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CASE REPORT

Solitary pituitary metastasis resulting from pulmonary large cell neuroendocrine carcinoma

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Abstract

Solitary pituitary metastasis is a rare phenomenon in human neoplasms. We report a case of lung cancer with the initial manifestation of endocrinopathy resulting from pituitary metastasis. The patient's initial diagnosis was a poorly differentiated carcinoma, however, morbid anatomy revealed a definite diagnosis of large cell neuroendocrine carcinoma (LCNEC). Clinical physicians should be aware of potential initial manifestations such as endocrine abnormalities including panhypopituitarism and diabetes insipidus due to solitary pituitary metastasis. This case demonstrates that an endocrine abnormality such as panhypopituitarism could be an initial manifestation of LCNEC.

Key words: Large cell neuroendocrine carcinoma; Pituitary metastasis; Solitary; Endocrinopathy

Core tip: Solitary pituitary metastasis is a rare phenomenon in human neoplasms. An endocrine abnormality such as panhypopituitarism could be an initial manifestation of large cell neuroendocrine carcinoma.

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INTRODUCTION

Pulmonary neuroendocrine tumors consist of typical carcinoid, atypical carcinoid, large cell neuroendocrine carcinoma (LCNEC) and small-cell lung carcinoma (SCLC). LCNEC is an uncommon malignancy with aggressive features and a dismal prognosis. Although brain metastasis is often observed in patients with LCNEC, to our knowledge, there is no description of solitary pituitary metastasis due to LCNEC. Here, we describe a case of LCNEC with the initial manifestation of endocrinopathy secondary to pituitary metastasis.

CASE REPORT

A 74-year-old man with a smoking history presented with anorexia, vomiting, fever and thirst. Physical examination revealed dry mouth, decreased skin turgor and hypotonia with a blood pressure of 80/50 mmHg. Laboratory investigations revealed thyroid stimulatory hormone of 0.05 U/mL [normal range (NR): 0.5-5.5 U/mL], luteal hormone

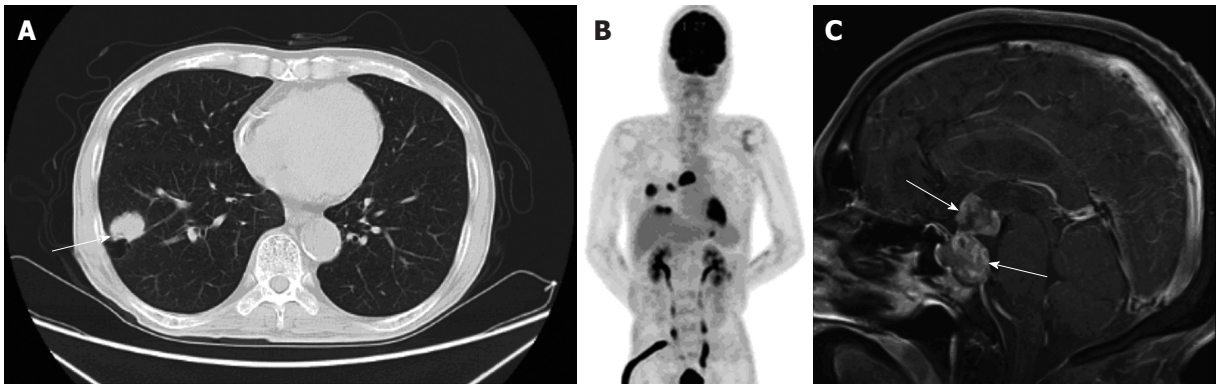

Figure 1 A 74-year-old man with a smoking history presented with anorexia, vomiting, fever and thirst. A: Chest computed tomography reveals a mass on the right upper lobe (white arrow); B: Fluoro-2-deoxy-D-glucose (FDG) positron emission tomography image shows FDG accumulation at the primary site, hilar and mediastinal lymph nodes, and liver; C: Sagittal view of gadolinium-enhanced brain magnetic resonance imaging shows irregularly enhanced dumbbell-shaped tumor in the intrasellar and suprasellar areas (white arrows).

< 0.07 IU/mL, follicle stimulating hormone of 0.6 mIU/mL, testosterone of 2.51 ng/mL (NR: 1.31-8.71 ng/mL), growth hormone of 1.00 ng/mL, insulin-like growth factor 1 of 11.0 ng/mL (NR: 121-436 ng/mL), adrenocorticotropic hormone of 2.4 pg/mL (NR: 1.0-5.2 pg/mL), and urinary free cortisol < 0.5 μg/d (NR: 11.2-80.3 μg/d), suggesting panhypopituitarism including secondary adrenal failure. The patient had symptoms of thirst, polyposia and increased urination (over 3 L/d). Laboratory investigations revealed low urine specific gravity of 1.004, plasma osmolarity of 319 mOSM, low urine osmolarity of 194 mOSM (< 300 mOSM/kg), and the ratio was 0.686 (< 1). The administration of 1-desamino-8-*D*-arginine vasopressin resulted in urine volume reduction and urine condensation. A definite diagnosis of diabetes insipidus was made following these laboratory investigations and physical examination.

Computed tomography of the chest showed a mass on the right upper lobe and swelling of mediastinal lymph nodes (Figure 1A). Percutaneous needle biopsy diagnosed a poorly differentiated adenocarcinoma. Brain magnetic resonance imaging showed a dumbbell-shaped gadolinium-enhanced tumor in the pituitary (Figure 1B). 2-^{18}F-fluoro-2-deoxy-*D*-glucose (^{18}F-FDG) positron emission tomography (PET) revealed an increased accumulation of ^{18}F-FDG in the lung, pituitary, liver and mediastinal lymph nodes (Figure 1C). A definite diagnosis of primary lung cancer stage Ⅳ (cT1bN2M1b) was made. However, the patient had pan hypopituitary symptoms with a performance status of 4. Therefore, palliative radiation therapy was administered for the solitary pituitary mass in order to improve the patient's quality of life. Following radiotherapy of 50 Gy/25 fr, the patient experienced an improvement in appetite and nausea. On the 58th hospital day, the patient was discharged from our institution due to improving quality of life. However, he died as a result of severe pneumonia and disseminated intravascular clotting due to progression of the primary disease 10 d after discharge. Evaluation of morbid anatomy was performed following permission from the bereaved family. The immunohistochemical findings of primary lung tumor and solitary pituitary metastasis revealed marked positive staining of chromogranin A, CD56 (NCAM) and synaptophysin. The final diagnosis was solitary pituitary metastasis resulting from LCNEC.

DISCUSSION

Postmortem studies have shown that pituitary gland metastasis is observed in 0.14% to 28.1% of all brain metastases and patients with breast and lung cancer account for approximately two thirds of these metastases[1]. Although solitary pituitary metastasis is an extremely rare condition, the histology of adenocarcinoma or small-cell carcinoma is often seen in patients with lung cancer[2]. In our patient, the diagnosis was poorly differentiated adenocarcinoma by percutaneous needle biopsy, however, a definite diagnosis of LCNEC was subsequently made. The diagnosis of LCNEC is difficult to establish based on small biopsies or cytology, because there is a limit to evaluating a neuroendocrine pattern morphologically[3]. Recently, Shimada *et al*[4] proposed the term "high-grade neuroendocrine carcinoma-probable LCNEC (HG-pLCNEC)" from biopsy findings and aimed to elucidate the clinical features compared with SCLC, suggesting that therapeutic efficacy in HG-pLCNEC is similar to that of SCLC. The diagnostic criteria of LCNEC are problematic in biopsy specimens, and our patient was initially diagnosed with poorly differentiated adenocarcinoma.

The patient developed the primary symptom of panhypopituitarism due to pituitary metastasis. Radiologically, it is important to differentiate between pituitary metastasis derived from primary lung cancer and pituitary carcinoma. As primary pituitary carcinoma has an occurrence of 0.1%[5,6], its definite diagnosis requires pathological evidence of a pituitary mass. In our case, the pituitary mass was not treated surgically due to the patient's poor performance status.

A retrospective study demonstrated that 10 of 1639 lung cancer patients (0.61%) had the initial manifestation of central diabetes insipidus[7]. Panhypopituitarism due to solitary pituitary metastasis is relatively rare, therefore,

may be overlooked as an initial symptom of lung cancer. Although multiple brain metastases due to LCNEC are a frequent occurrence, a single pituitary metastasis may also occur. These symptoms can be masked by systemic complications of malignancy, including nonspecific symptoms (malaise, weakness, vomiting, weight loss) and central nervous system involvement. There may be a number of patients with primary cancer whose pituitary insufficiency is not appropriately diagnosed. The possibility that lung cancer has metastasized to the pituitary gland should be considered, and the administration of appropriate endocrine replacement in a timely manner can improve symptoms due to these lesions.

Clinical physicians should be aware of potential initial manifestations such as endocrine abnormalities including panhypopituitarism and diabetes insipidus due to solitary pituitary metastasis.

COMMENTS

Case characteristics

A 74-year-old man with a smoking history presented with anorexia, vomiting, fever and thirst.

Clinical diagnosis

The diagnostic criteria of large cell neuroendocrine carcinoma (LCNEC) are problematic in biopsy specimens, and the present case was initially diagnosed with poorly differentiated adenocarcinoma.

Differential diagnosis

Panhypopituitarism due to solitary pituitary metastasis is relatively rare, therefore may be overlooked as an initial symptom of lung cancer.

Treatment

Clinical physicians should be aware of potential initial manifestations such as endocrine abnormalities including panhypopituitarism and diabetes insipidus due to solitary pituitary metastasis.

Experiences and lessons

This case demonstrates that an endocrine abnormality such as panhypopituitarism could be an initial manifestation of LCNEC.

Peer review

The pituitary metastasis of LCNEC is a very rare condition and the message derived from the case is clinically useful.

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