic disease, meningitis carcinomatosa is a rare metastatic manifestation, and gastric cancer is the most common primary lesion (3). However, there have been no previous reports of meningitis carcinomatosa caused by AFP-producing gastric cancer. In this report, we describe a case of AFP-producing gastric cancer in which deadly meningitis carcinomatosa occurred even though the liver metastasis had been reduced to 30% of pretreatment size following chemotherapy.

Case Report

A 68-year-old man was admitted to our hospital on January 4, 1996. About 6 months before admission, he had developed a poor complexion and appetite. He had visited another hospital, and ultrasonography revealed the thickening of the gastric wall with multiple liver tumors. He was referred to our hospital immediately. On admission, his body temperature was 36.5°C, blood pressure 120/70 mmHg, heart rate, 80/minute and regular. Physical examination revealed anemic conjunctiva, no cardiopulmonary abnormalities, no abdominal tumor and slight pretibial edema. Hemoglobin (Hb) was 5.3 g/dl, serum total protein (TP), 6.2 g/dl; serum albumin (Alb), 3.0 g/dl; total cholesterol 80 mg/dl; aspartate aminotransferase, 40 IU//; alanine aminotransferase, 50 IU//; AFP, 584 ng/ml; carcino embryonic antigen (CEA), 38.9 ng/ml. The upper gastrointestinal series showed advanced gastric cancer (type 3) which had expanded from the cardia to the angulus (Fig. 1). Histological diagnosis of the biopsy specimen by endoscopy revealed a moderately differentiated tubular adenocarcinoma (tub 2) (4). On abdominal computed tomography (CT), multiple metastatic lesions (H3) (4) were recognized in the liver (Fig. 2A). According to the TNM systems at classification of gastric cancer, he was stage IV. Chemotherapy was chosen under informed consent. The patient was treated with cisplatin (CDDP) and doxifluridine (5’DFUR), resulting in a decrease in the serum levels of CEA and AFP (Fig. 3). Though the primary lesion was reduced in size by 70% and was considered as “No Change” (NC) (5), the metastatic liver lesions were reduced to 30% of the original size and judged to be “Partial Response” (PR) (5) (Fig. 2B) after 6 courses of treatment. The patient was discharged on April 23. His general condition was good by the middle of May, but anorexia and dizziness appeared on May 23. He was admitted again on May 27. On second admission, gait disturbances were recognized, but there was no nuchal rigidity. He was initially conscious, but lapsed into a coma within 7 days of admission. Both anemia (Hb; 10.0 mg/dl) and hypoproteinemia (5.4 mg/dl) were evident. C-reactive protein was high (6.2 mg/dl), and both AFP and CEA levels had also increased again (Fig. 3). Brain MRI revealed conspicuous expansion of the cerebral ventricles and regions of high intensity,
which were parallel to the cerebellar sulci, on the T1-weighted image after meglumine gadopentetate enhancement. Compression of the pons toward the front was also indicated, and meningitis carcinomatosa was subsequently suspected (Fig. 4A, B). Although the cerebrospinal fluid was normal in appearance and the initial pressure was within normal limits (180 mmH$_2$O), Pandy’s reaction was positive, and the protein concentration was high (85 mg/dl). AFP levels in the cerebrospinal fluid were also high (24.3 ng/ml). Papanicolaou staining revealed the presence of large abnormal cells, suggesting meningeal dissemination of the gastric cancer. Although intrameningial injection of

Figure 1. Upper gastrointestinal series demonstrates a large tumor which expanded from the cardia to the angulus.

Figure 2. A) Abdominal computed tomography (CT) scan shows multiple metastatic lesions in the liver. B) multiple liver tumor almost disappeared after 6 courses of chemotherapy.

5’ DFUR + CDDP

Figure 3. Time course of carcino embryonic antigen (CEA) and alpha fetoprotein (AFP). 5’DFUR: doxifluridine, CDDP: cisplatin.
methotrexate (10 mg) was repeated, his general condition gradually deteriorated. He died 32 days after the second admission.

Autopsy revealed the primary gastric lesion to be a moderately differentiated tubular adenocarcinoma (Fig. 5A) that had invaded the serosa. Although we surveyed all the cancer tissues, lesions of poorly differentiated adenocarcinoma or signet ring cell carcinoma could not be identified. Immunostaining of gastric cancer cells for AFP was positive (Fig. 5B). Most of the metastases became changed to fibrous tissue of the liver, although some tumor cells were found among the hepatic cells

Figure 4. A) Brain magnetic resonance imaging (MRI) shows remarkable expansion of the cerebral ventricles. B) Brain MRI with meglumine gadopentetate enhancement demonstrates high intensity signals along to cerebellar sulci (arrow).

Figure 5. Histological examination of the gastric tumor shows A) moderately differentiated tubular adenocarcinoma (HE stain, ×100), B) immunostaining of alpha fetoprotein (AFP) is positive (methyl green stain, ×200).
ous cancers. On the other hand, 1.7-5.5% of all gastric cancer cases are considered to be complicated by meningitis carcinomatosa, such as poorly differentiated adenocarcinoma or signet-ring cell carcinoma. Because meningitis carcinomatosa occurred after chemotherapy, we speculated the following possibilities: 1) fragility of the choroid vessel due to chemotherapy, 2) transformation of cancer cells to become chemo-resistant to the anticancer drug (19). Chemotherapy for AFP-producing gastric cancer is not established, but the combined use of CDDP and 5-fluorouracil has been reported to be effective (20, 21).

In conclusion, we encountered a case of AFP-producing gastric cancer which was complicated by meningitis carcinomatosa after chemotherapy. Immunostaining of AFP and MRI were useful for the diagnosis of meningitis carcinomatosa.

Discussion

According to the report of Oomura et al, the most common primary lesion in cases of meningitis carcinomatosa is gastric cancer, accounting for 53% of all cases in Japan (6). In Europe and North America, breast cancer and small cell lung cancer are the most common primary lesions (7, 8). These differences seem to be related to differences in the frequency of the various cancers. On the other hand, 1.7-5.5% of all gastric cancer cases are considered to be complicated by meningitis carcinomatosa (9), and the histological type is signet-ring cell carcinoma in most cases (10). There have been no previous reports of meningitis carcinomatosa caused by AFP-producing gastric cancer cells, suggesting that the present case is rare. The neurological symptoms at onset are mainly headache and vomiting. Dizziness which was reported in the present patient is rare (3%) (11). A diagnosis of meningitis carcinomatosa can only be proven by the presence of cancer cells in the cerebrospinal fluid. However, the positivity rate at the time of first inspection is only about 50% (12). In the present case, malignant cells were detected in the first analysis and AFP levels in the cerebrospinal fluid were also high, facilitating rapid diagnosis. Concerning the diagnosis by imaging, meningitis carcinomatosa is often difficult to detect using CT (13). We detected high intensity areas along the cerebellar sulci in the T1-weighted MR image after meglumine gadopentetate enhancement, which is known to be specific for meningitis carcinomatosa (14). The prognosis in cases of meningitis carcinomatosa is generally poor and the one-year survival rate is reported to be only 10% (15). Although intrameninginal injection of methotrexate is recommended (16), most cases become invalids like our patient. The optimum treatment has not yet been established because the rarity of this complication has led to the publication of mostly small and non-controlled trials.

AFP-producing gastric cancer is known to be relatively rare and accounts for only 1.2-3.9% of all gastric cancers, but is commonly associated with liver metastasis (1, 17). Although the reason for liver metastasis is not clear, a possible cause is considered to be that cancer cells producing AFP appear to have biological affinity for the liver (18). The present case was a typical AFP-producing gastric cancer with multiple liver metastasis and was completely different from the histological type of gastric cancer that most commonly causes meningitis carcinomatosa.

Figure 6. Immunohistochemistry of the spinal cord shows alpha fetoprotein (AFP) positive cells exist along the pia mater (methyl green stain, ×400).

References

Meningitis of AFP Gastric Cancer