Pituitary and pineal gland metastases from pulmonary neuroendocrine carcinoma: A case report and literature review

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Abstract. Neuroendocrine neoplasms are a group of tumors originating from neuroendocrine cells that can occur in endocrine or non-endocrine organs. Metastatic pituitary neuroendocrine carcinomas are uncommon in clinical practice, with female breast cancer and male lung cancer being the most common primary sources of pituitary metastases. Pituitary and pineal gland metastases from pulmonary neuroendocrine tumors are extremely rare. The current study describes the case of a 68-year-old male patient who first presented with a headache and a small and limited pituitary lesion on saddle MRI, which was initially considered to be a primary pituitary microadenoma and was recommended to be reviewed on an ongoing basis. A total of 4 months later, the patient presented again after worsening of the headache and visual disturbances with diabetes insipidus. On review of the saddle MRI, which showed a significantly enlarged pituitary and pineal regions, the patient was treated with transsphenoidal surgery to completely excise the tumor. However, histopathological and immunohistochemical results suggested a pituitary metastasis from a pulmonary neuroendocrine tumor. Although the pineal region lesion did not undergo surgical pathology to confirm its origin from a pulmonary neuroendocrine tumor, it was highly suspected to be homologous to a pituitary metastasis in combination with the monist diagnostic and treatment concepts, and the imaging manifestations of the lesion. This case highlights the importance of the differential diagnosis of invasive lesions in the saddle region combined with the pineal region. Clinicians should be alert to this rare disease and a multidisciplinary consultation should be performed should be performed.

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Introduction

Neuroendocrine neoplasms (NENs) are tumors that originate from neuroendocrine cells and are classified into two categories: i) Neuroendocrine organs, such as the pituitary, thymus and adrenal glands, and ii) non-neuroendocrine organs, including the gastrointestinal tract, pancreas, lungs, thymus, skin and genitourinary tract. According to the 5th edition of the World Health Organization (WHO) Classification of Thoracic Tumors (May 2021), NENs account for ~1-2% of primary lung tumors and primarily originate from bronchial mucosal epithelial K-cells, which are distributed in large bronchial tubes and bifurcation mucosa. Lung NENs are classified into four subtypes: Typical carcinoid tumors, atypical carcinoid tumors, large-cell neuroendocrine carcinoma (NEC), and small-cell lung carcinomas (1). These tumors can metastasize to the lymph nodes, liver, lungs and bones, with brain metastases occurring in ~1-5% of cases (2-4). The incidence of pituitary metastases is extremely low, accounting for ~1% of all metastatic brain lesions (5). However, simultaneous metastases to both the pituitary gland and the pineal region are exceedingly rare. In the present study, a case of a pulmonary neuroendocrine tumor with simultaneous metastases to these regions was reported, aiming to provide a reference for clinical diagnosis and treatment.

Case report

A 68-year-old man first presented to the neurosurgery clinic of Gansu Provincial Hospital (Lanzhou, China) with intermittent headaches, fever and anorexia that had persisted for 1 month. The patient had been a smoker for >30 years, at 20 cigarettes per day. A neurological examination revealed no positive signs. Hormone levels and other laboratory results are presented in Table I; demonstrating that pituitary hormone secretion was significantly suppressed with enlargement of the pituitary and pineal region lesions. Ancillary examinations revealed the following findings: X-ray chest radiographs showed no obvious abnormalities (chest CT was not performed). MRI of the pituitary gland showed that it was full in shape, with a maximum height of ~1.1 cm in the coronal position. A slightly hyperintense T1 signal shadow, round in shape and measuring ~0.57 cm in diameter, was observed in the middle and upper part of the pituitary gland. Enhancement scans showed early

peripheral enhancement of the lesion, with inconspicuous enhancement in the center and sustained enhancement of the lesion. The pituitary stalk was shifted and showed enhancement (Fig. 1A-C). The preliminary diagnosis of pituitary microadenoma was made based on the patient's history and auxiliary examinations. It was recommended that a pituitary MRI be repeated every 3 months to observe dynamic changes in the lesion.

More than 4 months after the first consultation, the patient reported a progressive worsening of headache symptoms, accompanied by deteriorating vision and diabetes insipidus; therefore, the patient visited the Department of Neurosurgery of Gansu Provincial Hospital (Lanzhou, China) for further evaluation. The patient was admitted with blurred vision in both eyes and diabetes insipidus, with no other significant findings. Auxiliary examinations revealed that visual evoked potentials indicated a delayed P100 latency in both eyes and a peripheral visual field defect in the right eye was observed. Chest CT revealed a nodular soft tissue density shadow in the hilar region of the upper lobe of the left lung, measuring ~1.8x3.2 cm (Fig. 2A). Abdominal CT image revealed no significant abnormalities in the pancreas, spleen, or gastrointestinal tract, with preserved anatomical architecture and absence of focal lesions (Fig. 2C and D). MRI of the pituitary gland, both on plain scan and with contrast enhancement, showed a full pituitary morphology, with a maximum height of ~1.5 cm in the coronal position. The corset sign was observed in the middle and upper portion of the pituitary gland. The stalk of the pituitary gland was thickened in a nodular shape and showed significant enhancement after contrast administration. The pituitary MRI foci size had notably increased compared with 4 months ago. In the pineal region, a nodular abnormal signal measuring ~1.2 cm in diameter with clear borders was observed, which demonstrated significant and uniform enhancement after contrast administration (Fig. 1D-F). Based on the patient's medical history and auxiliary tests, the preliminary diagnoses included tumors of the sellar region, pineal gland and lung.

After multidisciplinary diagnosis and treatment (neurosurgery/imaging center/thoracic surgery) discussions, it was decided that the pituitary lesion should be resected first to relieve optic nerve compression and alleviate symptoms of blurred vision and diabetes insipidus. After ruling out contraindications to surgery, the trans-nasal butterfly approach neuro-endoscopic-assisted resection of the sellar region lesion was performed under general anesthesia. The tumor tissue was soft, grayish-red in color and had a general blood supply. Postoperative pathology suggested metastatic NEC (atypical carcinoid tumor). Hematoxylin and eosin (H&E) staining was performed as follows: Samples (thickness, 3.5 μm) were fixed using neutral buffered formalin (pH 7.2-7.4) at 25˚C for 12 h. Hematoxylin staining was performed for 8 min and eosin staining for 2 min (both at 24˚C). (H&E) staining revealed a solid tumor involving the pituitary gland, characterized by small cells with high-grade nuclear atypia and a mitotic index >30/2 mm^2 (magnification, x400; light microscope) (Fig. 3A). Immunohistochemical analysis was then performed. Normal goat serum (10%, diluted in PBS pH 7.4) was used for blocking at 25˚C for 45 min.

Primary antibodies included CKP (1:100; cat. no. M3515; Agilent; temperature and duration of incubation: 60 min at 25˚C), TTF-1 (1:100; cat. no. M3575; Agilent; temperature and duration of incubation: 4˚C for 16 h), Syn (1:200; cat. no. 790-4464; Roche Diagnostics; temperature and duration of incubation: 60 min at 25˚C) and CgA (1:500; cat. no. 760-2539; Roche Diagnostics; temperature and duration of incubation: 60 min at 25˚C). Secondary antibodies included anti-mouse IgG (H+L) antibody (biotin-conjugated; 1:200; cat. no. BA-9200; Vector Laboratories, Inc.; temperature and duration of incubation: 30 min at 25˚C) and anti-rabbit IgG (H+L) antibody (biotin-conjugated; 1:200, cat. no. BA-1000; Vector Laboratories, Inc.; temperature and duration of incubation: 30 min at 25˚C). A light microscope (Olympus Corporation) was used for observation (scale bar, 40 μm).

Immunohistochemistry showed the following results: Pan cytokeratin (CKP)(+), synaptophysin (Syn)(+), chromogranin A (CgA)(+), thyroid transcription factor (TTF-1)(+) and Ki-67 expression (index 40%) (Fig. 3B-F). Given the presence of multiple nodules in the patient's lungs, the pituitary NEC was considered to have originated from the lungs. To further confirm the primary tumor, a percutaneous CT-guided aspiration biopsy of the left hilar mass was performed under local anesthesia (Fig. 2B). The pathological results of the lung mass indicated that the tumor was a primary pulmonary neuroendocrine tumor (atypical carcinoid tumor). Histopathological evaluation of the pulmonary neuroendocrine tumor is presented in Fig. 4A-F, encompassing H&E staining and immunohistochemical profiles [CKP(+), Syn(+), CgA(+), TTF-1(+), Ki-67 (index 40%)].

The histopathological concordance between the pulmonary and pituitary lesions (Figs. 3 and 4) provides robust diagnostic evidence supporting pituitary metastasis originating from a pulmonary NEC. Specifically, both lesions exhibited identical histomorphological features. Immunohistochemical profiling demonstrated strong diffuse positivity for Syn, CgA and CKP in both lesions, with a Ki-67 proliferation index of >30%. Crucially, nuclear TTF-1 immuno-expression was unequivocally detected in tumor cells at both anatomical sites, definitively establishing metastatic dissemination from a primary lung origin. TTF-1, a lineage-specific nuclear transcription factor expressed in thyroid follicular epithelium and pulmonary respiratory epithelium, serves as a diagnostic marker for adenocarcinomas of lung/thyroid origin while being absent in neoplasms arising from other organs. In summary, the co-expression of Syn, CgA and CKP, coupled with nuclear TTF-1 immunoreactivity, provides robust evidence for the metastatic nature of the sellar tumor and its derivation from a primary pulmonary NEC.

Therefore, the final diagnosis was established by combining the medical history with the pathological results, confirming that the pituitary and pineal region metastases originated from a pulmonary neuroendocrine tumor. Due to the small size and deep location of the pineal region lesion, the patient did not undergo further surgical treatment or pathological tests. However, from the imaging analysis, the MRI signal characteristics of the lesion were consistent with those of the sellar region. Following the monist approach to diagnosis and treatment, the pineal region lesion was considered homologous to the metastatic tumor of the

Table I. Laboratory results.

Indexes	First lab test	Second lab test	Reference range
Urinary free cortisol (nmol/24 h)	0	0	100-379
Cortisol (nmol/l)	60.2	16.9	102.0-536.0
Human growth hormone (ng/ml)	0.485	0.329	0.970-4.700
Insulin-like growth factor-1 (ng/ml)	62	58	127-424
Thyroid stimulating hormone (mIU/l)	0.75	0.02	0.35-4.94
T3 (nmol/l)	1.53	1.07	0.98-2.33
T4 (nmol/l)	82.35	91.91	62.80-150.84
Adrenocorticotropic hormone (pg/ml)	15.57	4.37	7.00-64.00
Testosterone (nmol/l)	<0.45	<0.45	4.94-32.01
Dehydroepiandrosterone sulfate (μg/dl)	12.5	7.0	48.8-361.8
Prolactin (ng/ml)	115.19	76.70	3.46-19.40
Luteinizing hormone (IU/l)	0.45	0.33	0.57-12.07
Gastrin-releasing peptide precursor (pg/ml)	393.0	317.5	<63.7
Neuron-specific enolase (ng/ml)	22.10	25.27	<17.00
α-fetoprotein (ng/ml)	-	1.41	<8.78

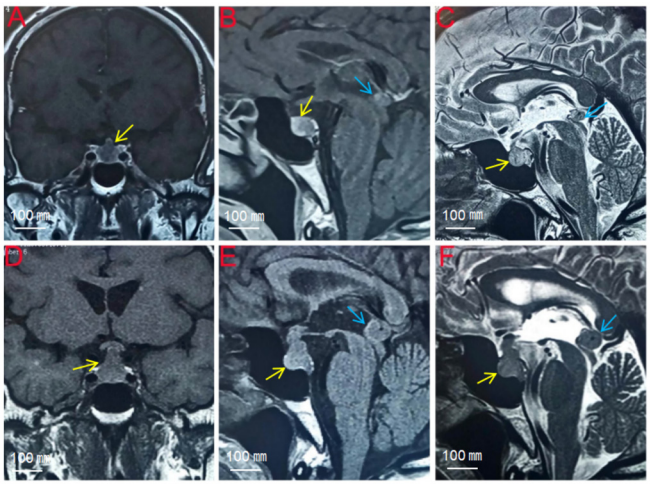

Figure 1. Magnetic resonance imaging. (A-C) First pituitary MRI: The pituitary gland is full, the maximum height of the pituitary gland is ~1.1 cm in the coronal position, and a slightly longer T1 signal shadow can be observed in the middle and upper part of the pituitary gland, which is ~0.57 cm in diameter. The enhancement scan shows peripheral enhancement of the lesion. (D-F) Second pituitary MRI: The pituitary gland is full, the maximum height of the pituitary gland in the coronal position is ~1.5 cm, the corset sign can be observed in the middle and upper part of the pituitary gland, and the pituitary stalk is thickened in the form of a nodule, which is obviously strengthened after enhancement. The pineal region can be seen in the form of a nodular abnormality, with a diameter of ~1.2 cm, with clear borders, and it is obviously and uniformly strengthened after enhancement. The signals of the lesion are the same as that of pituitary tumor (metastatic pituitary NEC: yellow arrows; metastatic pineal region NEC: blue arrows).

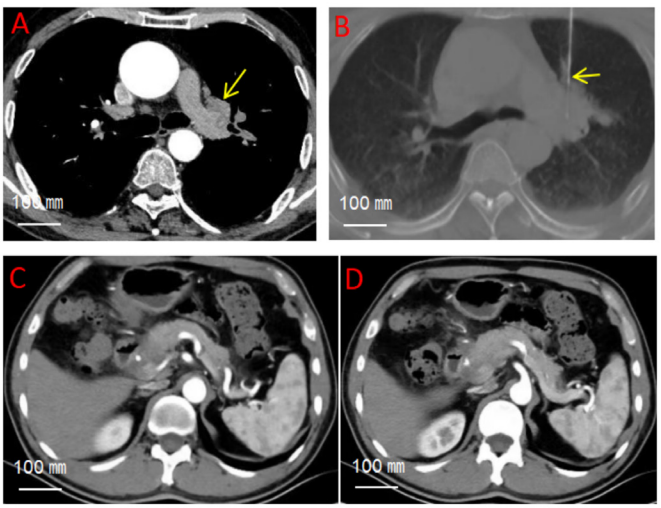

Figure 2. Chest CT. (A) Nodular soft tissue density shadow in the hilar region of the upper lobe of the left lung, ~1.8x3.2 cm in size. (B) Percutaneous CT-guided percutaneous left hilar mass aspiration biopsy under local anesthesia (arrow shows the puncture needle). (C and D) Abdominal CT. The pancreas and spleen demonstrate unremarkable size and morphological characteristics. The gastric lumen exhibits adequate distention with no evidence of localized wall thickening. Similarly, the rectal wall shows no apparent pathological thickening.

pituitary gland. Hormone replacement therapy (hydrocortisone 100 mg once daily via intravenous infusion, with dosage adjustment guided by serial hormonal level monitoring) was administered after surgery, and after a favorable recovery, further radiotherapy and chemotherapy were recommended. However, the patient refused additional treatment, was discharged from the hospital and succumbed 4 months after surgery.

Discussion

Neuroendocrine tumors are a heterogeneous group of malignant tumors that originate from the diffusely distributed neuroendocrine system. Pulmonary neuroendocrine tumors are classified into two categories based on their histomorphology, the Ki-67 proliferation index and differences in necrosis (6,7). The first category consists of well-differentiated neuroendocrine tumors, including low-grade G1 typical carcinoids and intermediate-grade G2 atypical carcinoids. These tumors are commonly found in young women without a history of smoking. The second group consists of poorly differentiated

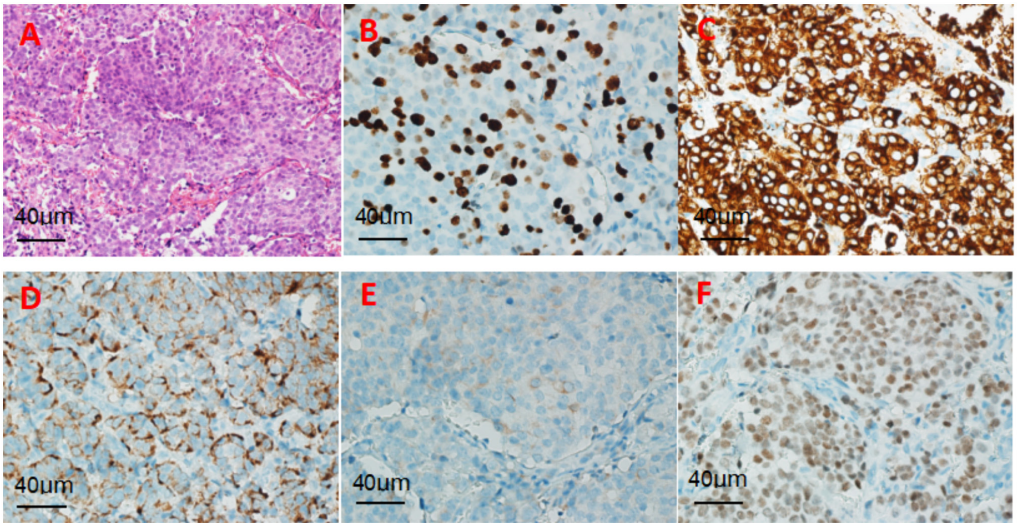

Figure 3. Histological features of the metastatic pituitary neuroendocrine carcinoma and immunohistochemistry results. (A) Hematoxylin and eosin staining revealing a solid tumor involving the pituitary gland, characterized by small cells with high-grade nuclear atypia, mitotic index >30/2 mm^2 (magnification, x40). Positive staining for (B) Ki-67 (index 40%), (C) synaptophysin, (D) pan cytokeratin, (E) chromogranin A and (F) thyroid transcription factor 1.

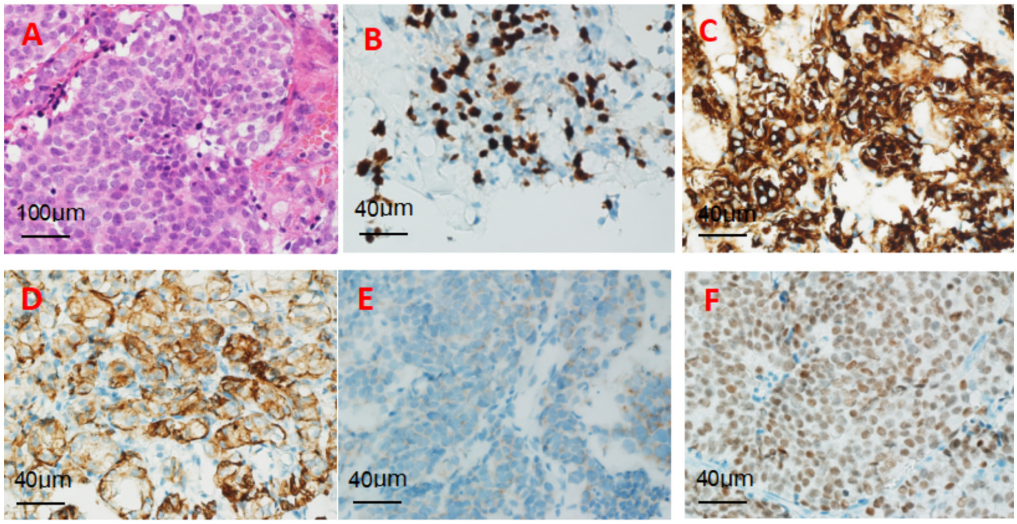

Figure 4. Histological features of the primary pulmonary neuroendocrine carcinoma and immunohistochemistry results. (A) The number of mitotic divisions in hematoxylin and eosin staining was found to be >30/2 mm^2 (magnification, x20). Immunohistochemical analysis suggested positive staining for (B) Ki-67 (index 40%), (C) synaptophysin, (D) pan cytokeratin, (E) chromogranin A and (F) thyroid transcription factor 1.

NEC, including high-grade small-cell lung carcinoma and high-grade large-cell NEC. These tumors are common in older men with a history of smoking (6,8,9). In the present case, the patient had a history of smoking, and the lesion progressed rapidly, had a poor prognosis and exhibited atypical carcinoid morphology. Moreover, H&E staining showed only small patchy areas of necrosis, and immunohistochemical profiling demonstrated strong diffuse positivity for Syn, CgA and CKP in both lesions, with a Ki-67 proliferation index of >30%. These findings indicate that the metastatic NEC of the pituitary gland originated from a primary pulmonary tumor.

To date, no reported cases of pulmonary NEC with synchronous metastases to both the pituitary gland and pineal region have been identified. In the present case, the patient was initially misdiagnosed with a primary pituitary adenoma and a pineal region tumor due to the clinicians' insufficient preoperative diagnostic experience. The definitive diagnosis of pituitary and pineal region metastases originating from a pulmonary neuroendocrine tumor was established based on pathological findings after surgery. Due to the deep location of the pineal region, its complex anatomical structure, the small size of the lesion and its possible homology with pituitary lesions based on imaging analysis, surgical pathology did not confirm that the pineal region lesion originated from pulmonary NEC. However, based on a monist diagnostic and treatment approach, the following evidence supports the diagnosis of pineal metastasis: i) The possibility that the same patient suffers from two tumors with different natures in the same period is extremely low; and ii) the growth rate of the pineal lesion in this patient was consistent with that of the pituitary lesion, and the imaging findings were consistent with those of the pituitary lesion. At present, neuroendocrine

Table II. Summary of cases with malignant neoplasm metastasis within pituitary neuroendocrine tumors.

First author, year	Patient characteristics		Primary tumor site	Other intracranial metastasis	Treatment	Outcomes		(Refs.)
	Age, years	Sex				Pathological findings	Survival time/status	
Van der Zwan *et al*, 1971	73	F	Breast adenocarcinoma	No	TCS	Hormone-negative	POD 28/dead	(13)
Richardson and Katayama, 1971	70	F	Breast adenocarcinoma	No	TCS	N/A	3 months/dead	(14)
Burns and Kadar, 1973	78	M	Renal pelvis ureter carcinoma	No	No	Hormone-negative	1 month/dead	(15)
James *et al*, 1984	77	M	Renal carcinoma	No	TSS	Hormone-negative	N/A	(16)
van Seters Arnoud *et al*, 1985	66	F	Stomach adenocarcinoma	No	TCS	PRL-positive	POD 12/dead	(17)
Molinatti *et al*, 1985	71	M	Lung small cell carcinoma	No	Radiation	FSH/LH-positive	1 month/dead	(18)
	67	F	Stomach adenocarcinoma	No	TCS	PRL/GH-positive	POD 2/dead	(18)
Zager and Hedley-Whyte, 1987	56	F	Breast adenocarcinoma	No	Radiation	FSH/LH-positive	3 weeks/dead	(19)
Post *et al*, 1988	61	F	N/A	No	TSS	ACTH-positive	N/A	(20)
	77	M	Lung carcinoma	No	TSS	N/A	6 months/dead	(20)
Ramsay *et al*, 1988	67	M	Prostate carcinoma	No	No	Hormone-negative	N/A	(21)
	50	F	Pancreatic carcinoma	No	TSS	ACTH-positive	7 months/dead	(21)
Hurley *et al*, 1992	76	M	N/A	No	TSS	GH-positive	6 months/dead	(22)
Abe *et al*, 1997	46	F	Malignant carcinoid	No	Medication	PRL-positive	6 months/dead	(23)
Bret *et al*, 2001	75	F	Breast carcinoma	No	TSS	FSH/LH/α-SH-positive	18 months/alive	(24)
	87	F	N/A	No	TSS	FSH/LH-positive	6 months/alive	(24)
Noga *et al*, 2001	60	M	N/A	No	TCS	Hormone-negative	Few days/dead	(25)
Weber *et al*, 2003	62	F	Renal carcinoma	No	TSS	Hormone-negative	8 months/dead	(26)
Nasr *et al*, 2006	44	F	GHRH producing carcinoid	No	TSS	GH-positive	N/A	(27)
Jung *et al*, 2007	70	M	Melanoma	No	TSS	Hormone-negative	N/A	(28)
Hoellig *et al*, 2009	71	M	Lung small cell carcinoma	Yes	TSS	N/A	POD 12/dead	(29)
Nassiri *et al*, 2012	55	F	Neuroendocrine tumor	No	TSS	GH-positive	21 months/dead	(30)
Rotondo *et al*, 2013	66	M	Bronchial non-small cell carcinoma	Yes	No	PRL/GH-positive	POD 1/dead	(31)
Thewjitcharoen *et al*, 2014	65	M	Colorectal carcinoma	No	TSS	PRL-positive	9 months/dead	(32)
Sogani *et al*, 2014	64	M	Lung adenocarcinoma	Yes	TSS	ACTH/PRL-positive	>1 month/alive	(33)
Magnoli *et al*, 2014	76	F	Renal carcinoma	No	TSS	FSH/LH/α-SU-positive	24 months/dead	(34)
Fujimori *et al*, 2014	80	M	Lung carcinoma	No	TSS	N/A	7 months/dead	(35)
Yang *et al*, 2017	62	M	Melanoma	No	TSS	PRL-positive	22 months/alive	(36)
Andreev *et al*, 2020	55	F	Breast carcinoma	No	TSS	FSH/LH-positive	POD 14/dead	(37)
Donofrio *et al*, 2023	68	M	Colon adenocarcinoma	No	TSS	FSH/LH/SF-1-positive	9 months/dead	(38)
Castle-Kirszbaum *et al*, 2020	51	F	Breast adenocarcinoma	Yes	TSS	N/A	6 months/alive	(39)

Table II. Continued.

First author, year	Patient characteristics		Primary tumor site	Other intracranial metastasis	Treatment	Outcomes		(Refs.)
	Age, years	Sex				Pathological findings	Survival time/status	
Liu *et al*, 2021	65	F	Lung NEC	No	TSS	N/A	POD 7/Dead	(40)
Mills *et al*, 2022	65	F	Breast carcinoma	Yes	TSS	FSH-positive	POD 12/Dead	(41)
Suzuki *et al*, 2024	75	M	Lung adenocarcinoma	No	TSS	α-SU/SF-1-positive	12 months/alive	(42)
Present study	68	F	Lung NEC	Yes	TSS	N/A	4 months/dead	

M, male; F, female; PRL, prolactin; GH, growth hormone; FSH, follicle-stimulating hormone; LH, luteinizing hormone; GHRH, growth hormone-releasing hormone; ACTH, adrenocorticotropic hormone; TCS, transcranial surgery; TSS, transsphenoidal surgery; α-SU, α-subunit; SF-1, steroidogenic factor-1; POD, postoperative day; NEC, neuroendocrine carcinoma; N/A, not available.

metastatic carcinoma in the pineal region is extremely rare, which may be related to the fact that, as a highly vascularized endocrine gland, the pineal gland is not easily seeded by tumor cells through hematogenous dissemination (10,11). Some scholars have suggested that this may be related to the following mechanisms (12): i) The pineal gland lacks a blood-brain barrier; and ii) pineal cells are in direct contact with the cerebrospinal fluid of the third ventricle, and pineal metastases are mostly derived from lung cancers, potentially indicating organ specificity.

As demonstrated in Table I, hormonal levels in the second pituitary function test exhibited widespread suppression. Metastatic pituitary NEC typically induces single or multiple anterior pituitary hormone deficiencies, primarily attributed to tumor-induced mechanical compression of the anterior pituitary and/or pituitary stalk. This compression disrupts hypothalamic regulatory signaling essential for pituitary cell stimulation. Notably, initial pituitary MRI in this case revealed a microadenoma without indications for surgical intervention due to the absence of significant neurological deficits. Subsequent re-evaluation following a 4-month active surveillance period revealed substantial progression of the pituitary lesion, characterized by both volumetric expansion and nodular thickening of the pituitary stalk. These morphological changes likely intensified compressive effects on the pituitary stalk, thereby amplifying the inhibitory impact on hypothalamic-pituitary axis signaling and downstream hormone secretion.

Since Benjamin discovered the first case of pituitary metastatic carcinoma through autopsy in 1857, numerous researchers have studied the condition. A review of national and international literature reveals that only 34 cases (13-42) of neuroendocrine metastatic carcinoma of the pituitary gland have been reported (Table II). However, no cases of simultaneous pulmonary neuroendocrine tumor metastasis to both the pituitary gland and pineal region have been documented.

There are several views on the pathogenesis of metastatic pituitary carcinoma (43-45). Metastasis to the posterior pituitary lobe occurs through hematogenous dissemination via the inferior pituitary artery. Parasellar malignant tumors can invade the perihypopituitary bony structures and extend into the pituitary fossa, leading to thickening of the pituitary stalk and metastasis to the anterior pituitary lobe (43). Pulmonary NEC with synchronous metastases to both the pituitary gland and pineal region has a poor prognosis, with survival primarily dependent on the grade of the primary tumor. Currently, no standardized guidelines or expert consensus exists for the treatment of pulmonary NEC with secondary metastases to the pituitary and pineal regions, and its management remains a topic of debate (44). It is considered by some scholars that surgical resection should be followed by adjuvant radiotherapy, chemotherapy or targeted therapy. Others consider that surgery does not prolong the patient's survival and that a biopsy of the primary tumor should be performed to determine the nature of the lesion, followed by comprehensive treatments such as stereotactic radiotherapy and chemotherapy (45). In the present case, the patient was followed up after surgery but succumbed 4 months later, as the patient's family refused the use of further adjuvant treatments, such as radiotherapy and chemotherapy, for personal reasons.

The mechanisms underlying the transformation of adenocarcinoma into NEC within the pituitary gland remain poorly understood and involve complex interactions among tumor heterogeneity, phenotypic plasticity and microenvironmental cues. Based on a comprehensive review of the literature (39,41,43), potential mechanisms may primarily involve the following: i) Adenocarcinoma cells may acquire migratory capacity through epithelial-mesenchymal transition, followed by trans-differentiation into NEC phenotypes under the influence of pituitary-specific microenvironmental factors (for example, hypoxia and neuroendocrine-derived cytokines); ii) the neuroendocrine-rich pituitary niche may orchestrate phenotypic conversion through localized activation of developmental signaling pathways and the secretion of lineage-directing growth factors; and iii) global DNA methylation remodeling (hypermethylation of CDH1/E-cadherin promoters) and histone modification shifts (H3K27me3 demethylation) may drive the transcriptional silencing of adenocarcinoma-associated genes while activating neuroendocrine-specific transcriptional programs.

A limitation of the present study is the absence of serum/plasma arginine vasopressin (AVP) quantification due to technical constraints in clinical assay availability (AVP testing is not routinely supported by the institutional laboratory infrastructure). While direct AVP measurements were unavailable, the diagnosis of diabetes insipidus was rigorously supported by the following: i) Concordant clinical manifestations (for example, polyuria and polydipsia); ii) characteristic pituitary stalk thickening and loss of the posterior pituitary bright spot on MRI (Fig. 1); and iii) symptomatic and biochemical resolution following desmopressin challenge. Nevertheless, it should be acknowledged that the lack of AVP data restricts pathophysiological granularity in distinguishing central vs. nephrogenic etiologies. Future investigations will incorporate standardized AVP assays to refine diagnostic precision and enhance mechanistic insights. A further methodological limitation of this study is the absence of somatostatin receptor scintigraphy (SRS) assessments. While SRS represents the gold-standard imaging modality for neuroendocrine tumor characterization, its implementation was precluded by current institutional constraints in radiotracer availability and dedicated γ camera instrumentation. To address this limitation, alternative diagnostic modalities were utilized to strengthen the diagnostic rationale: Histopathological and immunohistochemical analyses of the lung lesion confirmed a neuroendocrine origin [Syn(+), CgA(+) and TTF-1(+)], with no histological evidence of metastasis from other primary sites.

In conclusion, pulmonary NEC secondary to pituitary combined with pineal region metastasis is rare, and since most primary tumors have insidious symptoms, most patients present with metastases as their first symptom. Therefore, for cases of pterygoid or pineal tumors with relatively rapid progression of neurological symptoms, it is necessary to consider the nature of metastatic tumors that may be highly malignant, and it is recommended for patients to undergo surgery as early as possible to obtain sufficient pathological samples to clarify the diagnosis and to point out the direction of the subsequent treatment, so as to avoid delaying treatment of the condition.

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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

SP was involved in patient management, wrote the original manuscript, and contributed to conception, design and data analysis. JZ and JL contributed to supervision, writing, conception, design, data analysis, and reviewed and edited the manuscript. YF participated in patient treatment guidance, data collection, conception, and reviewed the article's final proofs. SP and JZ confirm the authenticity of all the raw data and participated in reviewing and approving the final manuscript proofs. JL guided and reviewed the writing of the manuscript. All authors 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.

Competing interests

The authors declare that they have no competing interests.

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