

Leptomeningeal carcinomatosis secondary to gastroesophageal adenocarcinoma: A case report and review of the literature

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BACKGROUND: Leptomeningeal carcinomatosis (LC) is a rare metastatic complication of solid tumours. It has been mainly described in association with breast cancer, lung cancer and melanoma.

CASE PRESENTATION: A patient presenting with progressive solid food dysphagia with documented adenocarcinoma of the lower esophagus and gastroesophageal junction is reported. One month after the initial diagnosis, the patient developed gradual onset of increasing headache and progressive decrease in the level of consciousness. Computed tomography of the head showed evidence of meningeal enhancement, and cerebrospinal fluid examination showed the presence of adenocarcinoma cells, making the diagnosis of LC. The patient died one month after LC was diagnosed.

DISCUSSION: LC is a poor prognostic sign in solid organ malignancies. It usually presents with headache, altered level of consciousness and focal neurological deficits. Diagnosis is established by finding malignant cells in the cerebrospinal fluid and supported by marked meningeal enhancement on computed tomography of the brain. A review of the English literature found only three reported cases of LC secondary to esophageal malignancy.

CONCLUSION: A case of LC complicating esophageal and gastroesophageal junction malignancy is described. A high index of suspicion and early diagnosis may influence the poor outcome of these patients.

Key Words: *Esophageal cancer; Gastroesophageal junction cancer; Leptomeningeal carcinomatosis*

Carcinomatose des leptoméninges secondaire à un adénocarcinome gastro-oesophagien : exposé de cas et examen de la documentation

CONTEXTE : La carcinomatose des leptoméninges (CL) est une complication métastatique rare des tumeurs solides. Elle est le plus souvent associée au cancer du sein, au cancer du poumon ou à un mélanome.

EXPOSÉ DE CAS : Voici le cas d'un patient qui consulte pour une dysphagie progressive aux solides et chez qui est diagnostiqué un adénocarcinome du bas œsophage et de la jonction gastro-oesophagienne. Un mois après la pose du diagnostic, le patient commence à éprouver des céphalées et une altération de son état de conscience. Une tomodensitométrie (TDM) de la tête révèle une prise de contraste des méninges, et l'examen du liquide céphalo-rachidien montre la présence de cellules d'adénocarcinome, d'où établissement du diagnostic de CL. Le patient meurt un mois plus tard.

DISCUSSION : La CL est signe de mauvais présage dans les cas de tumeur maligne des organes pleins. Elle se manifeste généralement par des céphalées, une diminution de l'état de conscience et des troubles neurologiques en foyer. La présence de cellules malignes dans le liquide céphalo-rachidien et la prise marquée de contraste des méninges à la TDM signent le diagnostic. La documentation médicale en anglais ne fait état que de trois cas de CL secondaire à un cancer de l'œsophage.

CONCLUSION : L'article décrit un cas de CL compliquant un cancer de l'œsophage et de la jonction gastro-oesophagienne. Une forte présomption et un diagnostic précoce peuvent influencer sur le sombre pronostic de la maladie.

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Leptomeningeal carcinomatosis (LC), or carcinomatous meningitis, is defined as multifocal seeding of the leptomeninges by malignant cells originating from a solid tumour or lymphomatous and leukemic meningitis (1). Although it was thought initially to be rare, this serious complication of cancer is seen with increasing frequency. Autopsy studies reveal that 19% of cancer patients with neurological symptoms have evidence of meningeal involvement (2). In most large series, breast cancer accounts for 11% to 64% of patients, followed by lung cancer (14% to 29%) and melanoma (6% to 18%) (3).

We describe a rare case of LC secondary to adenocarcinoma of the esophagus and gastroesophageal junction, without apparent central nervous system metastases.

CASE PRESENTATION

A 50-year-old, male construction worker presented with a two-month history of progressive solid food dysphagia accompanied by a 3 kg weight loss. He had no history of gastroesophageal reflux disease, caustic ingestion or scleroderma. He was a cigarette smoker of half a pack per day for at least 30 years and had been drinking one to two alcoholic drinks per day, but had stopped drinking for five years. He was otherwise healthy. The family history was positive for oropharyngeal cancer in his father.

On examination, his weight was 65 kg and height was 168 cm. His general physical examination including his abdominal examination was normal. He had no clubbing, lymphadenopathy or jaundice.

An upper gastrointestinal series showed evidence of a fixed irregular narrowing of the distal esophagus.

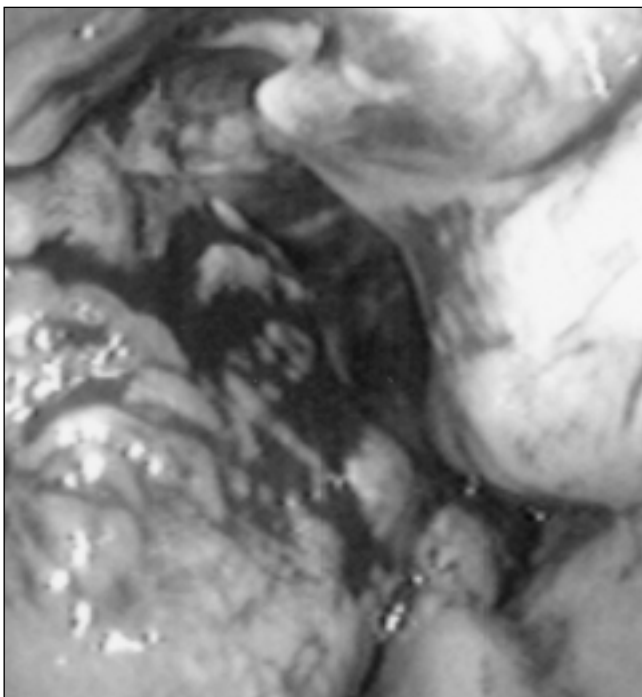


Figure 1) Endoscopic view of the lower esophagus and the gastroesophageal junction showing the cancer

Subsequently, upper gastrointestinal endoscopy was performed, which confirmed the presence of an ulcerated, stenotic mass lesion in the distal esophagus starting at 34 to 40 cm from the incisors (Figure 1). The stomach appeared to be normal. On retroflexed views of the gastroesophageal junction, the top of the gastric folds appeared to be spared, although the gastroesophageal junction was involved. Biopsies of the lesion revealed a moderately differentiated invasive adenocarcinoma.

Computed tomography (CT) demonstrated an area of severe circumferential thickening involving the distal 6 cm of the esophagus, extending to the gastroesophageal junction (Figure 2). No regional lymphadenopathy was noted. The lungs and liver were clear of metastases. Endoscopic ultrasound of the tumour confirmed the extension of the mass beyond the muscularis mucosa margin at approximately 40 cm. This was consistent with a stage T3N0.

Preoperative chemotherapy and radiotherapy were planned after consultation with an oncologist and esophageal surgeon.

The patient's dysphagia progressed rapidly. He was admitted to the hospital because of marked difficulty swallowing liquids and solids, which resulted in volume depletion and malnutrition. At that time he complained of extreme fatigue and a new symptom of mild occipital headache. There was no associated nausea, vomiting or visual disturbances. His level of consciousness was not affected and the neurological examination was normal. He had lost another 5 kg since presentation. His complete blood count, serum electrolytes, and calcium and magnesium levels were all normal. His albumin was low at 32 g/L. An enteral feeding tube was placed with radiological guidance. Arrangements were made for home enteral nutrition. Eight days after the feeding tube was inserted, the patient started to show signs of confusion and fluctuating levels of

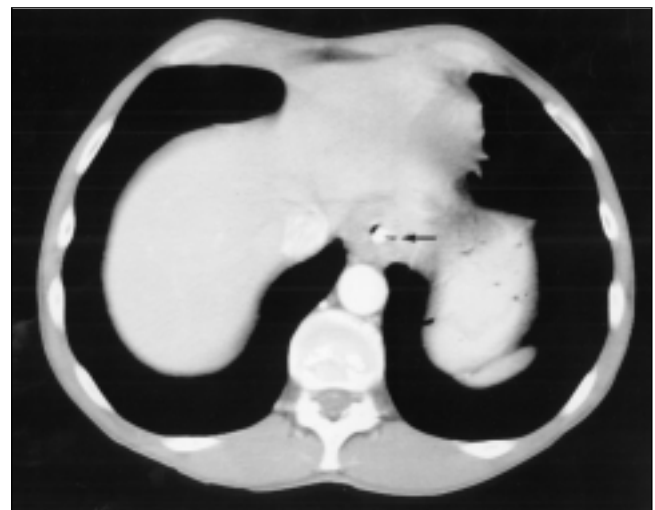


Figure 2) Computed tomography of the chest showing circumferential thickening of the lower esophagus and the gastroesophageal junction (arrow)

consciousness. His Glasgow coma scale was fluctuating during the day from normal down to approximately 10. His level of consciousness continued to deteriorate significantly over the next three days and he developed neck stiffness. He was placed on antibiotics in the form of ceftriaxone 2 g intravenously daily and a contrast head CT was obtained. This showed evidence of very prominent nodular enhancement involving the meninges overlying the cerebral hemispheres adjacent to the sagittal sinus and along the tentorium cerebelli (Figure 3). A lumbar puncture was performed. The white blood cell count was $35 \times 10^6/L$ (8% polymorphonucleocytes, 84% lymphocytes, 8% monocytes), red blood cell count was $2 \times 10^6/L$, glucose was 2.4 mmol/L (2.2 to 3.9 mmol/L) and protein was 1.35 g/L (0.15 to 0.45 g/L). Gram stain and culture were negative. Microscopic examination showed evidence of degenerate atypical cells with features of metastatic adenocarcinoma, confirming the radiological diagnosis of LC. Following oncological and neurological consultations, it was thought that there was no role for chemotherapy or radiotherapy, given the patient's clinical status and the level of consciousness, which had deteriorated further. Palliative care was started. Corticosteroids were given (dexamethasone [Decadron Phosphate Injection, Merck Frosst, Kirkland, Quebec] 4 mg every 8 h). The patient's level of consciousness continued to deteriorate. The patient died shortly thereafter, only two months after the time of his cancer diagnosis and five months after the onset of symptoms.

DISCUSSION

LC is a rare complication of metastatic cancer. It has been reported most commonly in adenocarcinomas of solid organs (4). Approximately 5% of all patients with breast cancer (5), 9% to 25% of patients with small cell lung cancer (6) and 23% of patients with melanoma (7) will develop LC. Of tumours from the gastrointestinal tract, it has been described rarely with metastatic adenocarcinoma of the stomach, a complication of this cancer that is thought to be rare (8). It has also been described with malignancies of the gallbladder (9) and cholangiocarcinoma (10). The most common presenting features of LC are headache, changes in mental status, cranial nerve palsies and neck stiffness. These symptoms are thought to result from either obstruction of normal cerebrospinal fluid (CSF) flow by focal tumour deposits, local tumour infiltration in the brain or spinal cord, or alteration in the metabolism of the underlying nervous system.

The mechanism of dissemination of the primary tumour to the leptomeninges is not clear. Multiple possible routes have been suggested, including direct invasion through the choroidal plexus (11) or leptomeningeal vessels (12), to indirect invasion through nerve roots (13), or retrograde dissemination along perineural lymphatics and sheaths (14). The pattern of meningeal involvement can be focal or diffuse (15).

The diagnosis of LC requires a high index of suspicion. CSF examination is the most valuable test. It should be performed in any patient with unexplained altered neurologi-



Figure 3) *Computed tomogram of the brain showing prominent nodular enhancement of the meninges*

cal status or focal neurological changes. Finding carcinoma cells in the CSF is diagnostic. Other common findings are increased opening pressure, pleocytosis and a modest elevation in the CSF protein (16). CSF may be normal in 5% of patients. An elevated CSF carcinoembryonic antigen may also be useful (17). Contrast enhanced CT of the brain or magnetic resonance imaging are positive in approximately 50% of patients. The most common radiological findings are contrast enhancement of the basilar cisterns, cortical convexities or hydrocephalus without an identifiable mass lesion. These findings are better seen with contrast enhancement.

The prognosis of patients with LC is very poor. This is largely due to the poor prognosis associated with the primary lesion and partially because of difficulties with penetration of the blood brain barrier by available chemotherapy. Estimated median survival is four to six weeks without treatment (16).

Early recognition and treatment of LC will not reverse fixed neurological deficits, but may improve general neurological status and prolong survival. Although not shown in randomized and prospective studies, it has been suggested that all patients with overt LC should be offered treatment except those patients with widespread and uncontrolled systemic neoplasia (18).

Standard therapy for LC is debatable. The three important components that are often used are: radiation therapy to the

TABLE 1
Review of the published cases of Leptomeningeal carcinomatosis (LC) from esophageal cancer compared with the present case

	Case 1*	Case 2*	Case 3*	Present patient
Age (years)	51	49	68	50
Sex	Female	Male	Male	Male
Type of cancer	Adenocarcinoma	Adenocarcinoma	Squamous cell carcinoma	Adenocarcinoma
Location in esophagus	Not clear	Lower third	Middle third	Lower third plus GE junction
CNS presentation	Vomiting, decreased LOC, hypertension	Headache, decreased LOC, rapid onset of blindness	Sudden bilateral hearing loss	Headache, decreased LOC
Time from diagnosis to CNS symptoms	6 months	4 months	Diagnosed at autopsy	3 months
CSF	Low glucose, high protein, malignant cells	Normal, no cytology		Normal biochemistry, 35 WBC, cancer cells
Brain CT	Enhancement in caudate nucleus	Normal	Thickening of meninges	Thickening of meninges
Treatment	Steroids, antihypertensives	Symptomatic	Intrathecal MTX and cis-platinum	Palliation plus steroids
Outcome	Died within 5 days of diagnosis	Died within 1 week of diagnosis	Died within 18 days of diagnosis	Died within 20 days of diagnosis
Autopsy	Confirmed LC	Confirmed LC	Confirmed LC	Not done

*Data from reference 28. CNS Central nervous system; CSF Cerebrospinal fluid; CT Computed tomography; GE Gastroesophageal; LOC Level of consciousness; MTX Methotrexate; WBC White blood cell count

affected sites (in an attempt to palliate symptoms), intrathecal chemotherapy and optimal therapy of the primary malignancy. Of the intrathecal agents, methotrexate (Methotrexate, Faulding, Kirkland, Quebec) has been the drug most commonly used. If methotrexate is combined with radiation, 50% of patients may improve initially and the median survival can be prolonged (19). Thiotepea has also been shown to be effective (20). Cytosine arabinoside has also been used mainly in leukemic and lymphomatous meningitis.

Generally, distant metastasis of esophageal cancer is rare, and metastasis to the central nervous system is unusual (21). Metastasis of esophageal cancer to the brain has been reported in at least 15 case reports (22,23). Central nervous system (CNS) involvement has been reported as a presenting feature (24), as isolated metastasis to the pineal region (25), as a second primary (26) and as a paraneoplastic syndrome in the form of cerebellar degeneration (27).

In a review of 334 esophagectomies performed in the authors' centre and 293 additional cases from surgical pathology files, Gabrielsen et al (28) found brain metastases in about 3.6% of cases. There was an increased tendency of CNS involvement, with large primary neoplasm, adenocarcinoma of the gastroesophageal junction, or findings of local invasion and lymph node metastases.

In terms of isolated cases of metastasis to the leptomeninges without apparent metastasis in the brain, we found only three case reports published in the English literature. A summary of the key features and comparison of these cases to our case is provided in Table 1.

In the present patient, the deterioration of the level of consciousness was sudden and rapidly progressive. There

was no evidence of any apparent metastases on the initial CT of the patient's chest and abdomen, and no apparent CNS metastases on the CT of the head. In consultation with the oncologist, it was decided not to offer the patient chemotherapy or radiotherapy because of his advanced neurological impairment and because of the relative poor prognosis of his primary tumour. The role of steroids in this case is not proven, especially in the absence of hydrocephalus, but we elected to try it in an attempt to decrease cerebral edema and provide some palliation.

CONCLUSIONS

The fourth case in the English literature of LC in a patient with esophageal and gastroesophageal junction carcinoma has been described. In patients with known esophageal cancer who present with a change in mental status or severe headache, a lumbar puncture should be done early in addition to a contrast enhanced CT of the head to detect LC.

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