Case report

Palliative approach to leptomeningeal carcinomatosis in oesophagogastric junction cancer

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SUMMARY

Leptomeningeal carcinomatosis (LC) is rare in solid tumours, particularly in gastrointestinal cancers. While other treatment strategies remain undefined, inclusion of palliative care is essential due to its very poor prognosis and variable manifestations. We report a case of oesophagogastric junction adenocarcinoma, previously submitted to surgery and chemotherapy, diagnosed with LC and followed in a palliative care unit. Treatment was comanaged with the oncology team and a palliative approach was decided. In this report, we review the literature and evaluate treatment options, with focus on the importance of palliative care and its potential benefits in patients diagnosed with this rare entity.

BACKGROUND

Gastric cancer (GC) and esophageal cancer (EC) present high incidence and mortality rates.^{1,2} Leptomeningeal carcinomatosis (LC) is rare and usually occurs in melanoma, lung and breast cancers.^{3,4} It is very rare in other solid tumours and comprises a poor prognosis.¹ Performance status (PS), age and presentation impact prognosis and treatment choice.⁵ Therefore, treatment remains challenging and palliative care is essential.³ Chemotherapy (ChT) and radiotherapy (RT) may be considered, but randomised trials and survival benefits are limited.^{5,6}

Although LC is rare, this case is important to understand the differences between available strategies and to support the palliative approach, with benefits for patients, both physical and psychosocial. As there are few publications on the subject, this report can shed some clarity for healthcare providers confronting similar situations.

CASE PRESENTATION

We report the case of a 51-year-old man, diagnosed with adenocarcinoma of the oesophagogastric junction, intestinal type, T1N0M0, submitted to esophagectomy, with free margins and 25 negative nodes.

After 1 year, routine CT scan identified subcentimetric lymph nodes (para-esophageal, supraclavicular, retrocrural and retroperitoneal), metabolically evident in positron emission tomography (PET). Cytology confirmed recurrence.

After 6 cycles of ChT (docetaxel 75 mg/m² day 1, cisplatin 25 mg/m² 1–3 and 5-fluorouracil 750 mg/m² 1–3), PET reported no abnormal metabolic activity.

After 18 months, he presented sudden hypoaesthesia, nausea and loss of balance. MRI showed an expansive lesion in the left cerebellum. Craniotomy with total removal of the tumour and ventriculoperitoneal shunting were performed, with confirmation of metastatic disease and was followed by stereotactic RT. Cerebrospinal fluid (CSF) did not present neoplastic cells.

At discharge, the patient presented loss of strength in inferior limbs, loss of balance and dysphagia. Consequently, he was admitted to our palliative care unit for symptom control.

Due to worsening of symptoms, particularly strength on lower limbs, MRI was repeated, reporting multiple nodular lesions in the subarachnoid space along the cerebellum, medulla and thecal sac, compatible with LC.

After multidisciplinary discussion, decision was that ChT or RT were not likely to show clinical benefit and had an elevated probability of toxicity, not being considered as options. While patient's PS (ECOG3) was poor for systemic ChT, intrathecal (IT) ChT was not indicated in multiple nodular lesions from a solid tumour and was considered to have low probability of survival benefit with high toxicity. Considering previous RT and extension of disease with need for high doses and target volume, RT was also considered technically impractical and with unfavourable safety profile. Hence, comfort was established as the main goal of care and lumbar puncture was not repeated for diagnosis confirmation, as it would not impact treatment strategy.

OUTCOME AND FOLLOW-UP

After initial worsening of strength in lower limbs, weakness and dysphagia, steroid doses were optimised and clinical stabilisation was achieved within 1 week. Symptomatic treatment focused on pain relief, anxiety control and physical rehabilitation.

During admission, frequent communication with the patient and family was ensued, guaranteeing knowledge about the situation, adaptation of our approach to patient's concerns, expectations, and desires and gradual reduction of anxiety with acceptance of patient's advanced condition.

He was discharged after 15 days, maintaining weakness in inferior limbs but showing satisfactory control of anxiety, pain and insomnia.

He stayed 21 days with good symptomatic control at home with support of his primary caregiver, his wife, and with one presential and one telephonic evaluation. He was then readmitted due to

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decreasing oral intake, increasing somnolence and incapability of the caregiver to provide the needed support.

The patient died after 4 days, 6 weeks after initial admission in our unit.

DISCUSSION

GC and EC have high incidence and mortality, representing the fifth and seventh most common cancers and the third and fifth causes of cancer-related deaths worldwide, respectively.^{1 2} Common metastatic sites are liver and peritoneum.¹ However, due to increased survival with new treatments, LC incidence is rising.^{3 7}

LC is rare, with an incidence of 3%–8%, higher in leukaemia, lymphomas, melanoma, lung and breast cancers and up to 20% in autopsy series.^{3 4 8 9} In GC, LC is even more rare, with incidence of 0.06%.¹⁰ Most commonly presents in signet ring cell carcinoma, with multiple metastatic sites and 12 months after initial diagnosis.^{4 11–13}

Clinical manifestations vary and include headache, nausea, vomiting, altered mental status, seizures, weakness and cranial nerves deficits, making differential diagnosis complicated.^{3 8}

Diagnosis is challenging, as imaging and CSF present low sensitivity.³ CT scans rarely show abnormal findings, while MRI sensitivity is around 65%–75%.^{9 13} LC diagnosis is probable with typical clinical and imaging signs, independently of the presence of tumour cells in CSF.^{5 14} MRI also has a role in the classification of LC which guides clinical decision-making.¹⁴

Definitive diagnosis includes the presence of malignant cells in CSF.⁸ However, sensitivity is 54%, increasing to 91% with repeated samples.³ Unspecific findings are elevated pressure, pleocytosis, decreased glucose, increased LDH and protein concentration.^{3 8} Since lumbar puncture is an invasive painful test with low sensitivity, clinicians should evaluate benefits and risks, including its implication on treatment strategy.

Prognosis is usually devastating, with median survival of 4 weeks in GC and 8 weeks in other solid tumours.^{1 3 8 9} Despite treatment, survival remains poor, averaging 3 to 6 months.⁶

PS at diagnosis of LC is the most important prognostic factor.⁵ While patients with good PS can endure aggressive treatments, including ChT, only 27% of patients with ECOG PS3–4 or Karnofsky score below 60% receive IT ChT and these present a survival around 2 months.^{7 14–16} Besides minor survival benefit, treatment also implies economic costs, invasive procedures and frequent admissions. Furthermore, guidelines for EC recommend best supportive care (BSC) for patients with stage IV disease and poor PS.¹⁵

Moreover, prolonged survival with treatment in LC is usually achieved in breast and lung cancer, while other solid cancers show very poor prognosis.^{5 7} Other poor prognostic factors include age over 50 years, major neurological deficits, high burden central nervous system (CNS) disease and high protein level in CSF.^{6 14 15} Guidelines propose BSC in these patients, except for chemosensitive tumours, such as lymphoma or specific cases where RT may help symptom control.¹⁵

Considering the dismal prognosis, primary goal of treatment should be quality of life and improvement of neurological deficits, while avoiding toxicities.^{6 14 17} Therefore, palliative care is essential.^{3 14} Symptomatic treatment may comprise steroids, anxiolytics, pain control, anticonvulsants and others.⁶

Besides palliative care, treatment strategies are RT, IT ChT and systemic ChT.^{6 7 14 17} Selection factors for these include good PS and younger age.⁶ However, treatments are based in uncontrolled case series and expert opinions, without 'gold standard'

guidelines due to lack of randomised clinical trials.^{5 7 17} Furthermore, studies include tumours with variable prognosis, mostly breast, lung or melanoma, with no specific data available for other tumours.^{5 17}

Focal RT may improve pain, bulky disease or obstructive lesions, and is commonly indicated in macroscopic disease.⁶ However, it did not show survival benefit in retrospective studies and may present CNS (somnolence, cognitive impairment, leukoencephalopathy) and haematologic toxicity, being reserved for circumscribed symptomatic nodular lesions.^{5 7 15} Cranio-spinal RT is avoided due to haematologic toxicity, mucositis and enteritis.^{6 14}

IT ChT, such as methotrexate, cytarabine and thioTEPA, is commonly used, although its efficacy and regimens are poorly understood due to limited randomised trials and absence of survival benefit against systemic ChT or BSC.^{5–7 17} IT has limited penetration into solid tumour lesions and is not indicated in nodular disease.^{5 14} Toxicities include mucositis and neurological complications (headache, meningitis, seizure and leukoencephalopathy).⁵

Since LC may disrupt the blood–brain barrier, systemic ChT could penetrate the CNS but few studies report survival benefit.^{5–7} It is indicated for palliative treatment in selected patients with good PS, particularly adenocarcinomas.¹⁸ However, lack of randomised trials and haematological toxicity are major limitations.^{5 14}

ChT has to be pondered considering that neurological symptoms and signs are usually fixed and rarely improved with these treatments.¹⁴

Surgical interventions include ventriculoperitoneal shunting for symptomatic hydrocephalus and intraventricular catheters for IT ChT.⁶

Treatment should be individualised and options should be discussed according to general and neurological status, primary tumour location and previous treatments.^{1 8 14} However, regardless of the strategy, patients have a poor prognosis.^{3 8}

Diagnostics that improve early detection and ChT tailored to the primary tumour, including newly developed molecular-targeted agents, will likely be significant advances in improving survival.^{6 7}

Learning points

- ▶ Leptomeningeal carcinomatosis (LC) in solid tumours is rare and comprises a poor prognosis.
- ▶ Chemotherapy (ChT) and radiotherapy (RT) lack evidence of survival benefit due to absence of randomised trials.
- ▶ Treatments present toxicities and should be reserved for patients with good performance status.
- ▶ Classification of nodular and linear LC helps to define indication for RT and intrathecal ChT.
- ▶ Therefore, palliative care presents as the essential pillar of treatment, providing symptom control, physical and psychosocial comfort and a dignifying end of life.

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