Cerebral infarctions caused by pulmonary vein metastasis from gastric cancer: A case report

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Abstract. Gastric cancer remains one of the leading causes of cancer-related mortality worldwide, particularly in East Asian countries, despite advances in systemic therapy and the development of novel targeted and immune-based treatments. Due to its aggressive biological behavior, gastric cancer frequently metastasizes to the liver, peritoneum, lymph nodes, lungs and bone. Although extremely rare, pulmonary vein metastasis is clinically significant as it can cause embolic events in vital organs, including multiple cerebral infarctions. The present report describes an extremely rare case of cerebral infarction secondary to pulmonary vein metastasis originating from a gastric adenocarcinoma. To the best of our knowledge, the current case is the first documented case of its kind.

Introduction

Gastric cancer has a relatively high prevalence, especially in East Asia, and it is one of the most common causes of cancer-related death worldwide. Despite many improvements in its diagnosis and treatment, the prognosis of gastric cancer remains poor, especially in its advanced stages. It exhibits several distinct metastatic patterns depending on the histological subtype, tumor location, and disease progression. The metastatic spread of the primary gastric cancer can occur through four pathways: peritoneal dissemination, hematogenous dissemination, lymphatic spread, and direct tumor invasion. Based on previous registration studies evaluating the hematogenous metastasis of gastric cancer, 17, 6, 5, and 1% of patients present with liver, lung, bone, and brain metastasis at the time of diagnosis, respectively (1). This report describes a very rare case of gastric cancer with metastasis to the pulmonary veins, which has not been reported previously. Tumor embolization of the pulmonary vein is a precarious condition because it can cause serious embolism if it migrates to the arteries.

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Case report

A 71-year-old male with a 20-year smoking history underwent laparoscopic distal gastrectomy, D1 lymph node dissection, and Billroth-I reconstruction for gastric cancer at a previous hospital in March 2021. The histological examinations revealed moderately differentiated tubular adenocarcinoma with No4d lymph node metastasis; pT1b(SM)N1M0 pStage1B (UICC TNM 8th edition). Seven months after the first surgery, partial hepatic resection was performed for a solitary S7 hepatic recurrence, followed by a 12-month course of postoperative chemotherapy with S-1 and docetaxel.

In December 2023, the patient presented with weakness and numbness of the right lower extremity and was admitted to our hospital. Non-contrast magnetic resonance imaging (MRI) of the brain demonstrated multiple small acute infarcts, characterized by diffusion restriction and low ADC values, located in the left cerebellar tonsil, right cerebellar hemisphere, and bilateral frontal watershed regions (Fig. 1A). Contrast-enhanced computed tomography (CT) of the chest revealed right-sided pleural effusion with no apparent lung metastatic nodules, but with a filling defect in the right inferior pulmonary vein (Fig. 1B). The vital signs upon admission were as follows: oxygen saturation, 99% on room air; blood pressure, 138/88 mmHg; heart rate, 61/min; and body temperature, 37.0˚C. Physical examination revealed no murmurs or abnormal sounds during respiration, and echocardiography showed no evidence of valvular disease or intracardiac thrombus. Positron

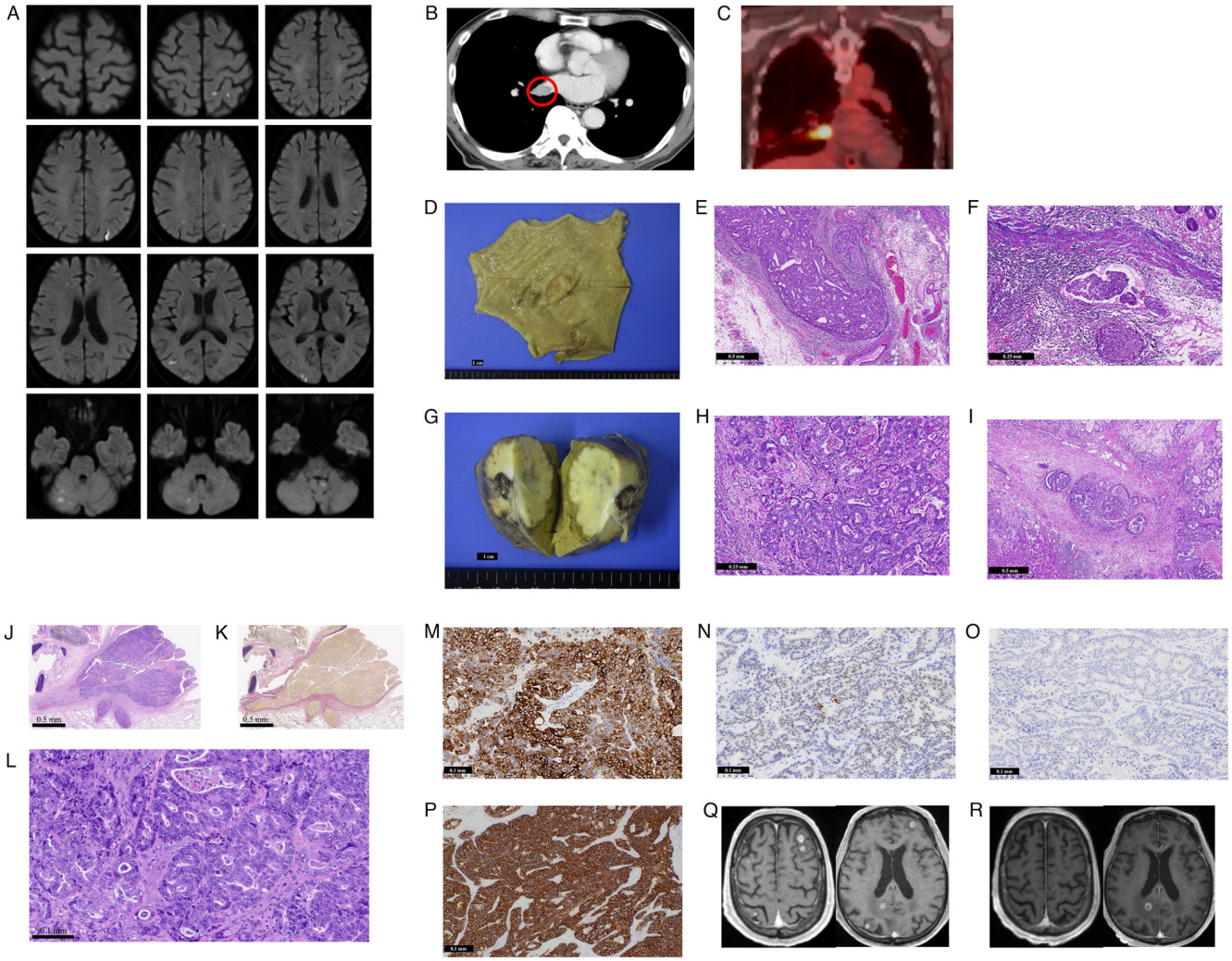

Figure 1. (A) Diffusion-weighted imaging of non-contrast brain MRI demonstrating multiple small acute infarcts characterized by diffusion restriction. Lesions were observed in the left cerebellar tonsil, right cerebellar hemisphere and bilateral frontal watershed regions. (B) Contrast-enhanced CT revealed a filling defect in the right inferior pulmonary vein (red circle) (C) Positron emission tomography/CT revealed abnormal uptake in the right inferior pulmonary vein with a maximum standardized uptake value of 13.0, as well as right-sided pleural effusion. (D) Gross image of the primary gastric carcinoma specimen after formalin fixation. Scale bar, 1 cm. (E) H&E-stained section of the primary gastric carcinoma demonstrating vascular invasion by adenocarcinoma. Scale bar, 0.5 mm. (F) H&E-stained section of the primary gastric carcinoma demonstrating lymphatic invasion by adenocarcinoma. Scale bar, 0.25 mm. (G) Gross image of the liver metastatic tumor after formalin fixation. Scale bar, 1 cm. (H) H&E-stained section of the liver metastatic tumor demonstrating adenocarcinoma with morphological features similar to those of the primary gastric carcinoma. Scale bar, 0.25 mm. (I) H&E-stained section of the liver metastatic tumor demonstrating vascular invasion by adenocarcinoma. Scale bar, 0.5 mm. (J) H&E-stained section of the tumor metastasized to the pulmonary vein. Scale bar, 0.5 mm. (K) Elastica van Gieson-stained section of the tumor metastasized to the pulmonary vein, demonstrating tumor invasion into the pulmonary vein. Scale bar, 0.5 mm. (L) H&E-stained section of the tumor metastasized to the pulmonary vein at a magnification of x100 (objective lens, x10; ocular lens, x10). The adenocarcinoma exhibited complex tubulopapillary structures with a stromal reaction. The tumor morphology was similar to that of the previously identified primary gastric carcinoma and liver metastasis. Scale bar, 0.1 mm. (M) Immunohistochemical staining of the pulmonary vein metastatic tumor showing positivity for cytokeratin 7. Scale bar, 0.1 mm. (N) Immunohistochemical staining of the pulmonary vein metastatic tumor showing partial positivity for caudal type homeobox 2. Scale bar, 0.1 mm. (O) Immunohistochemical staining of the pulmonary vein metastatic tumor showing negativity for cytokeratin 20. Scale bar, 0.1 mm. (P) Immunohistochemical staining of the pulmonary vein metastatic tumor showing strong positivity for HER2. Scale bar, 0.1 mm. Contrast-enhanced brain MRI performed in (Q) October 2024 and (R) March 2025. After initiating trastuzumab deruxtecan, a partial radiological response was observed, with some metastatic brain lesions disappearing on the follow-up MRI. CT, computed tomography; H&E, hematoxylin and eosin; MRI, magnetic resonance imaging.

emission tomography/CT demonstrated FDG accumulation [maximum standardized uptake value (SUVmax) 13.0] at the right inferior pulmonary vein (Fig. 1C). Based on these findings, the patient was suspected to have multiple cerebral tumor emboli, likely induced by pulmonary vein metastasis. The acute cerebral infarctions were managed with rehabilitation and aspirin therapy, and the patient's right lower extremity weakness and numbness had improved by two weeks after treatment initiation. A follow-up contrast-enhanced brain MRI revealed multiple enhancing lesions in the bilateral cerebellum and cerebrum, which were consistent with brain metastases. Stereotactic radiotherapy (35 Gy/5 fractions) was delivered to the 9 brain lesions. Subsequently, video-assisted thoracoscopic right lower lobectomy, pulmonary vein tumor resection, and left atrial repair were performed in February 2024. Pulmonary vein resection was done for diagnostic purposes, as well as to prevent any further cerebral infarctions caused by tumor emboli.

The resected specimen measured 16x12x7 cm. The pulmonary vein was dilated to 2.0 cm and filled with a grayish-white mass, which had similar histologic features as the previously resected gastric and hepatic tumors (Fig. 1D-L). Immunohistochemical staining was positive for CK7, partially positive for CDX2, and negative for CK20, confirming the diagnosis of pulmonary vein metastasis from gastric adenocarcinoma. Additionally, HER2 immunohistochemistry was strongly positive (IHC 3+) (Fig. 1M-P). Because the surgical margins of the pulmonary vein were positive, chemotherapy with S-1, oxaliplatin, and trastuzumab was subsequently initiated in March 2024. In August 2024, the patient developed new brain metastases, which were treated with additional stereotactic radiotherapy (SRT/SRS). In October 2024, the brain metastases further progressed, prompting a switch in the chemotherapy regimen to trastuzumab deruxtecan for its potential efficacy against brain metastases, resulting in partial regression of the brain lesions (Fig. 1Q and R). In June 2025, however, chemotherapy was discontinued due to a decline in the patient's performance status. As of July 2025, the patient remains alive under best supportive care.

Discussion

The most common metastatic sites of gastric cancer are the liver, peritoneum, lungs, and bones (1). Although several reports have described metastases to the pericardium and heart (2-4), pulmonary vein metastasis is extremely rare. The current literature describes pulmonary vein metastases from other malignancies such as hepatocellular carcinoma, chordoma, breast cancer, and melanoma (5-8), but no reports have described pulmonary vein metastasis from a gastric adenocarcinoma primary. Thus, this appears to be the first documented case of its kind.

In this case, the patient presented with acute right lower extremity weakness and numbness, and brain MRI revealed multiple infarcts involving the left cerebellar tonsil, right cerebellar hemisphere, and bilateral frontal watershed regions. Because the lesions were multiple and small, it was not possible to identify a definitive responsible focus that could clearly account for the patient's right lower extremity weakness and numbness. No notable cerebellar symptoms, such as ataxia or balance disturbance, were observed.

The distribution of infarcts across both supratentorial and infratentorial regions suggests that embolic material reached the brain via more than one arterial route. The coexistence of watershed infarcts in the frontal lobes and infarcts in the cerebellum indicates potential involvement of both the internal carotid and vertebrobasilar arterial systems. In this patient, it was not possible to definitively determine whether these multiple cerebral infarctions were caused by tumor emboli originating from the pulmonary vein, as thrombus retrieval was not performed. However, previous reports in other malignancies have described pulmonary vein tumor emboli as a cause of cerebral infarction (8). Therefore, in clinical situations where pulmonary vein metastasis is suspected, careful monitoring for cerebral embolic events is warranted.

For gastrointestinal cancers to metastasize to the pulmonary vein, the tumor cells must traverse the portal vein, pass through the right heart, and enter the pulmonary artery before finally reaching the pulmonary vein. Since gastric cancer cells are approximately 10 μm in diameter, it is unlikely that they can pass directly through the pulmonary capillaries, which typically have a smaller diameter. Additionally, there was no apparent pulmonary metastasis that could have trapped the tumor in the lungs in this patient, nor was there definitive evidence of the tumor invading the myocardium and pericardium. One hypothesis is that microscopic pulmonary artery-vein shunts could promote the migration of tumor cells into the pulmonary veins. However, Elastica van Gieson staining revealed tumor proliferation in the pulmonary veins and the stroma around the ruptured pulmonary veins, but there was no obvious pulmonary artery infiltration. Furthermore, a bubble test echocardiogram performed postoperatively revealed no macroscopic arteriovenous shunt.

Pulmonary vein metastasis can predispose patients to hematogenous brain metastases. In this case, nine metastatic lesions were identified bilaterally in the cerebrum and cerebellum. After multidisciplinary discussion, the patient underwent stereotactic radiotherapy and pulmonary vein tumor resection with left atrial repair, considering the possibility of further brain metastasis from the pulmonary vein, which could cause a decline in performance. By preventing appearance of new brain metastases in a short period of time, HER2-based chemotherapy could have been introduced, which could improve the chances of long-term survival (9,10).

This case highlights the importance of recognizing pulmonary vein metastasis as a potential source of tumor embolism and brain metastasis in gastric adenocarcinoma. Multimodal treatment with a combination of surgery, radiotherapy, and systemic therapy can help achieve long-term disease control even in such rare and challenging clinical situations.

This case was previously reported in part by the Department of Thoracic and Cardiovascular Surgery, focusing on the surgical technique (JTCVS Tech. 2025;29:103-105) (11). The present report offers a distinct perspective on the oncological and neurological aspects of the same case, including the clinical course, cerebral complications and systemic therapy, and does not overlap with the previous publication.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

NH and MT confirm the authenticity of all the raw data. NH conceived and designed the study. Acquisition and interpretation of data was performed by NH, YY, YK, RS, MO, SO,

HN, JT, RM, MHa, MHo, FO, AY and MT. Writing of the original draft was undertaken by NH, and writing, review and editing of the manuscript were carried out by NH and MT. All authors agree to be accountable for all aspects of the research in ensuring that the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for publication of this case report and the accompanying images. The patient was informed that all identifying information would be removed to ensure anonymity.

Competing interests

MT received honoraria from Chugai Pharmaceutical, AstraZeneca K.K., Bristol-Myers Squibb Company, Novartis Pharma K.K., and Ono Pharmaceutical. The other authors declare that they have no competing interests.

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