Caspian Journal of Internal Medicine 2025 (Spring); 16(2): 369-374
DOI: 10.22088/cjim.16.2.369

Case Report

A rare neurological odyssey: Gastric adenocarcinoma and leptomeningeal carcinomatosis – A Peruvian case study

Juan Eduardo Quiroz-Aldave (MD) [1]
María del Carmen Durand-Vásquez (MD) [2]
Ramiro Herrera Cabezas (MD) [3]
Rossana Jimenez Asto (MD) [4]
Carlos Cerrón Aguilar (MD) [3]
Julia Cristina Coronado-Arroyo (MD) [5]
Francisca Zavaleta-Gutiérrez (PhD) [6]
Luis Alberto Concepción-Urteaga (PhD) [7*]
Benjamín Alberto Leiva (MD) [8]
Marcio José Concepción-Zavaleta (MD) [9]

1. Division of Medicine, Hospital de Apoyo Chepén. Chepén, Perú
2. Division of Family Medicine, Hospital de Apoyo Chepén. Chepén, Perú
3. Division of Internal Medicine, Hospital Nacional Guillermo Almenara Irigoyen. Lima, Perú
4. School of Medicine "Manuel Huamán Guerrero", Universidad Ricardo Palma. Lima, Perú
5. Clínica Internacional, Lima, Perú
6. Division of Neonatology, Hospital Belén de Trujillo. Trujillo, Perú
7. Division of Internal Medicine, Hospital Regional Docente de Trujillo. Trujillo, Perú
8. Division of Surgical Oncology, Hospital Eleazar Guzmán Barrón. Nuevo Chimbote, Perú
9. Universidad Científica del Sur, Lima, Perú

*** Correspondence:**
Luis Alberto Concepción-Urteaga, Division of Internal Medicine, Hospital Regional Docente de Trujillo, Trujillo, Perú

E-mail: lconcepcion@unitru.edu.pe
Tel: +51 949 652 720

Received: 13 Dec 2023
Revised: 7 Feb 2024
Accepted: 4 March 2024
Published: 17 March 2025

Abstract

Background: Leptomeningeal carcinomatosis involves the diffuse infiltration of neoplastic cells in the central nervous system, affecting 5-8% of leukemia, breast, and lung cancer cases. Gastric cancer instances are rare, mostly in poorly differentiated adenocarcinomas. We report the first Peruvian case, featuring gastric adenocarcinoma.

Case Presentation: A 51-year-old woman presented with severe headache, vomiting, dizziness, blurred vision, tinnitus, bradyphrenia, reduced verbal fluency, sixth cranial nerve paresis, and non-reactive anisocoric pupils. Pleocytosis was found, with positive cytology for metastatic adenocarcinoma in cerebrospinal fluid, and a solid gastric mass defined as poorly differentiated adenocarcinoma. Due to her condition, the patient did not receive oncological management, evolving unfavorably and passing away twenty days later. Leptomeningeal carcinomatosis should be considered in patients with advanced cancer and meningeal symptoms. It is more predominant in women, with an average age of 53.84 years. Clinical presentation of leptomeningeal carcinomatosis varies, and diagnosis involves neuroimaging and cerebrospinal fluid cytology. Prognosis is unfavorable, often leading to fatality. Treatment protocols lack standardization, and personalized approaches, including targeted and systemic therapies, are explored for improved outcomes. The exceptional aspect of our case lies in the unique diagnosis of an abdominal tumor following the manifestation of neurological symptoms.

Conclusion: It is important to suspect this condition among the causes of meningitis, especially in the presence of an underlying malignancy.

Keywords: Meningeal carcinomatosis, Meningeal neoplasms, Cerebrospinal fluid, Gastric cancer, Neoplasms.

Citation:
Quiroz-Aldave JE, Durand-Vásquez MC, Herrera Cabezas R, et al. A rare neurological odyssey: Gastric adenocarcinoma and leptomeningeal carcinomatosis – A Peruvian case study. Caspian J Intern Med 2025; 16(2): 369-374.

Leptomeningeal carcinomatosis refers to the diffuse infiltration of neoplastic cells in the leptomeninges and the cerebrospinal fluid (1). This complication has been reported in 5-8% of cases of leukemia, breast cancer, and lung cancer (2, 3) and is rare in patients with gastric cancer, affecting 0.16-0.69% of them. In these cases, it primarily occurs in poorly differentiated adenocarcinomas and signet ring cell carcinomas (4–6).

The pathophysiological mechanisms remain incompletely understood, involving dissemination by contiguity, hematogenous spread, or through the fenestrated pores of the choroid plexus (1). Additionally, dissemination may occur retrogradely from peripheral nerves (2) or by lymphatic spread (7) (figure 1). The definitive diagnosis is usually established by finding neoplastic cells in the cerebrospinal fluid (CSF), in addition to hyperproteinorrachia and hypoglycorrhachia (8, 9). We present the first case of leptomeningeal carcinomatosis described in Peru, with the primary tumor being gastric adenocarcinoma.

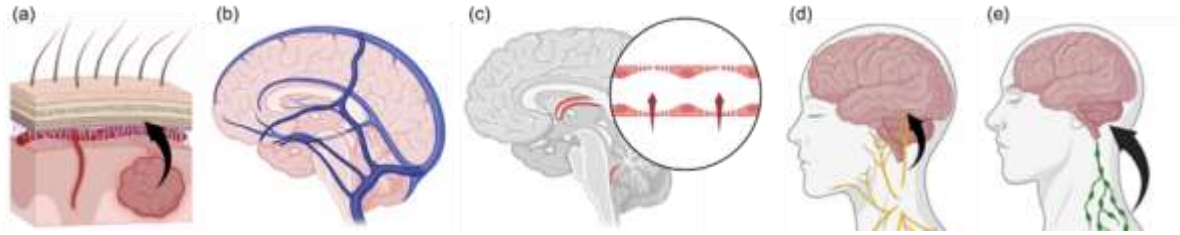

Figure 1. Proposed pathophysiologic mechanisms for the onset of leptomeningeal carcinomatosis. (a) Dissemination by contiguity, (b) hematogenous spread via venous vasculature, or (c) fenestrated pores of the choroid plexus, (d) retrograde spread from peripheral nerves, and (e) lymphatic spread.

Case Presentation

A 51-year-old woman from Lima, with no significant medical history, presented to the emergency department reporting a severe, persistent holocranial headache of sudden onset over the last 10 days, along with nausea, vomiting, dizziness, blurred vision, and tinnitus. In the clinical evaluation, she was awake but with bradypsychia, limited verbal fluency, bilateral sixth cranial nerve paresis more prominent on the left, and non-reactive anisocoric pupils, with a normal consensual reflex, and no motor deficit. Babinski sign, ataxia, dysmetria, sensory deficit, or meningeal signs were absent.

Initially, a non-contrast brain CT revealed no abnormalities. A lumbar puncture was performed, and cerebrospinal fluid (CSF) analysis showed adenosine deaminase: 12.65 IU/L, glucose: 62 mg/dL, protein: 35.8 mg/dL, acid-alcohol-resistant bacilli: negative, GeneXpert: negative, 1800 cells/µL (100% mononuclear), and India ink staining: negative. The patient had a torpid evolution, with persistent headache, altered sensorium, and a positive Brudzinski sign. Mannitol and broad-spectrum antibiotic therapy with meropenem and vancomycin were added due to suspected bacterial meningitis.

A repeat lumbar puncture for Papanicolaou staining in CSF resulted in metastatic adenocarcinoma. Primary tumor investigation with a whole abdominal CT scan revealed a solid, exophytic growth lesion depending on the gastric antrum wall toward the greater curvature (figure 2), along with multiple lytic and blastic lesions in the dorsal and lumbar vertebral bodies (figure 3). A bone scan showed multifocal metastatic bone involvement (figure 4). Tumor marker measurement found elevated CA19-9 (10115 U/mL) and normal levels of alpha-fetoprotein, CA125, and CA15-3. Subsequently, a biopsy of the abdominal mass was performed, yielding a histopathological diagnosis of poorly differentiated gastric adenocarcinoma, confirming the metastatic origin and the diagnosis of leptomeningeal infiltration. Due to the advanced stage of the disease, the patient did not receive chemotherapy or radiotherapy, evolving unfavorably and died 20 days after admission to the emergency department due to an overlaid bacterial infection.

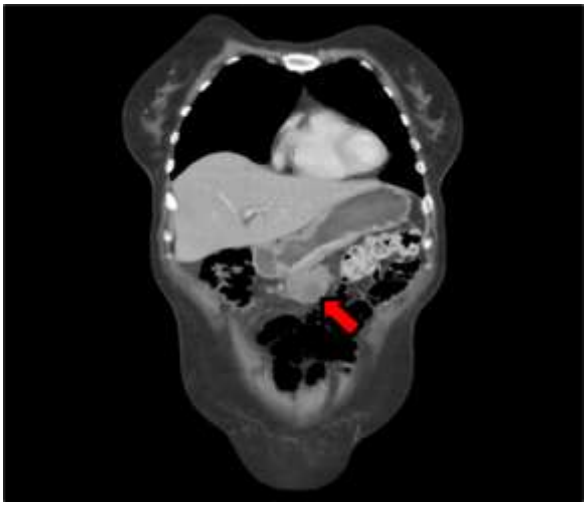

Figure 2. Coronal section of contrast-enhanced abdominal and pelvic computed tomography. A solid exophytic growth lesion is observed, arising from the wall of the gastric antrum toward the greater curvature (red arrow).

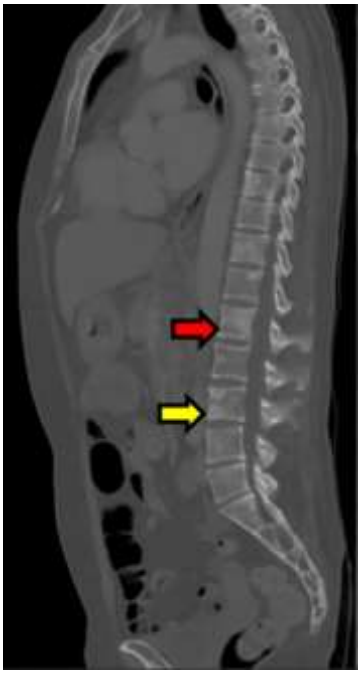

Figure 3. Sagittal section of the computed tomography of the thoracolumbar spine. Multiple lytic lesions (red arrow) and blastic lesions (yellow arrow) are observed in the dorsal and lumbar vertebral bodies.

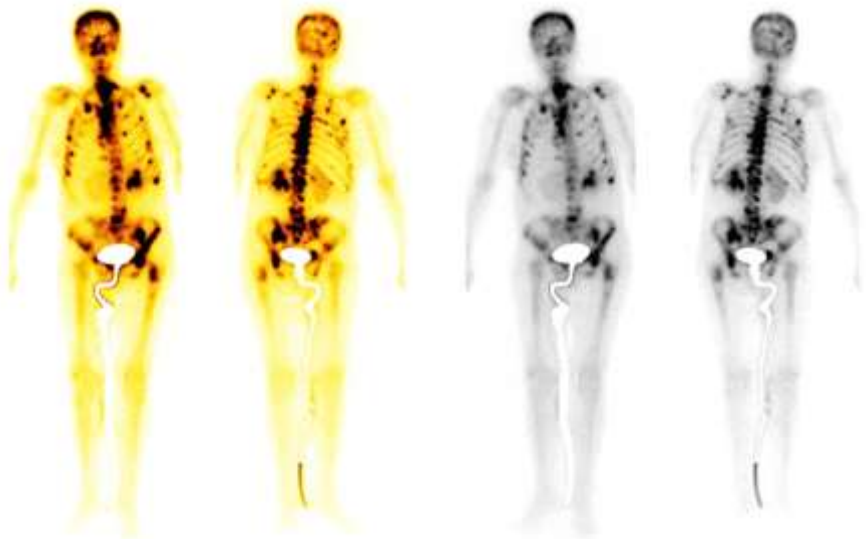

Figure 4. Bone scintigraphy with 99mTc. Note the multifocal metastatic bone involvement

Discussion

The clinical presentation of leptomeningeal carcinomatosis is highly varied, encompassing vague and nonspecific findings, particularly in the early stages of the disease, or neurological deficits in patients with known metastatic disease, raising suspicions of leptomeningeal carcinomatosis. It is rarely diagnosed in asymptomatic patients (1, 7). Typically, it involves meningeal and intracranial hypertension signs, such as headache, emetic syndrome, cognitive deficits, cranial nerve paralysis, auditory and visual disturbances, and seizures (7, 10). The headache is usually intense, lacks specific localization, and is predominantly in the morning, caused by the pressure of metastases on the meninges, stimulating the local sensory nerve (11). Rare cases of arginine vasopressin deficiency have been reported (12). Our patients presented with sudden, severe holocranial headache, nausea, vomiting, dizziness, blurred vision, and tinnitus. Cognitive deficits,

cranial nerve paralysis, and visual disturbances were also observed.

Various diseases can mimic leptomeningeal disease. Sarcoidosis, characterized by non-caseating sarcoid granulomas, may present with systemic symptoms, necessitating careful consideration of any organ involvement before neurological symptoms arise. Neuroborreliosis and giant cell arteritis have also been reported as rare mimics, with distinctive features and diagnostic challenges, requiring thorough evaluation and exclusion (1). Leptomeningeal carcinomatosis should be considered in patients with advanced cancer and meningeal signs (13). Typically, leptomeningeal carcinomatosis manifests when the primary tumor is already established, serving as an initial presentation in rare cases (13). Our patient is a unique case because the abdominal tumor was diagnosed during her hospitalization, with no prior gastrointestinal symptoms.

The reported cases in the literature are summarized in **Supplementary table 1**, indicating that the average age of patients with leptomeningeal carcinomatosis secondary to gastric cancer was 53.84 years (95% CI = 49.39–58.29), with a slight predominance in women (57%), similar to our patient. Concerning the histopathological diagnosis of gastric cancer, signet ring cell adenocarcinoma was reported in 49% of cases, poorly differentiated adenocarcinoma in 32%, and moderately differentiated adenocarcinoma in 5%. Our patient presented with the second most frequent histopathological form, poorly differentiated adenocarcinoma. Regarding the primary tumor location, 14% were reported as linitis plastica, 11% in the gastroesophageal junction, 8% in the pylorus, 5% in the lesser curvature, 5% in the greater curvature, and 5% in the antrum. In our patient, the tumor was located on the gastric antrum wall toward the greater curvature. The average time from the diagnosis of gastric cancer to the onset of neurological symptoms was 12.48 months (95% CI = 7.86–17.09). In 6 (16%) cases, both entities appeared simultaneously. The rarity of our patient lies in the diagnosis of an abdominal tumor after the onset of neurological symptoms. The main symptoms in the reported cases were headache (86%), cranial nerve abnormalities (49%), nausea (35%), and dizziness (35%). Eighty-four percent of patients with leptomeningeal carcinomatosis died. Confirmation of leptomeningeal carcinomatosis is achieved through neuroimaging studies and cerebrospinal fluid (CSF) cytology, with malignant cells expected to be found in the latter (14). Magnetic resonance imaging (MRI) with gadolinium contrast has a sensitivity of 70% and a specificity of 77% to 100%. It can reveal leptomeningeal enhancement, hydrocephalus, subependymal nodules or deposits, and irregular enhancement of nerve roots and extramedullary nodules (15). CSF cytology has a specificity of 95% for leptomeningeal carcinomatosis and is currently the gold standard for diagnosis (11). It is important to note that the cytochemical analysis of CSF resembles that found in bacterial meningitis, with increased opening pressure, pleocytosis, elevated protein levels, and decreased glucose levels (16). However, the identification of neoplastic cells in the CSF distinguishes it from infectious etiology (13, 17). In the context of high clinical suspicion and a negative cytological study, at least one additional cytological study should be performed, as the sensitivity of the first cytology is 50% to 60%, and it approaches 85% to 90% with the second collection (15). In this case, although no abnormalities were found on the non-contrast brain CT, we needed to perform two CSF tests to achieve the diagnosis; thus, an MRI was not required. The ThinPrep Plus Papanicolaou Stain Method, utilized in our patient, is the method of choice for analyzing CSF cytology in patients with leptomeningeal carcinomatosis due to its high sensitivity and specificity (18, 19). This method has been proven to be accurate in diagnosing leptomeningeal carcinomatosis in patients with malignant solid tumors. Additionally, it is effective for detecting primary tumor in patients with leptomeningeal metastasis of unknown primary origin (19).

The prognosis is unfavorable, even with chemotherapy and radiotherapy, with an overall life expectancy of approximately 3-6 months (20) and 3 to 4 weeks in cases secondary to adenocarcinomas of the digestive tract (21). Without treatment, life expectancy may be halved (22). This condition represents a significant oncological challenge as its incidence is increasing due to extended survival in certain types of cancer, where durable disease control is achieved outside the central nervous system. Additionally, it is particularly problematic due to the limited penetration of many antineoplastic drugs through the blood-brain barrier (23). Diagnosis and early treatment present the opportunity to control symptoms and prevent the onset of irreversible neurological deficits that significantly compromise the quality of life (10). According to the EANO – ESMO guidelines, the presence of tumor cells in the CSF is diagnostic for leptomeningeal metastasis from a solid tumor, as observed in the current case (18).

However, contemporary medical practice lacks standardized treatment protocols. Due to the limitation imposed by the blood-brain barrier, chemotherapy is often

used for palliative purposes with suboptimal results for patients (9). Better results are attainable through a personalized approach to treatment, emphasizing targeted and systemic therapies (22). Currently, ongoing investigations explore the efficacy of whole-brain radiation therapy in conjunction with intrathecal chemotherapy, with or without systemic chemotherapy (3). Concurrently, proton craniospinal irradiation emerges as a promising modality for managing leptomeningeal carcinomatosis from diverse histologic subtypes (22). We emphasize the importance of considering leptomeningeal carcinomatosis as a differential diagnosis among all causes of meningitis in patients presenting with neurological symptoms, particularly if they have an underlying malignancy. The cytological examination of cerebrospinal fluid is essential for the diagnosis.

Acknowledgments

None to declare.

Funding: None to declare.

Ethical approval: Authors commit to upholding the highest ethical standards in medical research. This commitment encompasses conducting research with honesty, accuracy, and objectivity, while avoiding fabrication, falsification, or plagiarism. Authors ensure proper authorship attribution and disclose any conflicts of interest. Informed consent was obtained, and confidentiality regarding personal information has been maintained.

Conflict of interest: The authors declare no competing financial interests.

Authors' contribution: JE Quiroz Aldave: conceptualization, methodology, investigation, writing – original draft, project administration. MC Durand-Vásquez: investigation, writing – original draft. R Herrera Cabezas: investigation, writing – original draft. R Jimenez Asto: investigation, writing – original draft. C Cerrón Aguilar: investigation, writing – original draft. JC Coronado-Arroyo: investigation, writing – original draft. F Zavaleta-Gutiérrez: investigation, writing – review & editing. LA Concepción-Urteaga: investigation, writing – review & editing. BA Leiva: investigation, writing – review & editing. MJ Concepción-Zavaleta: conceptualization, methodology, resources, investigation, writing – original draft, project administration.

References

1. Nguyen A, Nguyen A, Dada OT, et al. Leptomeningeal metastasis: A review of the pathophysiology, diagnostic methodology, and therapeutic landscape. Curr Oncol 2023; 30: 5906–31.
2. Rodríguez Mowbray JR, Macias Montero R, Gomez-Ulla Astray J. Carcinomatosis meníngea: distintos casos con los mismos resultados. Med Paliativa 2014; 21: 121–5. [in Spanish]
3. Liu Y. Leptomeningeal carcinomatosis from gastric cancer successfully treated by the intrathecal methotrexate plus temozolomide and simultaneous radiotherapy: Case report and literatures review. Cancer Biol Ther 2017; 18: 761–4.
4. Kim M. Intracranial involvement by metastatic advanced gastric carcinoma. J Neurooncol 1999; 43: 59–62.
5. Terasaki K, Mizuno C, Fujiishi S, et al. Garcin syndrome due to meningeal carcinomatosis from gastric cancer. Intern Med Tokyo Jpn 2021; 60: 855–8.
6. Kusumoto T, Kimura Y, Sugiyama M, et al. Leptomeningeal carcinomatosis originating from advanced gastric cancer--a report of three cases and review of the literatures. Fukuoka Igaku Zasshi Hukuoka Acta Medica 2013; 104: 456–63.
7. Mollica L, Leli C, Puglisi S, Sardi S, Sottotetti F. Leptomeningeal carcinomatosis and breast cancer: a systematic review of current evidence on diagnosis, treatment and prognosis. Drugs Context 2021; 10: 2021-6–6.
8. Yamada T, Furukawa K, Yokoi K, et al. Case of meningeal carcinomatosis with gastric cancer which manifested meningeal signs as the initial symptom; the palliative benefit of radiotherapy. J Nippon Med Sch Nippon Ika Daigaku Zasshi 2008; 75: 216–20.
9. Kim SJ, Kwon JT, Mun SK, Hong YH. Leptomeningeal carcinomatosis of gastric cancer misdiagnosed as vestibular schwannoma. J Korean Neurosurg Soc 2014; 56: 51–4.
10. Ajenjo González M, Cubelos Fernández N. Carcinomatous meningitis. J Negat No Posit Results 2019; 4: 436–53. Available from: https://revistas.proeditio.com/jonnpr/article/view/2931/html2931.
11. Chen G, Ma L, Xu M, et al. Meningeal carcinomatosis: three case-reports. World J Surg Oncol 2018; 16: 78.
12. Pan Z, Yang G, He H, et al. Leptomeningeal metastasis from solid tumors: clinical features and its diagnostic implication. Sci Rep 2018; 8: 10445.

13. Bastidas TÓ, Bravo HJ, Acosta MF, Linthon SA. Carcinomatosis meníngea, un desafío diagnóstico. Reporte de caso. Rev Fac Cienc Salud Univ Cauca 2018; 20: 46–9. [in Spanish]
14. Milburn-McNulty P, Michael B, Moxham N, Fletcher N, Crooks D. How to do it: How to get the most out of cerebrospinal fluid cytology. Pract Neurol 2012; 12: 241–3.
15. Batool A, Kasi A. Leptomeningeal Carcinomatosis. In: StatPearls. Treasure Island (FL): StatPearls Publishing 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK499862/. Accessed 27 Mar, 2023.
16. Park KK, Yang SI, Seo KW, Kim YO, Yoon KY. A case of metastatic leptomeningeal carcinomatosis from early gastric carcinoma. World J Surg Oncol 2012; 10: 74.
17. Ortapamuk H, Demir MK. Intracranial leptomeningeal carcinomatosis in three cases from breast cancer demonstrated on F-18 Fluorodeoxyglucose positron emission tomography/computerized tomography. Indian J Nucl Med 2017; 32: 16–8.
18. Le Rhun E, Weller M, Bent M van den, et al. Leptomeningeal metastasis from solid tumours: EANO–ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. ESMO Open 2023; 8: 101624.
19. Pan Z, Yang G, Wang Y, et al. Thinprep plus Papanicolaou stain method is more sensitive than cytospin-coupled Wright Giems stain method in cerebrospinal fluid cytology for diagnosis of leptomeningeal metastasis from solid tumors. PLoS One 2015; 10: e0122016.
20. Olmos-Jiménez R, Díaz-Carrasco MS, Cabañas-Perianes V, et al. Evaluación de la toxicidad tras la administración de quimioterapia triple intratecal estandarizada en pacientes onco-hematológicos adultos. Farm Hosp 2017; 41: 611–7.
21. Groves MD. New strategies in the management of leptomeningeal metastases. Arch Neurol 2010; 67: 305–12.
22. Marenco-Hillembrand L, Bamimore MA, Rosado-Philippi J, et al. The evolving landscape of leptomeningeal cancer from solid tumors: A systematic review of clinical trials. Cancers 2023; 15: 685.
23. Suki D, Khoury Abdulla R, Ding M, Khatua S, Sawaya R. Brain metastases in patients diagnosed with a solid primary cancer during childhood: experience from a single referral cancer center. J Neurosurg Pediatr 2014; 14: 372–85.