CASE REPORT

Leptomeningeal carcinomatosis from oesophageal cancer, presenting as meningitis

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SUMMARY

A 47-year-old woman presented with headache, neck pain, dizziness, nausea and vomiting for 4–5 days. She also had a history of weight loss and difficulty in swallowing. On physical examination, she had nuchal rigidity with a positive Kernig's sign. Cerebrospinal fluid analysis revealed mild pleocytosis but some atypical cells were also noted. Cytopathological analysis of the atypical cells showed high nuclear/cytoplasmic ratios and eccentric nuclei with prominent nucleoli, consistent with malignancy. A CT scan of the head and neck showed multiple lytic lesions involving the left calvarium, and diffuse thickening and enhancement of meninges over the left cerebral area. Extensive osteolytic lesions were also noted on the vertebral bodies, pedicles and lamina, at multiple levels of the cervical spine. An endoscopy revealed a mass at the gastro-oesophageal junction, and biopsy confirmed moderately differentiated adenocarcinoma of the oesophagus. The patient was started on chemotherapy along with radiation therapy.

oesophageal reflux disease in the past. On presentation, she appeared to be a healthy woman with significant distress due to headache and neck pain. Her blood pressure was 114/78 mm Hg, heart rate 107 bpm, respiratory rate 18/min, temperature 98.6°F and oxygen saturation 96% on room air. On physical examination, she had difficulty in active and passive movements of her head and neck. She had nuchal rigidity and a positive Kernig's sign. She was mildly tachycardic with dry oral mucosa. An ophthalmoscopic examination did not reveal significant papilloedema. Other than that, her heart and lung examination was normal. Her abdomen was non-tender and non-distended, with normal bowel sound and no palpable organomegaly. Her neurological examination did not reveal any cranial nerve deficit, or motor or sensory impairment, however, the examination was not conclusive—she could follow verbal commands, but she could not communicate well due to pain and delirium. Her Glasgow Coma Score was 15/15. Her gait was not tested at the time of admission because of her distress.

BACKGROUND

Leptomeningeal carcinomatosis (LC), also termed neoplastic meningitis, is a serious complication of cancer that carries substantial rates of morbidity and mortality. Approximately 1%–8% of patients with cancer are diagnosed with LC. Further, it is present in 19% of those with cancer and seen as neurological signs and symptoms on autopsy, usually found in those with disseminated systemic disease. LC is present in patients with solid tumours (1%–5%), leukaemia (5%–15%) and primary brain tumours (1%–2%). In this report, we present a case of LC from oesophageal cancer, which is a rare cause of LC. We also briefly reviewed the published literature with similar presentations.

CASE PRESENTATION

A 47-year-old woman presented with severe headache and neck pain for nearly 1 week. At presentation, she was delirious and restless. Most of the history was obtained from her husband, as the patient could not clearly describe her problems due to her restlessness and altered mental status. She also developed occasional dizziness, nausea and a few episodes of vomiting over the past 4–5 days. She took Tylenol and ibuprofen at home for pain, without much benefit. She had no fever, no chills and no upper respiratory symptoms, and had not recently travelled. Her medical history was only significant for hypertension. She was a non-smoker. She had never had such symptoms or gastro-

INVESTIGATIONS

On history and physical examination, meningeal involvement was suspected. Although the patient was initially sent to the emergency department for a CT scan of the head, the scan was postponed because of failure of the patient, due to pain and restlessness, to stay still within the scanner. Since meningitis was a possible diagnosis and antibiotics were planned to be started, a bedside lumbar puncture was performed before antibiotic administration. After that, the patient was started on broad spectrum antibiotics with vancomycin, ceftriaxone and acyclovir along with steroids. The cerebrospinal fluid (CSF) analysis revealed 93 polymorphonuclear cells with lymphocytic predominance of 73%. There were some atypical cells noted although their identification and characterisation were not ascertained. The fluid was sent for cytopathological analysis. The CSF protein was mildly elevated but glucose was normal. Gram stain was negative as well as *Cryptococcus* and acid fast bacilli stains. PCR for herpes simplex virus was negative. On the second day, another attempt to conduct a CT scan of the head was postponed, again due to pain and agitation.

On the fourth day of hospitalisation, the cytopathological analysis of the atypical cells in CSF revealed high nuclear/cytoplasmic ratios and eccentric nuclei with prominent nucleoli, consistent with malignancy (figure 1). The patient was given a high

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Figure 1 Cell block cytology from CSF revealed high nuclear/cytoplasmic ratios and eccentric nuclei with prominent nucleoli, consistent with malignancy. CSF, cerebrospinal fluid.

dose of narcotic analgaesic, and a CT scan of the head and neck was subsequently performed, showing multiple lytic lesions involving the skull, with the left side of the calvarium being the major area to be involved. There was diffuse thickening and enhancement of meninges over the left cerebral area (figure 2). Extensive osteolytic lesions were also noted on the vertebral bodies, pedicles and lamina at multiple levels of the cervical spine (figure 3). Since leptomeningeal metastasis was confirmed, the patient and her husband were once again asked about other symptoms and clinical conditions that might have been missed during the initial assessment. The husband admitted that, for the past few months, his wife was having difficulty in swallowing, which was progressively worsening, and the problem was more

Figure 2 CT scan of the head with contrast showing diffuse enhancement and thickening of the meninges over the left cerebral area.

with taking solids than with liquids. She also had unintentional weight loss of approximately 12–14 lb during this period. Considering her history of dysphagia, an endoscopy was performed on the day 7 of hospitalisation, which showed a mass at the gastro-oesophageal junction. The biopsy revealed moderately differentiated adenocarcinoma of the oesophagus (figure 4). A CT scan of the chest, abdomen and pelvis revealed no obvious metastasis elsewhere.

TREATMENT

The patient was referred to the oncology service. Since there was leptomeningeal metastasis at the time of diagnosis, the primary disease was determined to be unresectable. The patient was started on dexamethasone. Concurrent chemoradiation was planned as palliative therapy. A port-a-cath was placed on the right upper chest wall. The patient was started on external beam radiation therapy. Each treatment dose was 8 Gy. She took four treatments of radiation therapy initially, after which it was interrupted due to decline in her health and severe pain. She was admitted back to the hospital. The oncology team saw her in the hospital during the admission and decided to start the first cycle of chemotherapy with cisplatin and 5-fluorouracil. Opioid analgaesics and high-dose steroids were continued as well. After completion of the first cycle of chemotherapy, her overall condition deteriorated further and she became septic. Her blood culture grew methicillin sensitive *Staphylococcus aureus* on three different sets. It was suspected that her port-a-cath had become infected, so it was removed. Despite ongoing antibiotic treatment with vancomycin, her fever persisted and the leucocytosis was worsening. A transthoracic echocardiogram was performed, which did not reveal any vegetation in the heart and transoesophageal echocardiogram could not be carried out due to the patient's cervical metastasis and pain. The antibiotic was switched to nafcillin. Despite all efforts, the patient's general

Figure 3 CT scan of the neck showing extensive osteolytic lesions involving multiple cervical vertebral bodies.

Figure 4 Biopsy of the oesophageal mass showing moderately differentiated adenocarcinoma (low power).

condition did not improve. Her husband and other family members decided to adopt comfort measures for her. The hospice team was called and the patient was transferred to an in-patient hospice unit for comfort measures only. The patient expired after 5 weeks of initial presentation.

DISCUSSION

Oesophageal cancer is an uncommon clinical encounter. The number of cases of oesophageal cancer was 4.4/100 000 men and women per year in USA, based on cases reported between 2007 and 2011.¹ It is more common in men than in women, and is associated with old age, heavy alcohol and tobacco use. Oesophageal cancer is the 10th leading cause of cancer death in the USA.¹ The spread of oesophageal cancer to the leptomeninges is extremely rare. In LC, a solid tumour diffusely spreads to the leptomeninges. It may spread through a direct invasion from an adjacent tumour to the subarachnoid space or through a vascular and lymphatic channel. After initial invasion, the tumour spreads throughout the neuroaxis by the flow of the CSF.

The solid tumours known to cause LC are breast cancer, lung cancer, primary brain tumours, melanoma and non-Hodgkin's lymphoma.² Oesophageal cancer predominantly metastasises to the lymph nodes, liver, lungs, adrenal glands, stomach, kidneys and bones.³

Although uncommon, LC may present with symptoms of meningism and multiple cranial neuropathies. It is usually due to infiltration of tumour cells into the subarachnoid space, with increased intracranial pressure and damage to the cranial and spinal nerve roots. The numbers of reported cases of LC originating from oesophageal cancer are few. A review of previously reported cases revealed that age ranges from 39 to 68 years (mean, 44.1 years), and most cases involve males. The commonest symptoms are headache, vertigo,³ hearing loss,⁴ focal neurological deficit, spinal haematoma,⁵ lumbago, dysuria,⁶ seizure, vision loss⁷ and vocal cord paralysis.⁸ Squamous cell type was the commonest histological variant in previous case reports, but a recent series of seven cases revealed predominance of adenocarcinoma (77%).⁹ There is only one report describing signet ring type cancer.⁴ In an article by Kizawa *et al*,¹⁰ the authors reported three cases of signet ring type gastric cancer that metastasised to leptomeninges.

Diagnosis is mainly based on imaging study (CT and MRI) and CSF examination, though in early spread, it may be difficult to find visible evidence. Contrast-enhanced MRI is preferred over CT scan, if available. It is important to supplement MRI

study with CSF analysis since either of them may be falsely negative.¹¹ Okumura *et al*¹² reported a case, diagnosed by qRT-PCR, of a carcinoembryonic antigen in CSF, which was confirmed by anticytokeratin antibody.

Unfortunately, therapeutic options remain limited. The median survival is only 4 weeks in patients with leptomeningeal metastasis from gastric cancer.¹³ Intrathecal chemotherapy along with radiation is preferable. High-dose steroids may help with symptomatic relief, but their effects are short lived.¹⁴ Although intrathecal chemotherapy is often used, the survival benefit is questionable.

Learning points

- ▶ Leptomeningeal carcinomatosis may present with symptoms and signs of meningitis.
- ▶ Although not very common, oesophageal cancer may metastasise to leptomeninges, such as breast cancer, lung cancer, primary brain tumours, melanoma and non-Hodgkin's lymphoma, which more commonly metastasise to meninges.
- ▶ Contrast enhanced MRI or CT scan along with cytopathological analysis of cerebrospinal fluid is helpful for diagnosis.
- ▶ Chemotherapy, radiation therapy and steroids are the mainstays of treatment. The prognosis is very poor.

Competing interests None declared.

Patient consent Obtained.

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REFERENCES

- 1 Howlader N, Noone AM, Krapcho M, *et al*. *SEER Cancer Statistics Review, 1975–2011*. National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2011/ based on November 2013 SEER data submission, posted to the SEER web site, April 2014.
- 2 Imauchi Y, Kaga K, Nibu K, *et al*. Metastasis of cervical esophageal carcinoma to the temporal bone- a study of the temporal bone histology. *Auris Nasus Larynx* 2001;28:169–72.
- 3 Anderson LL, Lad TE. Autopsy findings in squamous-cell carcinoma of the esophagus. *Cancer* 1982;50:1587–90.
- 4 Ikuta T, Tetsuro Y, Shugo A, *et al*. A case report of esophageal carcinoma metastasis to meninges. *Gastroenterol Endosc* 2000;42:1053–7.
- 5 Wagemakers M, Verhagen W, Van de Borne B, *et al*. Bilateral profound hearing loss due to meningeal carcinomatosis. *J Clin Neurosci* 2005;12:315–18.
- 6 Ellis MJ, McDonald PJ. Acute epidural hematoma secondary to skull metastasis from esophageal carcinoma. *Can J Neurol Sci* 2007;34:491–3.
- 7 Watanabi M, Tanaka R, Takeda N. Correlation of MRI and clinical features in meningeal carcinomatosis. *Neuroradiology* 1993;35:512–15.
- 8 Akhavan A, Navabii H. Leptomeningeal metastasis from squamous cell carcinoma of oesophagus with unusual presentation. *BMJ Case Rep* 2012;2012:pii: bcr0220125846.
- 9 Teare JP, Whitehead M, Rake MO, *et al*. Rapid onset of blindness due to meningeal carcinomatosis from an oesophageal adenocarcinoma. *Postgrad Med J* 1991;67:909–11.
- 10 Kizawa M, Mori N, Hashizume Y, *et al*. Pathological examination of spinal lesions in meningeal carcinomatosis. *Neuropathology* 2008;28:295–302.
- 11 Gomori JM, Heching N, Siegal T. Leptomeningeal metastases: evaluation by gadolinium enhanced spinal magnetic resonance imaging. *J Neurooncol* 1998;36:55–60.
- 12 Okumura H, Natsugoe S, Yokomura N, *et al*. A case of leptomeningeal carcinomatosis from esophageal basaloid carcinoma diagnosed by quantitative reverse transcription-polymerase chain reaction for carcinoembryonic antigen. *J Gastroenterol* 2005;40:87–93.
- 13 Lee JL, Kang YK, Kim TW, *et al*. Leptomeningeal carcinomatosis in gastric cancer. *J Neurooncol* 2004;66:167–74.
- 14 Lisenko Y, Kumar AJ, Yao J, *et al*. Leptomeningeal carcinomatosis originating from gastric cancer: report of eight cases and review of the literature. *Am J Clin Oncol* 2003;26:165–70.

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