Case Report

Neurologic Signs due to Leptomeningeal Involvement as the Presenting Manifestation of Gastric Adenocarcinoma

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Abstract

A 43-year-old female with a 5-month history of progressive neurological manifestations was admitted to our hospital. On examination, she was found to have multiple cranial nerve deficits and cerebellar syndrome. Laboratory investigations revealed a prominent increase in protein content with no significant pleocytosis in cerebro spinal fluid. Neuroimaging studies showed contrast enhancement on cerebellar cortex and leptomeningeal enhancement at brainstem. Although she had no complaints regarding gastrointestinal system, further investigations led to the diagnosis of gastric adenocarcinoma.

We report this case for the rare presentation of gastric adenocarcinoma with neurological manifestations due to leptomeningeal involvement.

Keywords: Gastric adenocarcinoma; leptomeningeal involvement; CSF findings; cerebral MRI

INTRODUCTION

The most common neurological complications seen in adult malignancies are respectively due to metastatic spread to the brain, the spinal cord and the leptomeninges. In recent years, effective chemotherapy caused prolongation of survival rates in malignancies and this has led to an increase in the frequency of leptomeningeal involvement. The involvement of cranial and spinal nerves, confusional state, headache, and less commonly bilateral progressive hearing loss are the manifestations of leptomeningeal carcinomatosis (LMC) (1,2). LMC occurs in 3-8 % of the patients with leukemia, breast cancer, lymphoma, lung cancer and malignant melanoma. Primary or secondary tumors of central nervous systems (CNS) have a tendency to leptomeningeal infiltration, too (1,2).

Rarely, the neurological symptoms may precede the systemic manifestations of malignancy (1). The frequency of central...
nervous system metastases in gastric adenocarcinoma is reported as 0.16-0.69%; leptomeningeal involvement is 0.17%. Moreover, LMC as the initial manifestation of any form of cancer, especially gastric adenocarcinoma, there have been only a few reported in literature (3-4).

We report a patient presenting with neurological symptoms and signs due to leptomeningeal involvement as the initial manifestation of gastric adenocarcinoma.

**CASE PRESENTATION**

A 43-year-old female was admitted to our department with complaints of headache, blurred vision, fatigue and imbalance. She had a 5-month history of right facial palsy. Two months later, she began to develop positional vertigo, hearing loss in the right ear, bilaterally diminished visual acuity and double vision. Her symptoms slowly progressed and she began to experience gait disturbance and imbalance within the last month. Her past medical history was significant for a thyroidectomy carried out ten years earlier. She was hypertensive for six years. Her family history was significant for her mother dying of breast cancer.

Neurological examination revealed bilateral optic atrophy, sluggish pupillary reaction to light, diminished visual acuity more on the left side, conjugate vertical upward gaze palsy, bilateral lateral gaze palsy, right peripheral facial palsy, right sensoryneural hearing loss, left-sided dysmetria, ataxia and positive Romberg test.

Laboratory blood analyses were significant for increase in ESR (71 mm/hour), anemia (Hb: 11.6 g/dl, Hct: 35%), and increase in hepatic enzymes (ALP: 447 U/L, GGT: 89 U/L). Some tumor markers have also increased (Ca-125: 192.73 UI/ml, Ca-15.3: 1800 UI/ml). Other serologic investigations including blood smear, protein electrophoresis, specific infections (brucellosis, salmonellosis, syphilis, HIV, toxoplasmosis, tuberculosis), collagen vascular diseases and bone marrow biopsy were within normal limits. Bence-Jones protein was negative in urine. A lumbar puncture revealed a xantochromic cerebrospinal fluid (CSF) with an opening pressure of 220 mm H2O, a protein content of 300 mg/dl, a glucose concentration of 63 mg/dl, a lactate concentration of 4.1 mEq/L, and no significant pleocytosis. Oligoclonal band was negative. CSF serology and culture were negative both for the specific infections mentioned above and fungi. CSF pop smear for cytology was negative.

EEG showed diffuse background slowing with prominent slow delta waves in bilateral temporocentral and left midfrontal regions. Visual evoked potentials were delayed bilaterally, brainstem evoked potentials showed a delay in 3rd and 5th waves on the right. Somatosensory evoked potentials were normal. EMG-NCV measurements revealed advanced partial degeneration of right facial nerve and a delay in the 1st and the 2nd blink reflex responses. on the right side. Normal nerve conductions were obtained in upper and lower extremities.

Computed tomography showed multiple lytic lesions in vertebral bodies (figure 1). Bone sintigraphy displayed increased activity in left acetabulum, sternum, and several thoracal vertebrae. Breast ultrasonography was normal. Abdominal ultrasonography and CT demonstrated peritoneal ascites and carcinomatosis and bilateral ovarian masses. Endoscopy revealed severe hyperemia in antrum and total gastritis. Cranial MRI showed periventricular and subcortical hyperintense lesions, more widespread in bilateral frontal areas. Contrast enhancement on cerebellar cortex and leptomeningeal enhancement at brainstem were detected (Figure 2). Mild hydrocephalus was also evident.
Endoscopic biopsy material from antrum demonstrated antral adenocarcinoma. Medical oncologists considered the case as inoperable and intratechal chemotherapy with etoposide, doxorubicine, cisplatine was initiated. The patient showed no significant improvement and died 6 months later.

DISCUSSION

Leptomeningeal involvement, also known as meningeal carcinomatosis or neoplastic meningitis, is verified with malignant cells in the CSF. The CNS metastasis is a very rare complication of gastric cancer, occurring in these patients. Gastric adenocarcinoma which generally spreads to peritoneum, liver and intraabdominal lymph nodes rarely shows leptomeningeal involvement. Presenting with leptomeningeal involvement is far more uncommon in gastric adenocarcinoma. The female frequency rate of gastric carcinoma in Turkey is 6.99%, being the second most frequent cancer type after breast carcinoma \(^{15}\). Despite its frequency rate, LMC due to gastric cancer has not been reported in Turkish population to date. This patient is one of the rare cases reported in literature presenting with neurological signs due to leptomeningeal involvement preceeding systemic findings of gastric adenocarcinoma \(^{5,14}\). In the literature, Lee et al. reported the widest series of LMC due to gastric cancer. However, of the 19 patients in their series, LMC was the initial manifestation only in 2 cases.

Its clinical course is slowly progressive. Initial symptoms can be headache, lowback pain, radiculopathy, paresis, cranial nerve involvement, nausea, vomiting, seizure, and impairment in cognitive functions \(^{1,2}\). Headache is a complaint of 1/3 of the patients \(^2\). Pain can be aggravated by neck and waist movements. Cranial nerves are affected in more than 50% of these patients causing diplopia, vision loss, hearing loss, vertigo, tinnitus, facial palsy or dysphagia. In our case, the presenting symptoms were diffuse headache, facial palsy, vision and hearing loss, and gait disturbance, and neurologic examination showed multiple cranial nerve involvement with cerebellar syndrome.

Leptomeningeal involvement can be diagnosed with lumber puncture and contrast enhanced MRI. CSF findings are very important to exclude chronic meningitis \(^{16}\). If it is excluded, then increased CSF pressure and protein content, decreased glucose concentration, and positive CSF cytology are significant for a malignancy. However, it should not
be forgotten that CSF cytology can be negative initially, and may become positive in the successive analyses; sensitivity of CSF cytology is 60% in the initial and 85% in the third investigation and may increase up to 95% in the following tests. Radiological investigations are very important in such malignancies. Contrast-enhanced CT and especially contrast-enhanced MRI are reported to be positive up to 56% and 71% respectively. In some studies contrast enhanced MRI has been reported to be more effective than lumbar puncture.

In our case, high ESR, increase in hepatic enzymes and some tumor markers, and CSF findings were suggesting malignancy. Chronic meningitis due to tuberculosis, syphilis, and AIDS were excluded with the specific tests in the differential diagnosis. CSF cytology was performed using pop smear only once in our patient and it was negative. Imaging studies, especially computed tomography and cerebral MRI, supported our diagnosis. Leptomeningeal involvement was diagnosed by MRI. Tumor markers were helpful in directing us to the primary tumor.

Malignancies with leptomeningeal involvement without any therapy can survive only for 4-6 weeks. Survival can be extended for a year with an aggressive chemotherapy. The survival ranges between 6 weeks to 6 months in patients with gastric adenocarcinoma presenting with leptomeningeal involvement. A combination of intrathecal chemotherapy and radiotherapy should be administered to systemic cancer patients with neurologic symptoms even though CSF cytology is negative for tumor cells. Our patient had intrathecal chemotherapy and survived for 6 months.

Neurological signs can be the initial manifestation of a gastric malignancy and early diagnosis is essential to prolong survival and delay morbidity. A negative CSF cytology does not rule out the possibility for leptomeningeal involvement and MRI can sometimes be more helpful for an early diagnosis.

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