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Brain Metastasis as the Initial Presentation of Carcinoid Tumor: Case Report and Literature Review

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Abstract

Neuroendocrine neoplasms of the lung include neuroendocrine carcinomas and neuroendocrine tumors (NETs). NETs are also known as carcinoid tumors (CaTs), which are categorized as typical carcinoid and atypical carcinoid (AC). Pulmonary CaTs often metastasize to various sites, including regional lymph nodes, lungs, liver, and bone; however, metastasis to the brain is relatively rare. It is even rarer for patients with CaTs to present with signs of brain metastasis initially. We report the case of a 50-year-old female patient who initially presented with neurological symptoms and magnetic resonance imaging findings suggestive of multiple sclerosis. Despite initial treatment for multiple sclerosis, further evaluation uncovered a rare case of bronchopulmonary AC tumor metastasis to the brain. This case highlights the importance of considering metastatic disease in patients presenting with atypical neurological symptoms, especially when initial management fails to yield expected outcomes. Our literature review revealed 7 cases of CaTs initially presenting with brain metastases, with our patient being the youngest among all published cases.

Keywords

neuroendocrine neoplasms, carcinoid, multiple sclerosis, brain metastasis, radiotherapy

Introduction

Neuroendocrine neoplasms (NENs) are a heterogeneous group of lung neoplasms with varying morphological patterns, biological traits, and clinical manifestations. Based on the differentiation grade, neuroendocrine tumors (NETs) and neuroendocrine carcinomas (NECs) are 2 categories of NENs. In this context, NECs correspond to high-grade carcinomas and comprise small-cell lung cancer (SCLC) and large-cell neuroendocrine carcinoma (LCNEC). On the other hand, NETs, also called carcinoid tumors (CaTs), are low- and intermediate-grade tumors that are referred to as typical carcinoid (TC) and atypical carcinoid (AC), respectively. CaTs correspond to well-differentiated NENs.[1]

Pulmonary CaTs account for roughly 1% to 2% of all invasive lung malignancies, corresponding to approximately one-fourth to one-third of all well-differentiated NETs throughout the body. There are 0.2 to 2 instances per 100 000 people in the United States and Europe.[2] CaTs are relatively rare and are marked by slow growth and distinctive symptoms. Patients usually exhibit symptoms and indicators associated with either carcinoid syndrome or a localized disease. As the disease progresses, these tumors often metastasize to various sites, including regional lymph nodes, lungs, liver, and bone; however, metastases to the brain are relatively uncommon.[3,4]

The majority of patients with brain metastases have a single intraparenchymal brain metastasis, and the median time between the main diagnosis and the emergence of a brain metastasis is 16 months. The documented incidence of central nervous system (CNS) metastases is 1.5% to 5%.[5] It is uncommon for patients with CaTs first to have signs of brain metastasis.[4]

We reported a case of a 51-year-old female patient who presented with CNS symptoms and radiological findings

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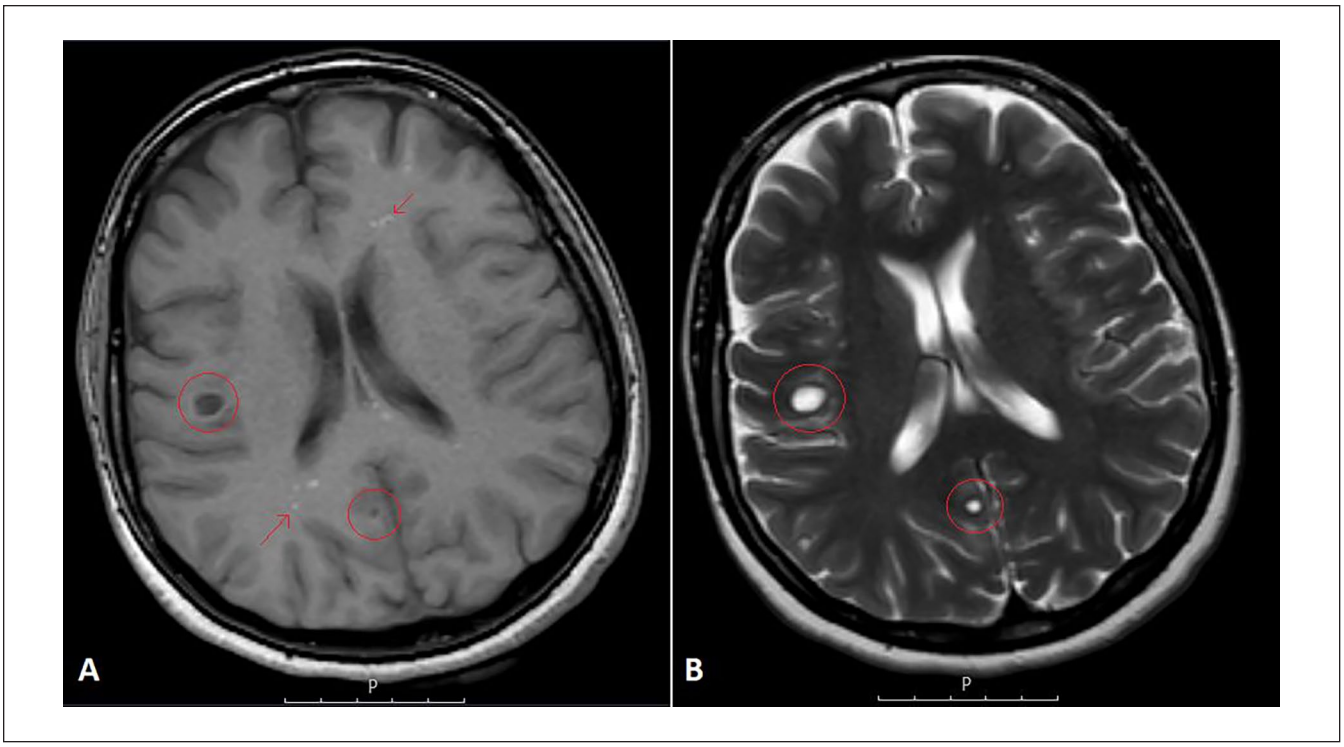

Figure 1. Selected axial cuts of the patient's brain MRI showing few well-defined rounded cystic lesions are noted with hypo-intense signal at T1W image (Circles; A) and hyper-intense signal at T2W image (Circles; B), in addition to multiple tiny foci of T1 hyper-intensities seen at the peri-ventricular white matter (arrows; A). MRI, magnetic resonance imaging.

resembling multiple sclerosis. Further investigation and worsening symptoms led to the diagnosis of a bronchopulmonary AC tumor metastasizing to the brain. To the best of our knowledge, the English literature has documented only 7 cases of CaTs initially presenting with brain metastases. The study attempts to shed light on this rare entity and emphasizes the significance of considering and ruling out atypical causes since they may lead to therapeutic delays.

Case Presentation

A 50-year-old female patient with a history of hypertension and paroxysmal atrial fibrillation presented with neck pain, dizziness, numbness, and paresthesia in her upper limbs for 2 months. Initial investigations, including a brain magnetic resonance imaging (MRI), showed few well-defined rounded cystic lesions, leading to a provisional diagnosis of multiple sclerosis (Figure 1). Despite treatment with immunosuppressants and steroids, her condition worsened, and she developed new symptoms such as cough and dyspnea. Repeated imaging 6 months later showed increased brain lesions (Figure 2). Subsequent evaluation with positron emission tomography-computed tomography (PET-CT) revealed a right lung lesion with mild hypermetabolic activity and a hypo-dense hepatic dome lesion (Figures 3 and 4) that prompted further investigation.

After 1 month, the patient underwent a CT-guided biopsy of the right lung lesion, but the sample was suboptimal. Therefore, a bronchoscopic biopsy was performed. Immunohistochemical staining showed positive markers for synaptophysin, TTF-1, pan-CK, and chromogranin A, a Ki67 index of approximately 15%, and no obvious necrosis (Figure 5). The histopathology revealed features consistent with an AC. A Gallium-DOTATATE PET/CT scan was done for staging, the right lung lesion and the ipsilateral hilar lymph nodes demonstrated positive high DOTATATE uptake (Figure 6).

Following the diagnosis of a radiological metastatic of AC, the patient was initiated on a multidisciplinary treatment approach. Given the extent of metastatic disease and the neuroendocrine (NE) nature of the tumor, the patient received radiotherapy for the brain delivered in 5 fractions and then started on a combination chemotherapy regimen consisting of etoposide and carboplatin. Additionally, Sandostatin (a somatostatin analog) was incorporated into the treatment plan to manage hormonal symptoms associated with the tumor. The patient completed 6 cycles of chemotherapy, demonstrating a good clinical response to treatment.

The most recent 68-Ga-DOTATOC PET/CT scan was performed to evaluate the patient's response to treatment 7 months after the previous scan. Interval changes were

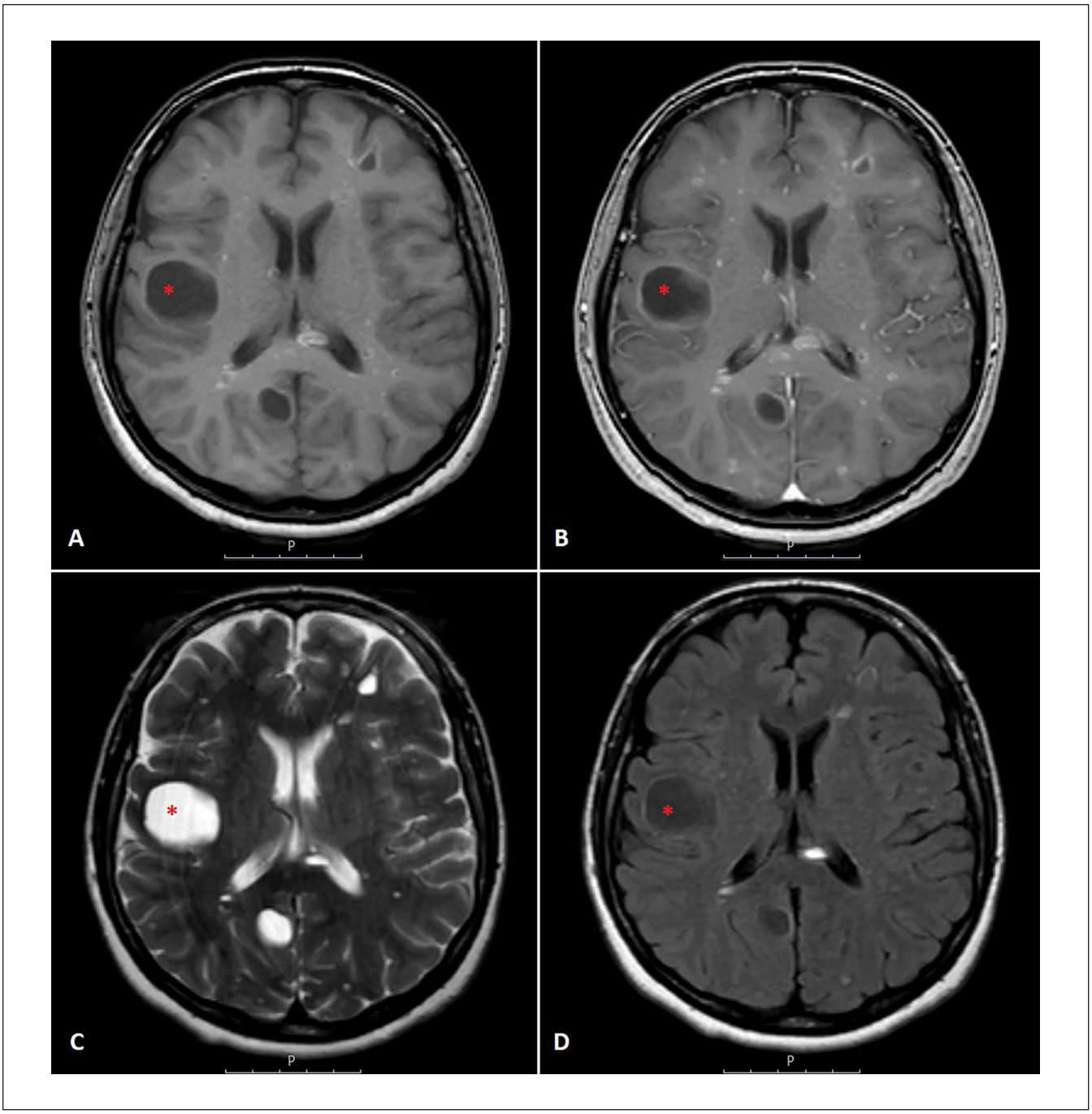

Figure 2. Selected axial cuts of the patient's follow-up brain MRI (A: T1W image, B: T1W C+ fat sat, C: T2W image, D: T2-FLAIR) showing progression in the sizes of the previously seen cystic lesions in addition to newly noted ones, all noted showing peripheral enhancement postcontrast administration (B) suggesting cystic metastatic lesions (asterisks in A, B, C, and D). MRI, magnetic resonance imaging.

observed in previously identified lesions at the chest level. The pulmonary nodule in the posterior segment of the right lower lobe and the right hilar lymph node demonstrated an increase in both size and uptake (Figure 7). However, these findings suggest stable disease with minimal progression in select lesions.

While no new lesions or significant disease progression were detected, the persistence of somatostatin receptor expression and lesion enlargement necessitates close monitoring. The patient will undergo regular follow-up 68-Ga-DOTATOC PET/CT scans every 6 to 12 months to assess disease stability and detect early recurrence.

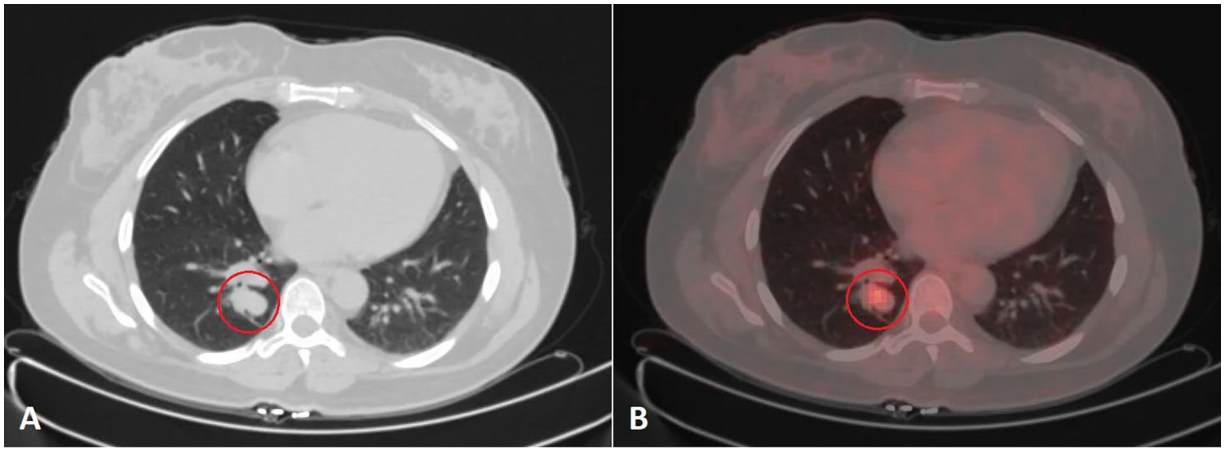

Figure 3. Selected axial cut of the patient's PET-CT scan showing a moderately hypermetabolic right lower lobe lung lesion (circle in A and B). PET-CT, positron emission tomography-computed tomography.

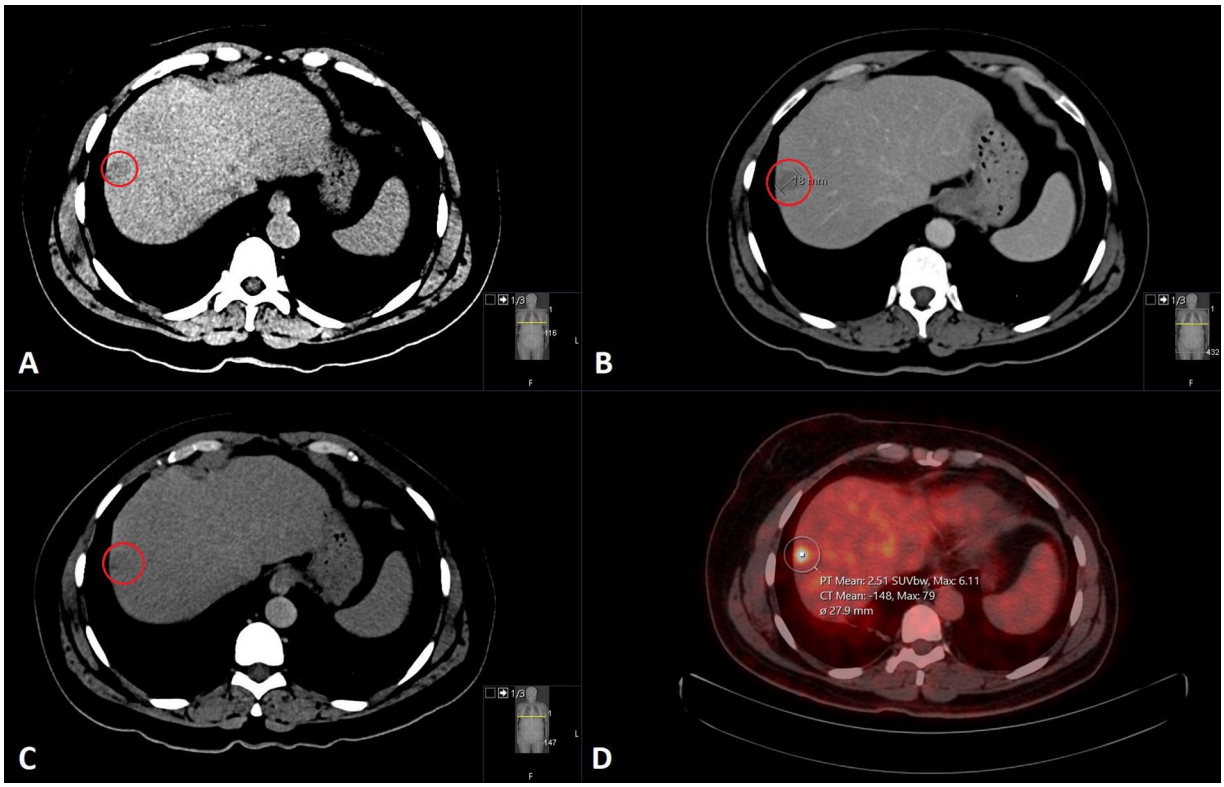

Figure 4. Selected axial cuts at the level of the liver of the patient's abdominal CT scan (A: precontrast, B: venous phase postcontrast, C: delayed phase postcontrast, and D: FDG PET-CT scan) showing a hypo-dense hepatic dome lesion demonstrating early wash-out at the delayed image (C) with corresponding moderate FDG uptake seen in (D) (circle in A-D). FDG, Fludeoxyglucose; PET-CT, positron emission tomography-computed tomography.

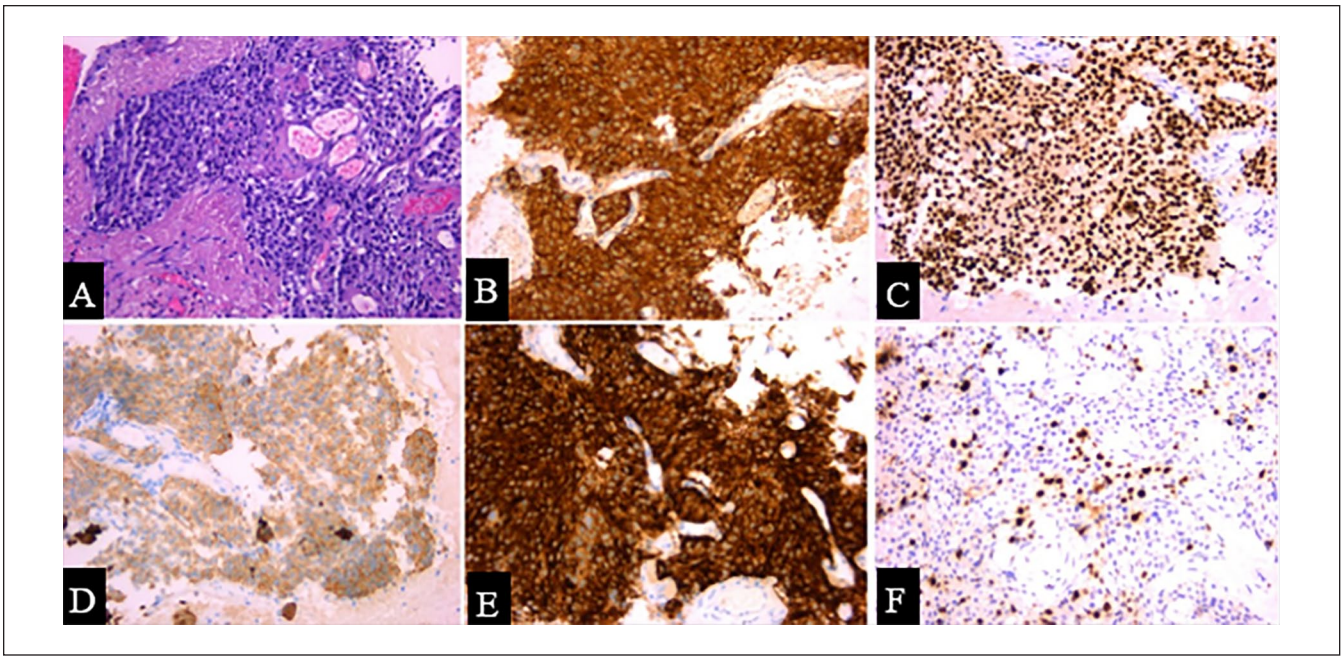

Figure 5. H&E staining shows tumor cells with hyperchromatic nuclei, without a significant increase in mitosis or necrosis (magnification ×20) (A). Immunohistochemical studies demonstrate positive immunostaining of tumor cells for (B) synaptophysin, (C) TTF-1, (D) pan-CK, and (E) chromogranin A. (F) The Ki-67 index is approximately 15%. (H&E staining, magnification ×20). H&E, hematoxylin and eosin.

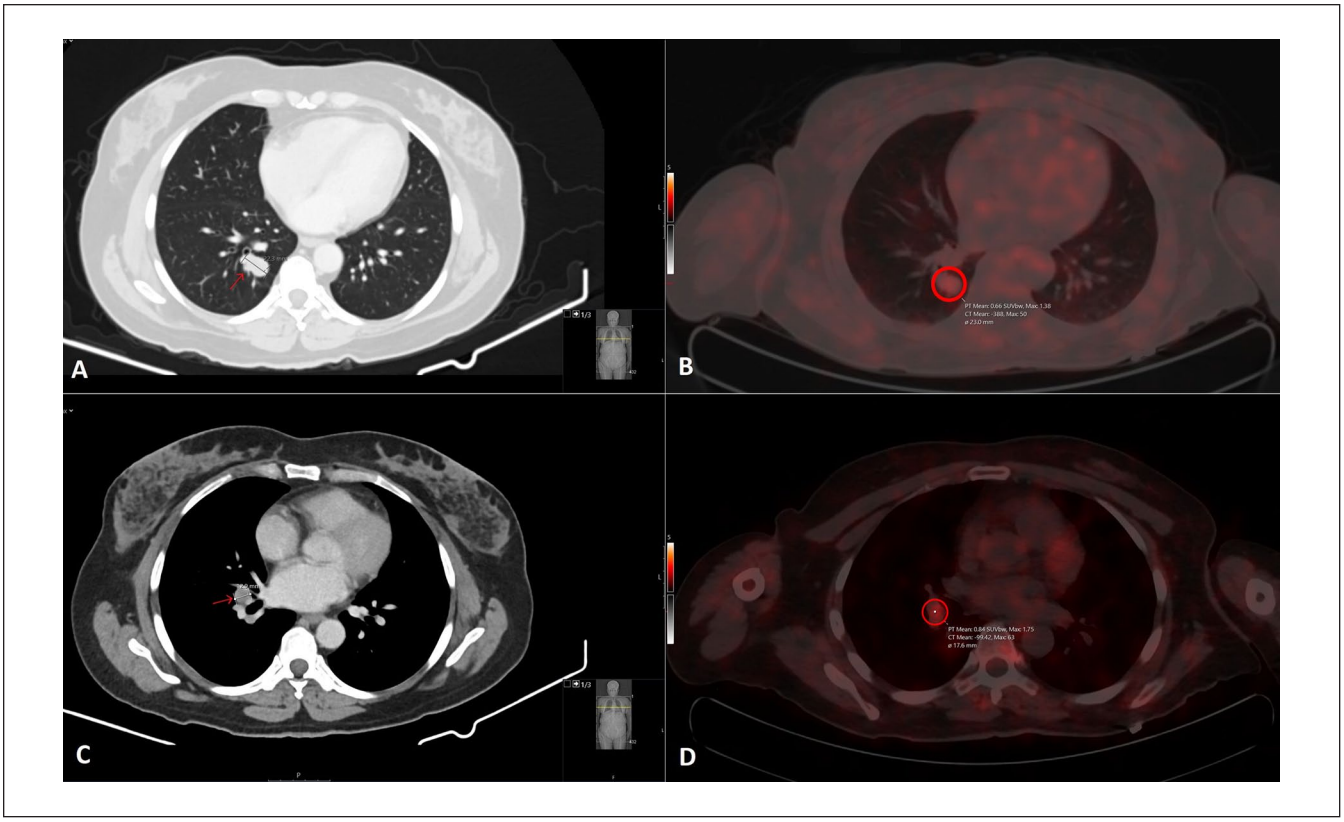

Figure 6. Selected axial cuts of the patient's 68-Ga-DOTATOC PET/CT scan at the level of the chest showing solitary pulmonary nodule within the posterior segment of the right lower lobe (arrow and circle in A and B, respectively) as well as a right hilar lymph node (arrow and circle in C and D respectively) with mild Ga68 DOTATOC activity. PET/CT, positron emission tomography/computed tomography.

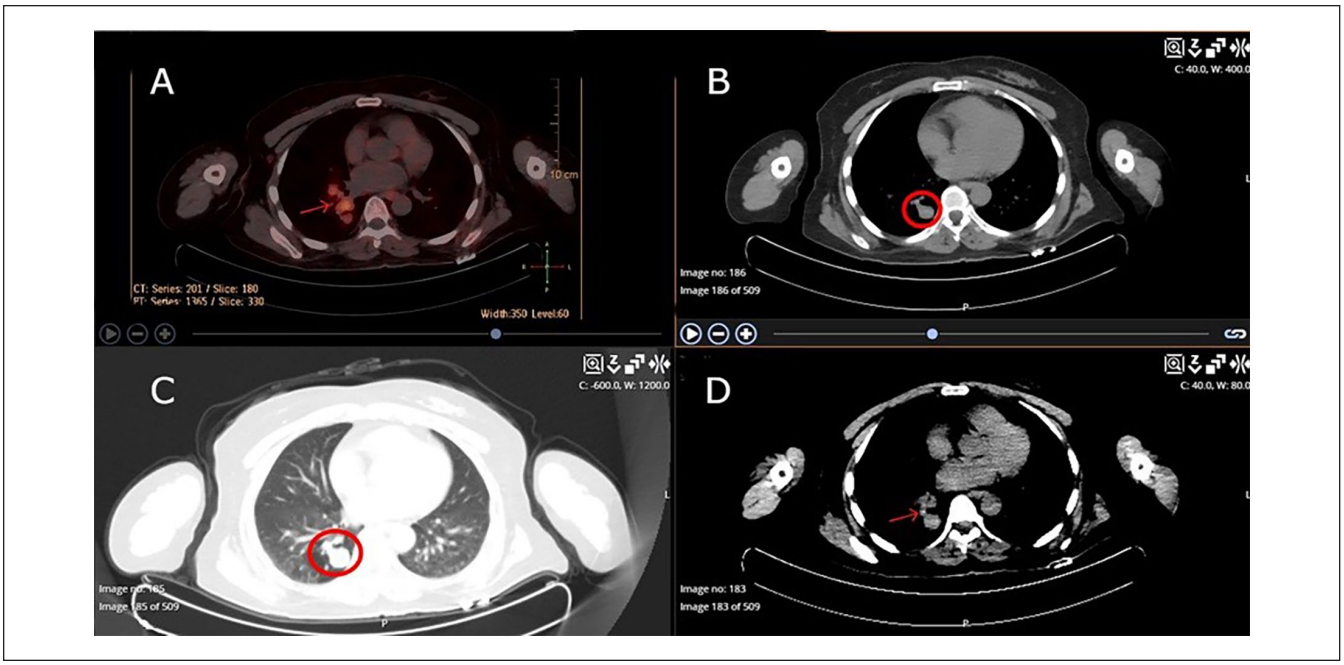

Figure 7. Selected axial Ga-68 DOTATOC PET/CT scan shows interval changes in the previously identified lesions in Figure 6. The pulmonary nodule in the posterior segment of the right lower lobe has slightly increased in size and uptake (2.0 cm × 2.0 cm, SUVmax 2.8) compared to the previous measurement (1.7 cm × 1.4 cm, SUVmax 1.38; circle in B and C). The right hilar lymph node also shows interval progression (2.3 cm × 1.9 cm, SUVmax 4.1) compared to the prior measurement (1.2 cm × 1.0 cm, SUVmax 1.75), indicating increased metabolic activity (arrow in A and D). PET/CT, positron emission tomography/computed tomography.

Discussion

NENs are a significant category, encompassing roughly 20% of primary lung cancers. SCLCs are the most common, accounting for about 15% of all cases. LCNECs and CaTs are less frequent, representing 3% and 2% of primary lung cancers, respectively. Mixed NE and non-NE carcinomas also exist. The ratio of TC to AC is around 10:1.[1,6]

CaTs can arise sporadically or as a component of an inherited condition.[5] Carcinoids are composed of cells that produce peptides and amines, originating from the embryonic neural crest.[7] Studies have shown that cough, dyspnea, recurrent respiratory infections, and hemoptysis are the main clinical symptoms of lung CaTs. However, most peripheral lung NETs are found accidentally and are asymptomatic. CaTs can exhibit 2 types of ectopic hormonal activity: they may secrete hormones or hormone precursors, or they may not.[8]

Hematogenous spread from the lung is the typical system via which metastases to the brain occur. But another mechanism might exist, particularly in patients whose tumors are in the abdomen or pelvis. A valveless network of veins that run in the spinal epidural region forms Batson's venous plexus, which links pelvic tissues with the brain.[5] As far as we are aware, there have only been 7 cases of CaTs initially presenting with brain metastases, and in 5 of these cases, the primary tumor is in the lungs[3-5,9-12] (Table 1).

Chest radiographs often show incidental detection of lung NETs. While lung NETs frequently appear as isolated, well-defined hilar or perihilar tumors, plain X-rays are nonspecific. A computed tomography (CT) scan of the chest and upper abdomen should be performed as soon as a suspicious lesion is identified on a chest X-ray. This will allow for the assessment of the primary tumor's features, size, and extent as well as the involvement of mediastinal lymph nodes and the possibility of distant metastases.[13] However, many patients do not undergo routine brain imaging as a component of metastatic study.[5]

In patients with TCs or ACs, MRI is recommended to identify and assess liver or bone metastases. Because lung CaTs express somatostatin receptors (SSTR), imaging with radiolabeled somatostatin analogs effectively localizes lung carcinoids and detects metastasis. Single-photon emission tomography (SPET)/CT, SPET/planar SSTR scintigraphy, andPET/CT have all been used as diagnostic techniques. For SSTR scintigraphy, PET using 68Ga-DOTATATE/TOC is preferred over Octreoscan if available. The predominant imaging technique for diagnosis, staging, and monitoring is frequently SSTR scintigraphy using ^{111}In-octreotide. Its sensitivity ranges from 80% to 100% when locating radiologically occult cancers.[5] Bronchoscopy can confirm the histologic subtype and diagnose centrally positioned lung carcinoids through biopsy.[2]

Mediastinal lymphadenectomy and extensive anatomical resection are part of the treatment for AC; sleeve or lobectomy is preferable. Surgery for liver or other solid organ metastases is typically used in this entity. Local radiotherapies such as microwave ablation, stereotactic ablative radiotherapy, and

Table 1. A Summary of the Characteristics of 7 Worldwide Cases, Along With Our Case of Metastatic Carcinoid Tumor Presenting as Brain Tumors at First Presentation, That Have Been Published Previously.

Author	Year	Age/Sex	Complain	Location of the primary tumor	Imaging	Treatment	Other sites of metastasis
Hussein et al[3]	1990	61/M	Bilateral frontal headache, weight loss, and anorexia	Lung	• Chest X-ray • Brain MRI • Abdominal CT	Patient refused treatment	• Liver • Thyroid gland • Bone marrow
Greene et al[9]	1993	68/F	Severe headaches and seizure disorder	Lung	• Brain CT • Brain MRI • Chest X-ray • Chest CT • Bone scan	• Anticonvulsant therapy • Craniotomy for exploration and decompression of the brain tumor. • Radiotherapy	• Bone
Porter et al[10]	2000	62/M	Headache with features of raised intracranial pressure	None Identified	• Brain CT • Brain MRI • Chest and abdominal CT • MIBG scan	• Subtotal resection of an extra-axial tumor	None
Nakamura et al[4]	2001	52/F	Sudden onset of severe headaches and ataxia	Lung	• Brain MRI	• Stereotactic radiosurgery • A middle lobectomy of the right lung	None
Maiuri et al[11]	2004	54/M	Ataxia, right dysmetria, speech disturbance, papilledema	Lung	• Brain MRI	• Complete resection of the brain lesion • Chemotherapy • Radiotherapy	None
Sundar et al[5]	2012	60/M	Headache, vomiting, and hemiparesis	None identified	• Brain CT • Brain MRI • Chest and abdominal CT	• Approximately total excision of brain tumor • Radiotherapy	None
Fazio et al[12]	2019	57/M	Mood swings and outbursts	Lung	• Brain MRI • Chest and abdominal CT • FDG PET-CT • 68-Gallium-DOTATATE PET/CT scan	• Chemotherapy • Total excision of brain tumor	None
Our case	2023	50/F	Neck pain, dizziness, numbness, and paresthesia in upper limbs	Lung	• Brain MRI • FDG PET/CT • 68-Gallium-DOTATATE PET/CT scan	• Radiotherapy • Chemotherapy • Octreotide	• Liver

Abbreviations: CT, computed tomography; F, female; FDG, fludeoxyglucose; M, male; MIBG, metaiodobenzylguanidine; MRI, magnetic resonance imaging; PET, positron emission tomography.

radiofrequency ablation are alternatives for patients declining surgery. Adjuvant therapy, which combines radiation and chemotherapy, is used after surgery for AC and has been shown to improve survival.[8] Patients with advanced or metastatic disease may benefit from complete surgical excision of the primary tumor and metastases, aiming for a cure. Cytoreductive surgery's effectiveness, with or without ablation, was documented in a global multiinstitutional review. This investigation focused on patients who had functional liver metastases.[2]

Currently, there are no recognized treatment guidelines for patients with CaTs that have metastasized to the brain.[5] Generally, several therapeutic options are available, including chemotherapy, whole brain radiotherapy, stereotactic radiosurgery, and surgery, either alone or in combination.[14] While surgery can be palliative, it is the preferred treatment for single-brain metastases, especially if they result in a focal neurological deficit.[15] External beam irradiation is recommended for patients with multiple brain metastases.[11,15] In certain circumstances, it can be used in conjunction with surgery unless the tumor is poorly differentiated. When neurosurgical intervention is not required for neurological impairments, systemic treatment is typically preferable to an intensive local approach.[5]

Conclusion

This report describes an uncommon initial presentation of a bronchopulmonary AC tumor metastasizing to the brain. It raises the importance of considering CaTs in differential diagnoses of CNS symptoms. The multidisciplinary approach, which includes surgery, chemotherapy, radiotherapy, and hormone treatment, emphasizes the complexity of managing metastatic CaTs. This case emphasizes the importance of early detection, careful investigation, and comprehensive management techniques in improving patient outcomes in such rare presentations, especially given their rarity in the existing literature.

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Declaration of Conflicting Interests

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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References

1. Vocino Trucco G, Righi L, Volante M, Papotti M. Updates on lung neuroendocrine neoplasm classification. *Histopathology*. 2024;84:67-85.
2. Hendifar AE, Marchevsky AM, Tuli R. Neuroendocrine tumors of the lung: current challenges and advances in the diagnosis and management of well-differentiated disease. *J Thorac Oncol*. 2017;12:425-436.
3. Hussein AM, Feun LG, Savaraj N, East D, Hussein DT. Carcinoid tumor presenting as central nervous system symptoms. *Am J Clin Oncol*. 1990;13:251-255.
4. Nakamura Y, Shimokawa S, Ishibe R, Ikee T, Taira A. Pulmonary carcinoid found in a patient who presented with initial symptoms of brain metastasis: report of a case. *Surg Today*. 2001;31:510-512.
5. Sundar I, Jain S, Kurmi D, Chopra S, Singhvi S. Malignant metastatic carcinoid presenting as brain tumor. *Asian J Neurosurg*. 2016;11:314-314.
6. Hung YP. Neuroendocrine tumors of the lung. *Surg Pathol Clin*. 2019;12:1055-1071.
7. Zeichner SB, Cusnir M, Francavilla M, Hirzel A. Typical bronchial carcinoid metastasizing to the brain: a case presentation. *Case Rep Oncol*. 2011;4:602-610.
8. Savu C, Melinte A, Diaconu C, et al. Lung neuroendocrine tumors: a systematic literature review (Review). *Exp Ther Med*. 2021;23:176.
9. Greene KA, Anson JA, Martinez JA, Spetzler RF, Johnson PC. Multicystic metastatic carcinoid to brain: case report. *J Neurooncol*. 1993;17:15-20.
10. Porter DG, Chakrabarty A, McEvoy A, Bradford R. Intracranial carcinoid without evidence of extracranial disease. *Neuropathol Appl Neurobiol*. 2000;26:298-300.
11. Maiuri F, Cappabianca P, Del Basso De, Caro M, Esposito F. Single brain metastases of carcinoid tumors. *J Neurooncol*. 2004;66:327-332.
12. Fazio N, Laffi A, Spada F, et al. Brain cystic metastases in a patient with advanced atypical lung carcinoid. *Case Rep Images Oncol*. 2020;1:1-5.
13. Gustafsson BI, Kidd M, Chan A, Malfertheiner MV, Modlin IM. Bronchopulmonary neuroendocrine tumors. *Cancer*. 2008;113:5-21.
14. Krug S, Teupe F, Michl P, Gress TM, Rinke A. Brain metastases in patients with neuroendocrine neoplasms: risk factors and outcome. *BMC Cancer*. 2019;19:362.
15. Hlatky R, Suki D, Sawaya R. Carcinoid metastasis to the brain. *Cancer*. 2004;101:2605-2613.