Rapidly Progressive Dementia due to Carcinomatous Meningitis Associated with Gastric Cancer

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ABSTRACT

Gastric cancer rarely presents with carcinomatous meningitis (CM) and rapidly progressive dementia. The authors report two cases of carcinomatous meningitis due to gastric cancer presenting with rapidly progressive dementia. The MRI of the brain was different between the two cases. The diagnosis of CM was confirmed by positive cerebrospinal fluid cytology.

Keywords: Gastric cancer, carcinomatous meningitis, rapidly progressive dementia

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CASE REPORT

Most dementias usually develop slowly which allow physicians to have time in the evaluation. Rapidly progressive dementia (RPD) is a dementia condition which accelerates progressively in less than 2 years, typically over weeks or months. A number of underlying causes may contribute to a RPD, including neurodegenerative, vascular, tumor, autoimmune, infectious, and toxic-metabolic conditions. Neurologists and primary physician are familiar with the diagnosis of Alzheimer disease and related neurodegenerative dementias. This leads to the delay in diagnosing the cause of RPD and subsequently in the treatment of the condition. The prognosis in RPD is variable depending on the underlying causes of which many are reversible. Malignancy is not a common cause of RPD and most malignancy-related causes of RPD have parenchymal involvement or paraneoplastic syndrome. Carcinomatous meningitis (CM) is estimated to occur in 3% to 8% of solid carcinomas and most of the primary sites are breast, lung and malignant melanoma. CM is rarely present with RPD. Here, the authors report two patients with an uncommon primary site of CM presenting with RPD.

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CASE REPORT

Case 1

A 76-year-old man presented with cognitive impairments for 3 weeks. He was diagnosed with poorly differentiated adenocarcinoma of his stomach (stage III B) 6 months ago and underwent subtotal gastrectomy and received adjuvant chemotherapy for 7 cycles. His baseline cognitive function was intact. Three weeks prior to presentation, he progressively developed memory problems, followed by diminishment of speech

fluency, refusal to eat or ambulate, and incontinence. Three days prior to admission, he developed ptosis of the right eye and had only trivial motor response to pain stimuli. Physical examination showed mute, E3V1M6. Cranial nerve examination revealed good papillary response to light and incomplete ptosis of the right eye. Motor tone increased and motor power was grade III/V.

Initial investigations were normal. The cranial CT scan showed non obstructive hydrocephalus and the Magnetic Resonance Imaging showed ventricular dilatation and leptomeningeal enhancement at posterior fossa (Fig 1). The cerebrospinal fluid cytology revealed a few tiny clusters of malignant cells with a few signet ring cell arrangements. These cells show large intracellular vacuoles pushing the nuclear aside (Fig 2).

The patient was diagnosed with carcinomatous meningitis (CM) from gastric cancer. After the admission, his general conditions progressively deteriorated and he developed aspiration pneumonia. Having discussed this with his family, the treatment plan was palliative care. The patient expired on the seventeenth day of admission.

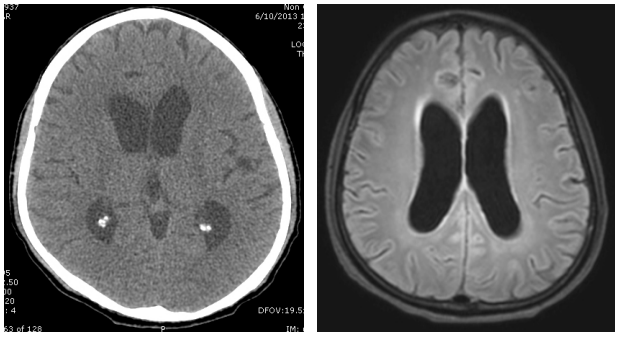


Fig 1. (Case 1) CT and MRI brain of case 1 showed dilated ventricular system.

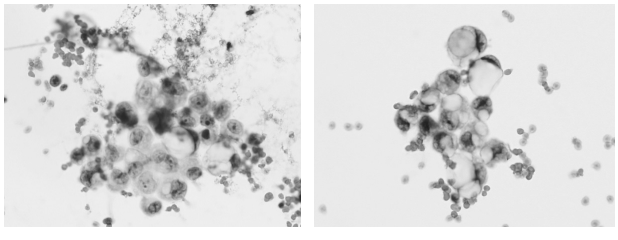


Fig 2. (Case 1) Cerebrospinal fluid (CSF) cytology reveals few tiny clusters of malignant cells with few signet ring cell arrangement. These cells show large intracellular vacuoles pushing the nuclear aside.

Case 2

An 86-year-old man had a complaint of gradually progressive forgetfulness over two years. The Thai Mental State Examination (TMSE) score was 27/30. His initial cranial CT scan showed leptomeningeal enhancement at the left occipital lobe with no space occupying lesion. He was scheduled for further MRI brain scan. Five days prior to admission, the patient had nausea and vomiting and decreased level of consciousness. He could follow only two-step commands and became bedridden. He was hospitalized for further investigations. Physical examination revealed drowsiness. The pupils and fundoscopic examination were unremarkable. Muscle tone, power and deep tendon reflex was generalized and decreased. Nuchal rigidity was positive.

Initial investigations were normal. MRI brain with gadolinium showed multiple masses at temporal, frontal, and cerebellar vermis with leptomeningeal enhancement (Fig 3). The cerebrospinal fluid (CSF) cytologic examination demonstrated the presence of metastatic poorly differentiated carcinoma with a suggestive morphological diagnosis of adenocarcinoma (Fig 4).

The CT whole abdomen demonstrated diffused circumferential wall thickening with heterogenous enhancing lesion at the gastric antrum, pylorus and duodenal bulb with extension through serosa and perigastric fat. His clinical data were compatible with gastric cancer with CM. The palliative whole brain radiation was scheduled. Over the course of his admission, his condition deteriorated rapidly. Eventually he became comatose and expired on the 25th day after admission.

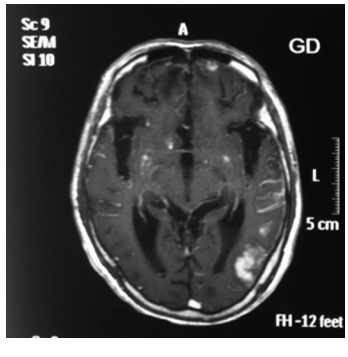
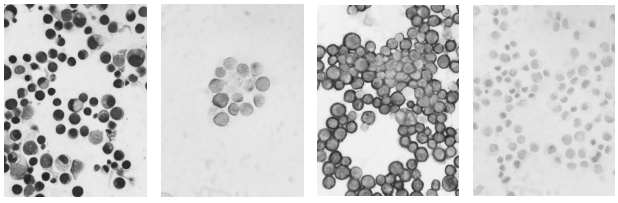


Fig 3. (Case 2) MRI brain with gadolinium showed enhancing mass at left temporo-occipital region with leptomeningeal enhancement.



A B C D

Fig 4. (Case 2) Cerebrospinal fluid (CSF) was processed in cytopathology laboratory and stained with Diff-Quik® stain. The cytologic material (Fig A) shows numerous individual enlarged round tumor cells mixed with small lymphocytes on clear background. Some tumor cells show signet-ring cell appearance characterized by large cytoplasmic vacuole compressed nucleus and eccentric nuclei. Immunostaining was performed on cytospin material and demonstrates that the neoplastic cells mark with AE1/AE3 (Fig B) and BER-EP4 (Fig C) but they do not mark with CD20 (Fig D).

DISCUSSION

These two patients had the clinical syndrome of rapidly progressive dementia (RPD) which deteriorated in few months. The prognosis of RPD is variable depending on the underlying cause of the symptoms. Identification of a reversible RPD is particularly important considering that delay in treatment may lead to permanent functional impairment or death.[1] Investigations including hematological or other chemical laboratory tests are important steps for excluding reversible causes of RPD. Furthermore brain imaging, electroencephalography, and brain biopsy are needed for providing the diagnosis in particular cases.[2]

From 9 studies in RPD, it was revealed that the major cause of this syndrome is Creutzfeldt–Jakob disease (69%). The prevalence of malignancy is only 3%.[3] A study in a tertiary center showed that the causes of RPD were non-prion neurodegenerative diseases (36.8%), Creutzfeldt–Jakob disease (30.6%), toxic-metabolic conditions (8.2%), and other disorders (16.2%).[4] Neoplastic disease accounted for only 2% of RPD in that report. Generally, the three most common malignancies presenting as RPD are primary central nervous system lymphoma, intravascular lymphoma and lymphomatoid granulomatosis. The prevalence of carcinomatous meningitis resulting in RPD was reported to be only 0.1%.[2]

Carcinomatous meningitis (CM) is rare and a devastating complication of malignancy. The incidence rate of CM ranges from 4-15% in breast, small cell lung cancer and malignant melanoma.[5-10] The prevalence of CM in gastric cancer patients is as low as 0.14-0.24%. The most common symptom of CM is headache from increased intracranial pressure (incidence 51-75%).[5,8,9] This is followed by decrease in mental status or cranial nerve palsies. The pathophysiology of decline in mental status is the disturbance of diffused brain metabolism.[6,8,10] The clinical manifestations of CM may be the malignancy's consequences or the first presentation of primary cancer. Because of clinical pleomorphism of CM, a delay in diagnosis may occur. Hence, early recognition of this uncommon manifestation of CM is essential. The standard investigation of CM is determining the presence of malignant cells in the CSF.[5-7,9,10] CSF cytology is positive in 44-58% of suspected cases of CM on the first CSF cytological analysis, but increases to 57-84% by the third analysis.[6,11,12] The volume of CSF is an essential factor for diagnostic accuracy. The sensitivity of CSF cytology rose from 68% to 97% for 3.5 and 10.5 ml of CSF sample, respectively.[5] Currently the CSF biomarkers including carcinoma-embryonic antigen, alpha-fetoprotein and beta-HCG have been suggested to favor the diagnosis in patients with normal routine CSF analysis.[5,7,9] Nevertheless, these biomarkers may be nonspecific and not available worldwide. Any cancer patient with clinical manifestations suggestive of CM and with rapidly progressive cognitive decline requires contrast enhanced brain imaging to exclude brain metastasis. The sensitivity is approximately 30% by the CT brain scan and 70% by the MRI brain scan.[7,8]

Treatment options for CM include radiation and intrathecal chemotherapy to stabilize the neurological status and prolong survival.[8,9] However, overall survival ranges from 4-11 weeks.[5,7,9,13] According to the National Comprehensive Cancer Network guideline (NCCN), the patients who have Karnofsky Performance Status (KPS) higher than 60%, no major neurological deficits, no CSF leak shown and minimal systemic disease usually have better response to treatment and thus are reason-

ably considered for treatment. Unfortunately, our two patients did not meet the criteria. Therefore, the goal of their treatments was palliative treatment in both cases.

CONCLUSION

RPD from CM can be a presenting symptom prior to the diagnosis of cancer. CM associated with gastric cancer, especially in its early stages, is exceedingly rare. However, it can present with RPD. Therefore, the finding from this study highlights the importance of the evaluation of CSF cytology in patients with RPD.

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