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Ring Cell Gastric Cancer Presenting with Headache

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Abstract: Headache, the most common symptom of cerebral dysfunction caused by leptomeningeal carcinomatosis, may be the only symptom. The headache usually results from increased intracranial pressure. Brain metastasis of gastric cancer in particular is rarely encountered and leptomeningeal carcinomatosis (LMC) is even less common. Presentation with isolated headache is a very rare condition in patients with gastric carcinoma. This 48-year-old man was admitted to the neurology outpatient clinic with headache that was present for nearly one month. The pain was felt in entire head particularly in the occipital and neck regions. The nature of the pain was throbbing, which worsened in the morning while the patient was in supine position. His headache persisted for all day. There was no nausea and vomiting. Neurological examination was normal. Brain MRI (contrast-enhanced) demonstrated triventricular hydrocephaly with transependymal edema. MR angiography and venography were also normal. Lumbar puncture revealed high cerebrospinal fluid (CSF) pressure (320 cm H_2O), normal biochemistry except for mildly elevated protein, and unremarkable microbiological and pathological examination five days, and fundus examination revealed papilledema. Abdominal tomography demonstrated a focal area of increased gastric wall thickening. Result of endoscopic examination was reported as giant ulcer. PET showed increased FDG uptake in the gastric antrum. Gastric biopsy revealed diffuse carcinoma. Ventriculo-peritoneal shunt was performed for hydrocephalus. His treatment continued at medical oncology department. We reported this case since clinical presentation with isolated headache in the patients with gastric carcinoma is a rare condition.

Keywords: Gastric Cancer, Headache, Leptomeningeal Carcinomatosis

1. Introduction

Leptomeningeal carcinomatosis (LMC) is one of the complications of systemic cancers and has poor prognosis. It is characterized by dissemination and growth of cancer cells within the leptomeningeal space [1]. Headache, the most common symptom of cerebral dysfunction caused by LMC, may be the only symptom [2, 3]. Headache is usually a consequence of increased intracranial blood pressure. Hydrocephalus is the consequence of increased intracranial pressure resulting from either obstructive or communicating hydrocephalus [4]. The most common primary tumors that involve leptomenings include breast and lung carcinomas, lymphoma, leukemia and melanoma [5]. Brain metastasis of gastric cancer in particularly is a rare condition and LMC is even less common [6]. Although LMC is a common finding of advanced carcinoma, we encountered a single case with early phase of gastric carcinoma that presented itself with LMC. Herein, we presented a previously healthy male, who developed isolated subacute progressive headache secondary to LMC and was later diagnosed with gastric carcinoma.

2. Case Report

A 48-year-old man was admitted to the neurology outpatient clinic with the complaint of headache that was present for nearly one month. The pain was felt in entire head particularly in the occipital and neck regions. The nature of the pain was throbbing, which worsened in the morning while the patient was in supine position. His headache persisted for all day. There was no nausea and vomiting. His medical history was unremarkable. There was no past history of migraine.

The patient was initially alert, cooperative and oriented. He was afebrile, and her vital signs were normal. There was no rash. His cognition was normal. The rest of his cranial

nerve examination was unremarkable. Tone, power, coordination, and sensation were all normal in both upper and lower limbs. Plantar reflexes were flexor bilaterally. There was no neck stiffness or nystagmus. He had normal venous pulsation of his retinal veins and no papilloedema was seen on fundoscopy examination. Other system examinations were unremarkable. Brain MRI (contrast-enhanced) demonstrated triventricular hydrocephaly with transependymal edema. MR angiography and venography were normal. A lumbar puncture and analysis of the cerebrospinal fluid (CSF) was performed. The results showed an elevated protein (80 mg/dL), high CSF pressure (320 mm H_2O), decreased glucose (25 mg/dL; simultaneous blood glucose was 80 mg/dL), and normal LDH and chloride concentrations. The initial CSF smear and culture were negative, and so were the subsequent CSF specimens. There was no evidence of acid/alcohol fast bacilli. All other microbiological investigations (throat swab, midstream urine, faecal specimen, and Cytomegalovirus/ Adenovirus/ Herpes/ Varicella Zoster/ Enterovirus/ Rotavirus/ Leptospira/ Treponema pallidum serology) were all negative. The rest of his full blood picture, renal function and liver function tests were all normal.

He developed nausea and vomiting after 10 days and fundus examination revealed papilledema. Brain MRI was re-performed on the 10th day after initial findings. Contrast-enhanced brain MRI showed no new lesion. The second lumbar puncture revealed high CSF pressure (370 mm H_2O), elevated protein (65 mg/dL), and decreased glucose (29 mg/dL; simultaneous blood glucose was 105 mg/dL).

Abdominal and thoracic tomography were performed to detect presence of either primary tumor or systemic disease. Abdominal tomography showed a focal area of increased gastric wall thickening. Result of the endoscopic examination was reported as giant ulcer. PET showed increased FDG uptake (SUVmax: 5.9) in the gastric antrum. Gastric biopsy revealed diffuse carcinoma. Ventriculo-peritoneal shunt was performed for hydrocephalus. Headache, vomiting and nausea disappeared after ventriculo-peritoneal shunt. Thereafter, he was transferred to the oncology department. He is already being treated at medical oncology department.

3. Discussion

LMC accounts for 3-8% of all solid cancers [7]. LMC originating from a gastric cancer is a very rare condition. Kim et al. [2] reported that the incidence of LMC secondary to a gastric cancer was 0.06% among all cases of gastric cancer. Presentation with headache as initial symptom has been rarely reported in patients with LMC secondary to gastric carcinoma [3, 4, 6]. Park et al. reported a case with early stage gastric cancer in remission, which presented with headache and nausea [8]. Lee et al. reported a case, who presented with headache, dizziness and melena [7] and diagnosed with signet ring cell carcinoma. Our patient was admitted to the hospital with isolated headache. He had no gastrointestinal or systemic illness. This feature is interesting as a presenting symptom.

Apart from a clinical suspicion of LMC, diagnosis is dependent upon demonstration of cancer in cerebrospinal fluid (CSF) or radiographic manifestations as revealed by neuraxis imaging. In our case, which was a persistent headache, imaging studies were performed primarily to monitor the pathologic lesions that may occupy space and contraindications to LP. Mass, cystic lesion, aneurysm, such as space occupied lesion was excluded. LP was used to investigate the factors in the etiology of the triventicular hydrocephalus. The first CSF microbiological and pathological examinations were unremarkable. However, progression was observed when the patient was waiting for the results of the examinations.

LMC may cause multifocal neurologic deficits, which may be associated with infiltration of cranial and spinal nerve roots, direct invasion of the brain or spinal cord, obstructive hydrocephalus, or some combination of these factors [2-4]. As the consequence, the patient may complain about nausea, vomiting, headache, diabetes insipidus, changes in mental status, diplopia, facial numbness, hearing loss, loss of visual acuity, paresthesia, pain in the back or neck, weakness of the legs, and bladder and bowel dysfunction, and may have a variety of other neurologic deficits. Isolated headache in patients with LMC is a rarely encountered condition. The nature of headache in LMC is generally throbbing, which worsens in the morning when the patient is in supine position and persists for all day because of high intracranial pressure. Nausea and vomiting may be accompanied by headache [2-4]. Our patient's headache was throbbing, worsened when he was in supine position, and persisted for all day as expected. Medical history of the patient revealed no presentation with headache that clinically worsened day by day. He developed nausea and vomiting after 10 days, and fundus examination revealed papilledema. The first lumbar puncture revealed elevated CSF protein and pressure and decreased glucose suggesting leptomeningeal involvement. Second LP was performed after ten days; CSF pressure was higher as compared to the first LP and protein was found elevated again (65mg/dl). Because of the progression of neurologic symptoms, ventriculo-peritoneal shunt was performed. His headache and nausea-vomiting were relieved after the surgery.

Radiologic imaging techniques play an important role in the diagnosis of LMC, but unfortunately do not always clearly identify LMC. Meningeal gadolinium uptake on cranial MRI is a meaningful finding but not specific. In the literature, the sensitivity of cranial MRI in the diagnosis of LMC was reported between 65% and 75% [9-11]. Although brain MRI demonstrated no sign of contrast uptake suggestive of leptomeningeal carcinomatosis, there were hydrocephalus and transependymal edema. Cytological examination of CSF is often considered as the gold standard diagnostic method for LMC [8]. However, one study found that the diagnosis of LMC could have been accurately made in only 54% (49/90) of the cases according to the initial examination of CSF specimen and in 91% (82/90) of the

patients according to the subsequent examination of the specimen [8]. Cytological specimens with sparse cellularity and minimal cytological atypia can be misleading.

Processing of CSF specimens in a timely manner is also critical to improve the sensitivity of CSF cytology. Glantz et al. summarized the recommendations for minimizing the factors that could lead to false negative results in LMC. Their suggestions; withdrawing at least 10.5 mL of CSF for cytologic analysis; processing the CSF specimen immediately; obtaining CSF from a site of known leptomeningeal disease; and repeating this procedure once if the initial cytology is negative [12]. Also determined the volume of CSF is 12 mL and the pathological processing the CSF specimen immediately, the cytological examination of CSF, was interpreted as negative for two times in our case.

The goals of treatment include palliating neurologic symptoms and whenever possible stabilizing or improving patient neurologic function as well as prolonging survival. The median survival for LMC varies depending on the source of the primary tumor and the organ systems involved including the central nervous system. Patient prognosis is reported to be poor for LMC arising from gastric cancer. Without treatment, carcinomatous meningitis has a median survival of about 4–6 weeks [13, 14]. Treatment options are very limited in LMC. Symptomatic treatment is directed at pain including headache, nausea, and vomiting, surgical (ommaya reservoir placement, ventriculo-peritoneal [V-P] shunt placement) whereas more specific LMC-directed therapies include intra-CSF chemotherapy, systemic chemotherapy, and site-specific radiotherapy (RT) [15-17].

Even in patients who underwent aggressive chemotherapy and RT following the diagnosis of LMC, the mean survival has been reported to be only approximately 2-3 months [18]. An early diagnosis of LMC, before fixed neurologic deficits are manifest, permits earlier and potentially more effective treatment, thus leading to a better quality of life in patients so affected. In 2011, Oh et al. performed a retrospective analysis of 54 patients who were diagnosed with LMC from gastric cancer. They reported that "although these patients had a fatal clinical course, cytologic negative conversion by intra-CSF chemotherapy may improve survival" [19]. A multidisciplinary approach should be considered to improve the symptoms of patients with meningeal carcinomatosis [20]. From an oncological perspective, neurosurgery can be used to aid in the administration of chemotherapy and address the issue of hydrocephalus. Zhao et al. was analyzed 5 meningeal carcinomatosis patients therapeutic process to evaluate the value of shunting surgery in the treatment for patients with meningeal carcinomatosis. They reported the V-P shunt surgery can effectively relieve the intracranial pressure caused by meningeal carcinomatosis, decrease the mortality and morbidity caused by intractable intracranial hypertension in these patients, and improve their live quality [21].

4. Conclusion

Brain metastasis of gastric cancer in particular is a rare condition and LMC is even less common. Presentation with isolated headache is a very rare condition in the patients with gastric carcinoma. Early LMC-directed treatment may allow maintenance of quality of life and potentially improve survival. A combined treatment approach (i.e., systemic and intra-CSF chemotherapy, site specific radiotherapy and surgical treatment) may provide better palliation in patients with LMC. Despite all treatments, LMC is a fatal disease. Before the start of LMC-directed therapy the patient should be informed about the realistically outline the course of disease and palliative treatment goals. Persistent neurological symptoms should alert the physician to any central nervous system involvement, and the appropriate diagnostic and therapeutic work-up should be established immediately. LMC should be suspected in persistent headache patients even in the absence of hydrocephaly and/or meningeal contrast enhancement in neuroimaging and CSF cytology must examined even if there is no history of cancer. CSF examination should be repeated if there is suspicion about LMC.

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