

Krukenberg Tumor with Leptomeningeal Carcinomatosis Misdiagnosed as Acoustic Neuroma

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Abstract

Objective: Leptomeningeal carcinomatosis (LMS) is defined as the diffuse infiltration of the leptomeninges and subarachnoid space by malignant cells metastasizing from systemic cancer. Patients usually have a known underlying malignancy, but primary presentation can be with symptoms of meningeal involvement. We describe a rare case of Krukenberg tumor with LMS initially presented as bilateral progressive sensorineural hearing loss, which was misdiagnosed as acoustic neuroma.

Patient: A 50 year old man with a history of cervical cancer was referred to the Ear Nose and Throat (ENT) clinic because of progressive hearing loss, tinnitus, dizziness and blurred vision for 5 months.

Results: A CT scan of the abdomen and pelvis showed a right adnexal mass, suspicious for an ovarian neoplasm. The patient underwent surgical resection of her pelvic mass. Surgical pathology revealed poorly differentiated adenocarcinoma with scattered signet ring cells, favorable with metastatic gastric adenocarcinoma. Magnetic resonance imaging revealed abnormal leptomeningeal enhancement. A lumbar puncture was performed, the CSF analysis showed elevated protein and positive for signet malignant cells.

Conclusion: Our case highlights the importance of the development of new diagnostic tools and treatment regimens for LMC.

Keywords: Gastric cancer; Krukenberg tumor; Leptomeningeal carcinomatosis; Intrathecal methotrexate therapy; Whole brain irradiation

Introduction

A Krukenberg tumor refers to the “signet ring” subtype of metastatic tumor in the ovary that metastasized from a primary site, classically the gastrointestinal tract, although it can arise in other tissues such as the breast [1]. Gastric adenocarcinoma, especially at the pylorus, is the most common source [2].

Leptomeningeal Carcinomatosis (LMC) is the dissemination and growth of cancer cells within leptomeningeal space [3]. It is a rare but devastating complication of malignancy. It is a more frequent manifestation of advanced or metastatic carcinoma and is commonly seen in patients with leukemia, breast cancer and lung cancer [4].

LMC has been rarely reported with gastric adenocarcinoma with a prevalence of only 0.14%-0.24% [4,5]. On average, LMC is diagnosed within 1 year of the diagnosis of the primary cancer [4]. However, the diagnosis of cancer for some patients may be delayed until after the onset of neurological symptoms.

We describe such a case of Krukenberg tumor with LMC initially presented as bilateral progressive sensorineural hearing loss, which were thought to be due to acoustic neuroma.

Case Report

A 50 year old female initially presented to the Ear Nose and Throat (ENT) clinic complaining of left ear fullness, bilateral hearing loss, dizziness and imbalance for five months. Magnetic resonance imaging (MRI) of the brain revealed a cerebellar vermis lesion and enhancement of bilateral auditory canals. Her symptoms were initially thought to be due to acoustic neuroma. Five months after her initial presentation, a computerized tomography (CT) scan of the abdomen

and pelvis showed a right adnexal mass, suspicious for an ovarian neoplasm. The patient was then referred to our hospital where she underwent exploratory laparotomy, bilateral salpingo-oophorectomy, left pelvic lymphadenectomy, omentectomy, appendectomy. The intraoperative findings show malignant appearing left adnexal mass, extensive adhesions of the omentum to the mass and to the anterior abdominal wall, nodules in the omentum and another firm mass in the posterior stomach. Surgical pathology of the left ovarian mass revealed poorly differentiated adenocarcinoma with scattered signet ring cells, favor for metastatic gastric adenocarcinoma. The tumor showed 1-2+ positivity for Her2Neu by immunohistochemistry. She subsequently underwent an esophagogastroduodenoscopy, which revealed two areas of prominent gastric folds and ulceration. Biopsy results of the ulcerated mucosa were consistent with invasive gastric adenocarcinoma in a background of goblet cell metaplasia. The immunohistochemical staining for *H. pylori* was positive.

Three weeks after surgery, she was evaluated at the Emergency Room for headaches, vertigo, worsening of her hearing and one episode of syncope. A CT of head revealed 6 × 5 mm ovoid hypodensity midline in the inferior cerebellar vermis. MR of the brain revealed multiple enhancing lesions within the posterior fossa including

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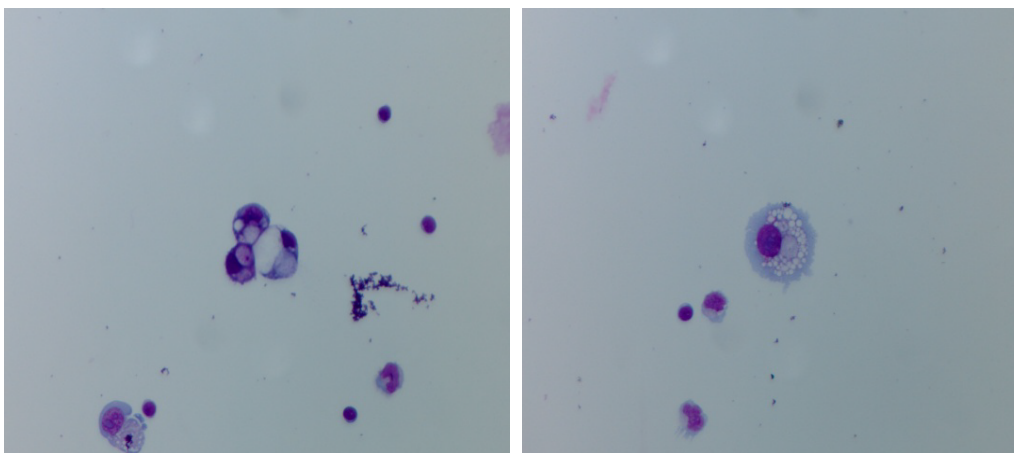


Figure 1: Slides representing metastatic malignant cells (signet ring cells) in cerebrospinal fluid cytology suggestive of leptomeningeal carcinomatosis.

within the internal auditory canals bilaterally and cerebellar vermis. A lumbar puncture (LP) was performed, and the Cerebrospinal fluid (CSF) analysis showed evidence of elevated protein and positive for signet malignant cells (Figure 1). A multi-disciplinary team involving a medical oncologist, neurosurgeon and a radiation oncologist was formed. Intrathecal chemotherapy with liposomal Cytarabine and systemic chemotherapy with oral Capecitabine were initiated after whole brain radiation and Ommaya reservoir placement. Unfortunately, her course was complicated by chemical meningitis and hydrocephalus requiring shunt placement and discontinuation of chemotherapy. This was followed by recurrent seizures and encephalopathy, which were attributed to the progression of LMC. At this time, patients' family opted for comfort measures and she deceased almost nine months after her initial presentation [6].

Discussion

LMC is defined as cancer cell invasion of the leptomeninges (pia mater and arachnoid membrane). It is a rare but devastating neurological complication of cancer that is associated with a poor prognosis [2,7]. Although originally considered to be a rare complication, it has become more commonly diagnosed as cancer patients live longer and our diagnostic tools improve. It is estimated that LMC is diagnosed in 5-8% of patients with metastatic disease but it can be as high as 20% at autopsy [7-9]. Most LMC cases are reported in patients who have leukemia, breast cancer, lymphoma, lung cancer or melanoma [3]. In contrast, LMC in gastric cancer patients is extremely rare with a prevalence of only 0.14%-0.24% [4,6].

A majority of patients with LMC present with headache (39-85%) or nausea and vomiting (25-58%). Other symptoms may include leg weakness, altered mental status, hearing loss, seizures and diplopia [4,10]. These symptoms are usually attributed to meningeal irritation, increased intracranial pressure, cerebral edema, direct invasion of brain parenchyma or direct invasion of cranial or spinal nerve roots.

Diagnosis of LMC can be difficult. Diagnostic evaluation usually starts with a Gadolinium-enhanced MRI which would show leptomeningeal enhancement [11]. Confirmation of the diagnosis is usually required by performing a single or multiple lumbar punctures. Ideally, CSF analysis would show high opening pressure, high protein, low glucose and positive cytology for malignant tumor cells [3,12,13].

Oh et al. [6] performed the largest retrospective study that included 54 patients who had LMC due to metastatic gastric cancer. According to this study, a majority of the patients had a diagnosis of gastric cancer prior to diagnosis of LMC. Additionally, hearing loss was reported in only two patients. Our case was unique in the way that the patient presented with a rare symptom (i.e., hearing loss) of a rare disease (i.e., Krukenberg tumor with LMC), with no known history of gastric cancer, that would have raised the suspicion of the diagnosis if it was present. This, unfortunately, was responsible for a misdiagnosis of bilateral acoustic neuroma, thereby leading to a delay in the diagnosis. Kim et al. [14] reported a similar case of LMC that presented with hearing loss and was initially misdiagnosed as bilateral vestibular Schwannoma. However, this case reported by Kim et al. [14] had a known diagnosis of gastric cancer two years prior to the onset of hearing loss.

Treatment of LMS includes a combination of intrathecal and systemic chemotherapy with or without radiation therapy [14,15]. Intrathecal chemotherapy is usually with either methotrexate or liposomal cytarabine. One study comparing the two drugs reported a significant delay in neurological progression and a non-significant increase in the median survival in the depot cytosine arabinoside liposomal injection arm [16]. However, another study reported no significant difference in the primary end point (progression-free survival) between the two drugs [17]. Our patient was initially treated with liposomal cytarabine, oral capecitabine and whole brain radiation. Unfortunately, her treatment was held due to a complication of chemical meningitis and delayed wound healing.

LMC is a serious complication of cancer and is associated with high rates of morbidity and mortality. The median overall survival in untreated patients is four to six weeks compared with two to four months in treated patients [18,19]. Good performance status, intrathecal chemotherapy and low CSF LDH concentration have been linked to better survival in univariate analysis. However, Intrathecal chemotherapy was the only independent predict factor for survival in multivariate analysis [20]. In patients with LMC due to metastatic gastric cancer, it is reported that cytological conversion was associated with longer duration of survival [4]. Our patient lived for nine months since the time she was diagnosed with LMC [21].

Conclusion

In conclusion, LMC may occur at any stage in the neoplastic disease, either as the presenting sign or as a late complication. The current case is unique not only because the patient presented at the ENT clinic with chief complaints of hearing impairment rather than neurological deficits such as headache, nausea, or seizure, but also because the initial MRI findings were suggestive of acoustic neuroma. Our case highlights the importance of the multidisciplinary disciplinary cancer care, and calls for the development of new diagnostic tools and treatment regimens for LMC.

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