

A Case of Gastric Adenocarcinoma Presenting as Meningeal Carcinomatosis

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Leptomeningeal carcinomatosis occurs in approximately 5% of patients with cancer. The most common cancers involving the leptomeninges are breast, lung cancer and melanoma. However, gastric adenocarcinoma has been rarely reported with leptomeningeal carcinomatosis. The presenting manifestations are usually headache, visual disturbances and seizures. We report a case of leptomeningeal metastasis that presented as a gastric cancer. A 49-year-old woman was admitted to our hospital with the symptoms of headache and melena for 10 days. The endoscopy showed a thickening of the folds of the stomach compatible with the diagnosis of a Borrmann type IV gastric cancer. The biopsy revealed a signet ring cell carcinoma. The MRI of brain showed no abnormal findings; however, the patient complained of an intractable persistent headache, nausea and vomiting on admission day 6. The cytology examination of the cerebrospinal fluid supported the diagnosis of metastatic signet ring cell carcinoma.

Key Words : Neoplasm, Leptomeningeal, Carcinoma, Signet Ring Cell

INTRODUCTION

Leptomeningeal carcinomatosis (LC), also called carcinomatous leptomeningitis, neoplastic (lepto)meningitis, leptomeningeal metastasis, or more commonly leptomeningeal seeding, is the dissemination and growth of cancer cells within the leptomeningeal space; it is one of the most serious complications that can occur in cancer patients¹. The incidence of LC is three to 8% of all solid cancers. LC is frequently found in patients with leukemia, breast cancer, lymphoma, and lung cancer².

Gastric cancer (GC) is one of the most common causes of cancer related death in Asian countries including Korea. However, the development of LC from a GC is very rare. Kim, et al³ reported that the incidence of LC with GC was 0.06% of all cases of gastric cancer. LC is a more frequent manifestation of advanced or metastatic carcinoma rather than associated with early disease. It is usually discovered during the treatment

period for the cancer. We report a rare case with LC as the presenting symptom and review the medical literature.

CASE REPORT

A 49-year-old woman was admitted to our hospital with headache, dizziness, easy fatigability, and melena for 10 days. She looked pale and acutely ill. There were no significant findings in the medical history. On physical examination, she was oriented to time, place and person. Her vital signs were as follows: a blood pressure of 130/75 mmHg, a pulse rate of 95 beats/min and a respiration rate of 21 breaths/min. There were no focal neurological signs or abnormal reflexes. The plantar responses were flexor. There was no neck stiffness or nystagmus. The sensory examination was normal. The conjunctivae were pale, but not icteric. The breathing sounds were clear

• Received : May 4, 2007

• Accepted : September 21, 2007

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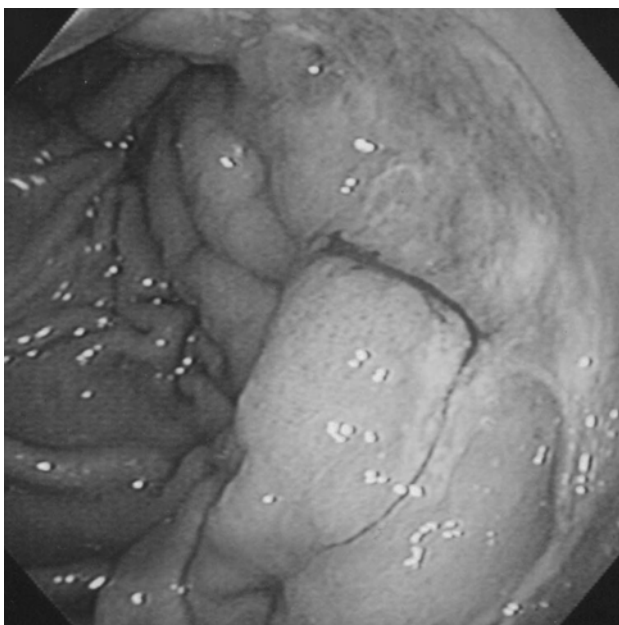


Figure 1. The gastroscopy showed a discrete ulcer with rugae like fold thickening on the high body and posterior wall of the stomach.

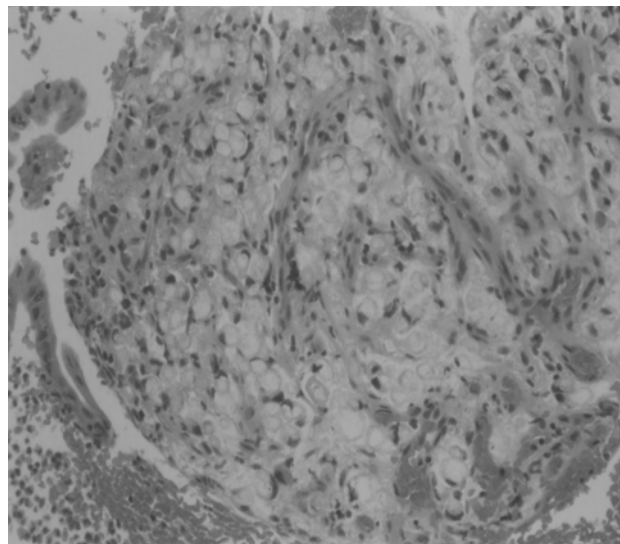


Figure 2. Diffuse infiltration of tumor cells shaped like a signet ring with intracytoplasmic mucin pooling, pushing the nuclei to the periphery in the gastric mucosa (H&E, $\times 400$).

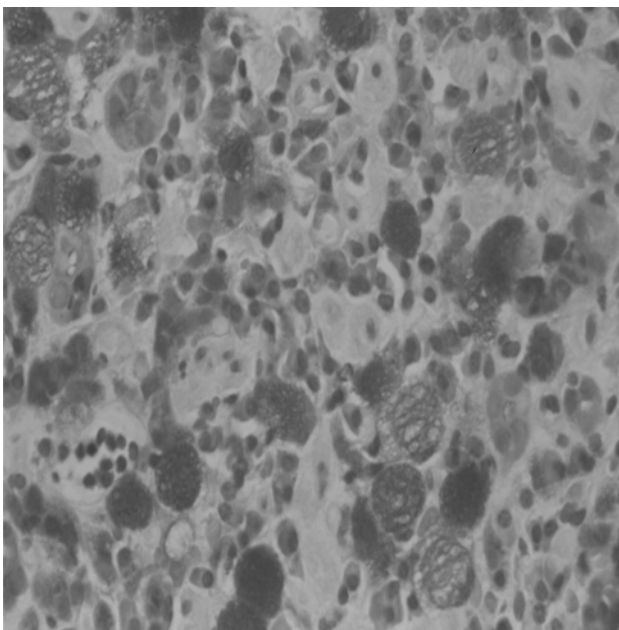


Figure 3. PAS (Periodic acid-Schiff) staining reveals abundant intracytoplasmic mucin in the individual tumor cells (PAS, $\times 400$).

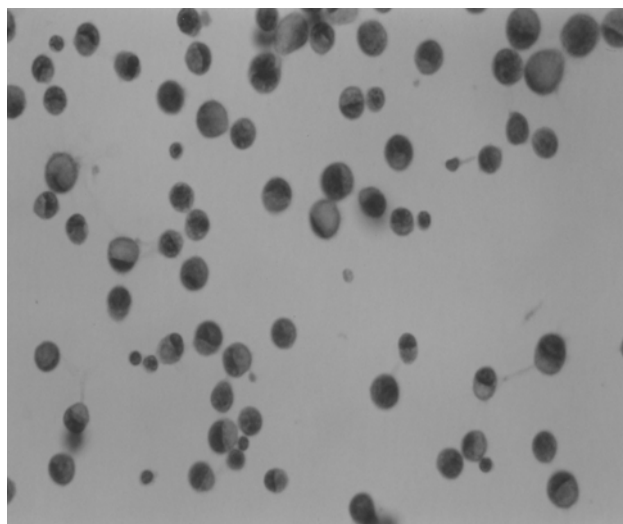


Figure 4. Cytology examination of the CSF shows many floating malignant cells with large mucous vacuoles and displaced hyperchromatic nuclei.

and the heart sounds were regular without a murmur. Hepatosplenomegaly was not noted. The symptoms were slightly improved with conventional analgesic agents. The MRI of brain showed no abnormalities, but the esophago-gastroduodenoscopy showed thickening of the gastric folds on the greater curvature of the stomach and on the posterior wall

of the stomach compatible with a Borrmann type IV gastric cancer (Figure 1). The biopsy revealed a signet ring cell carcinoma (Figure 2, 3). The CT scan of abdomen and pelvis showed an advanced gastric cancer involving the posterior wall of the lower body of the stomach; in addition, the angle and the antrum had extensive metastatic lymphadenopathy. The patient complained of an intractable persistent headache as well as nausea and vomiting on admission day 6. A lumbar puncture and analysis of the cerebrospinal fluid (CSF) was performed.

The results showed an elevated protein concentration with normal glucose content. There were many mucin-secreting cells and signet ring cell types, which were strongly positive for mucicarmin and alcian blue in the CSF (Figure 4). Symptomatic treatment was initiated with steroids and mannitol. A generalized tonic clonic seizure developed on day 11. The patient became stuporous and did not recover. Finally, the patient was discharged without further medical treatment.

DISCUSSION

Since the first report of leptomeningeal carcinomatosis (LC) in 1870, the incidence of LC has been increasing. The incidence of LC is three to 8% of all solid cancers. The most common causes of LC are breast and lung cancer and malignant melanoma. Gastric cancer is the most common cancer in Korea; however, LC associated with gastric cancer (GC) is relatively rare. In the Korean medical literature, the incidence of LC with GC has been reported to be 0.06% of all gastric cancers³. Among cases with LC, GC is reported as the most frequent cause of cancer in Korea^{4,5}. However, these results are based on the experience of one institution, so these findings may not be generalized to the entire Korean population.

The clinical manifestations of LC are very variable and depend on the site of involvement. Many patients complain of headache, nausea, vomiting, ataxia, and have a variety of neurological deficits. Some cases have presented with bilateral progressive blindness⁶ or bilateral hearing loss⁷. LC is usually a manifestation of advanced cancer discovered during follow-up after a cancer diagnosis; it is rarely the presenting symptom as it was in this case. The median time to the diagnosis of LC, from the initial cancer diagnosis, is very variable; reports have found a 76 day⁵ to 17 month⁴ time interval. Diagnosis is based on cytology examination of the CSF and imaging studies (especially, magnetic resonance imaging with gadolinium enhancement)⁸. The CSF findings include an increased opening pressure, elevated protein, the presence of tumor markers (for example, CEA, CA19-9 in gastric cancer), decreased glucose, and pleiocytosis. However, the diagnosis is frequently missed on the first trial but the diagnosis rate increases by 30% on a second one. In our case, the definitive diagnosis was achieved by the first CSF cytologic examination. Chang, et al. reported on patients with breast cancer metastasized to the central nervous system over 20 years. There were 43 cases with 38 parenchymal metastases and 5 leptomeningeal metastases. Out of five LC patients, only one (20%) patient was confirmed cytologically⁹. Pathologically, poorly differentiated adenocarcinoma with signet ring cell features is the most frequent type of LC associated with GC in Japan¹⁰ and this is likely true for

Korea³. LC was a more frequent finding in advanced disease with or without distant metastases; it is rarely reported with early gastric cancer¹¹. Imaging studies (MRI with gadolinium enhancement) show abnormalities in 67% of LC patients¹².

There are several treatment options for patients with LC including intrathecal (IT) chemotherapy with or without radiotherapy (RT). Most chemotherapeutic agents do not penetrate the blood-brain barrier (BBB), and are given by direct intrathecal administration. Agents that can be used for IT chemotherapy include methotrexate (MTX), cytarabine, thiotepa, and steroids. The benefit (i.e. the prolongation of survival) achieved by IT chemotherapy (single or multiple regimens) in LC patients continues to be debated. The median survival of LC is reported to be four to six months even with aggressive therapy. In one study, the objective response rate and median survival of IT MTX were 20% and 11 weeks; with sustained-release cytarabine they were 25% and 15 weeks. Therefore, the results did not confirm a definite benefit with the IT chemotherapy¹³. However, in a Korean study, there was a favorable outcome with combination IT chemotherapy, compared to the single IT chemotherapy¹⁴. MTX, one of most useful agents for IT chemotherapy, penetrates the blood brain barrier poorly in low doses, but can penetrate in the higher dose range. High dose intravenous MTX (3.5 g/m²) injection showed a 28% partial response and stable disease and 44% progressive disease. The median survival of patients with LC (with or without parenchymal disease) was 12.6 weeks; shorter than with isolated parenchymal disease (25.4 weeks)¹⁵.

The clinical risk factors that influence the survival of patients with LC are performance status, underlying malignant disease and previous responsiveness to anticancer therapy. The patients with disease that is more advanced, poor performance status (PS), chemoresistant tumors, pronounced neurological clinical findings, and a heavy pretreatment status have a poor prognosis and additional management should be with conservative treatment¹⁶. In our case, the patient had a poor PS, pronounced abnormal neurological clinical findings and a very rapidly deteriorating clinical course.

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