

Central Diabetes Insipidus: An Unusual Initial Presentation of Lung Cancer

Szu-Chun Yang, Chien-Chung Lin, Chin-Chung Tseng*, Han-Yu Chang

Central diabetes insipidus (DI) rarely occurs as the initial presentation of lung cancer. Lung cancer patients with the presentation of central DI often exhibit other central nervous system (CNS) symptoms. We reported a 54-year-old man with polyuria for 3 months. His physical and neurological examination results were unremarkable. Water deprivation test confirmed the diagnosis of central DI. A magnetic resonance image of the brain revealed multiple lesions consistent with metastases, including a lesion in the posterior lobe of the pituitary gland. A chest radiograph showed a nodule in the left upper lobe of the lung. Computed tomography-guided needle biopsy of the nodule confirmed the diagnosis of lung adenocarcinoma. The patient was treated with a nasal spray of desmopressin, cyber-knife radiosurgery followed by whole brain radiotherapy, and chemotherapy. His polyuria improved markedly and he was well without significant complications. In conclusion, if a patient initially presents with central DI without other CNS symptoms, physicians should consider the possibility of metastatic disease, especially that resulting from lung cancer. (*Thorac Med* 2010; 25: 305-310)

Key words: diabetes insipidus, lung cancer, pituitary metastasis

Introduction

Central diabetes insipidus (DI), occurring from injury to the hypothalamic-neurohypophyseal system, commonly results from head trauma, neoplasms, and granulomatous disease [1]. Pituitary metastasis frequently results from breast and lung cancer [2]. However, patients with pituitary metastases are often asymptomatic, and the metastasis is discovered accidentally. Symptoms of central DI are often complicated

with other central nervous system (CNS) symptoms that are caused by multiple CNS metastases. Central DI as the initial presentation of lung cancer has hitherto been reported in only a limited number of cases [3-6]. In most of these patients, central DI was accompanied by other neurological symptoms. We report a patient in whom the initial presentation of lung adenocarcinoma was central DI without other neurological symptoms.

Division of Pulmonary Medicine and Nephrology*, Department of Internal Medicine, National Chen Kung University Hospital, Tainan, Taiwan

Address reprint requests to: Dr. Chien-Chung Lin, Division of Pulmonary Medicine, Department of Internal Medicine, National Cheng Kung University Hospital, No. 138, Sheng-Li Rd., Tainan 704, Taiwan

Case Report

A 54-year-old non-smoking man presented to our nephrology outpatient department with a 3-month history of polyuria and polydipsia. He did not experience cough, shortness of breath, feverishness, or weight loss, and had an uneventful medical history except for diabetic mellitus. He took 500 mg of oral metformin twice daily.

The physical examination was unremarkable. Neurological and visual field examinations revealed no focal deficit. Initial investigation showed normal plasma glucose, and his hemoglobin A1c was 7.4%. His 24-hour urine volume was 5,800 ml; urine osmolality, 92 mOsm/kg; and plasma sodium, 149 mmol/L. These levels were consistent with those for DI. We therefore performed a water deprivation test (Table 1). After administration of desmopressin, urine osmolality increased (and urine output concomitantly decreased) by more than 100%. This result confirmed the diagnosis of central DI [7]. The patient's growth hormone, adrenocorticotrophic hormone, prolactin, follicle-stimulating hormone, luteinizing hormone, and

thyroid stimulating hormone levels were within normal limits.

A magnetic resonance image (MRI) of the brain showed multiple lesions consistent with metastases, including a lesion in the posterior lobe of the pituitary gland (Figure 1). Chest radiographs showed a nodule in the left upper lobe of the lung (Figure 2). A chest computed tomographic (CT) scan (Figure 3) showed a 2.8 cm × 1.9 cm speculated nodule in the left upper lobe of the lung with several fine nodules in both lungs, indicating metastases.

We performed a CT-guided needle biopsy of the nodule; the morphology confirmed the diagnosis of lung adenocarcinoma (Figure 4). A technetium-99m whole body bone scan showed multiple bony metastases. The disease was classified as stage IV according to the tumor-node-metastasis stage ($T_{1b}N_0M_{1b}$).

The patient was treated with a nasal spray of 10 µg desmopressin twice daily, which markedly improved his polyuria. He underwent cyberknife radiosurgery (12-24 Gy; pituitary metastatic tumor, 24 Gy) followed by whole-brain radiotherapy (3000 cGy/10 fractions for 2 weeks) and 4 cycles of cisplatin (60 mg/m²) and

Table 1. Water deprivation test

Time (hr)	Plasma osmolality (mOsm/kg)	Plasma sodium (mmol/L)	Urine osmolality (mOsm/kg)	Urine volume (ml)	Urine sodium (mmol/L)
0	295	141	112	250	18
Subcutaneous desmopressin 2.5 µg					
0.5	291	143	--	110	--
1	297	142	503	80	86
2	288	143	510	60	112
3	290	143	--	0	--
4	291	144	544	80	110

--: Not applicable

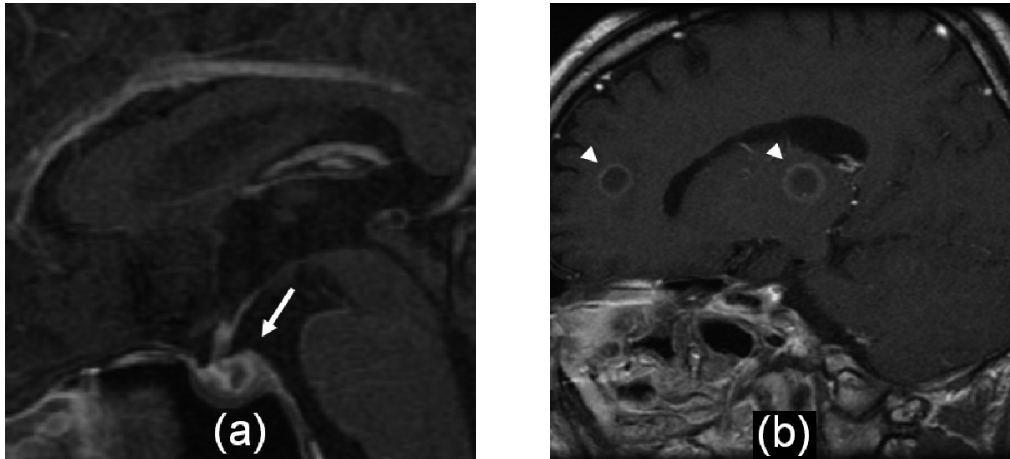


Fig. 1. MRI of the brain (sagittal view) shows: (a) A peripherally enhanced lesion (arrow) in the posterior lobe of the pituitary gland on a post-Gd T1-weighted image (T1WI). (b) Several lesions (arrow heads) with rim-enhancement are seen on a post-Gd T1WI, located at the right thalamus and the right frontal lobe. These findings are consistent with the presence of metastases.

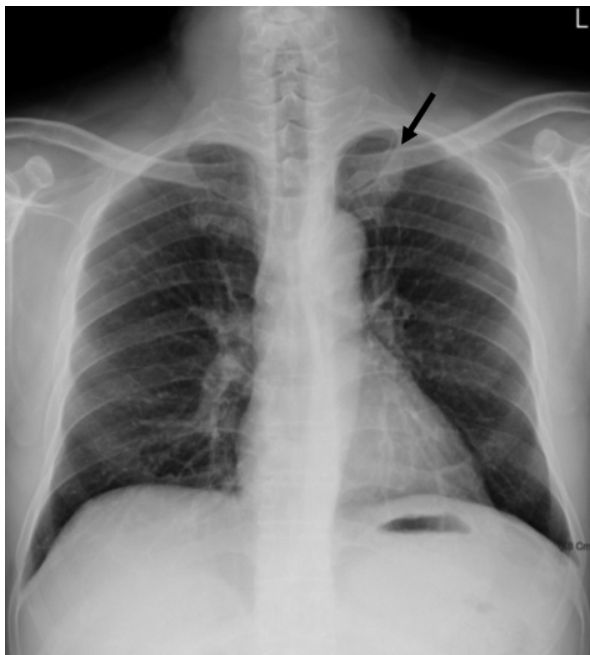


Fig. 2. Chest radiograph of the patient shows an obscure nodule (arrow) in the left upper lobe of the lung.

pemetrexed (500 mg/m²). As of this writing, the patient was well and had not developed significant complications.

Discussion

Pituitary metastases are observed at the time of autopsy in 1% to 5% of patients with advanced cancer [8]. The breast and lung are the most frequent primary sites in woman (66.0%) and men (62.9%), respectively [2]. However, pituitary metastases in most patients remain asymptomatic and are usually discovered as a postmortem finding [2]. More than 60% of pituitary metastases primarily affect the posterior lobe, 10% to 20% affect the anterior lobe, and only 1 to 2% involves the infundibulum [2]. The posterior pituitary receives blood supply from the systemic circulation, whereas the anterior pituitary is supplied by its portal system [3]. Symptoms of central DI are rare (6.8%) among patients with pituitary metastases [2]. These patients often experience other CNS complications, such as headache, cranial nerve palsy, and visual changes [9-11] that are caused by multiple CNS metastases.

Polydipsia, polyuria with hypotonic urine, low serum antidiuretic hormone (ADH) levels,

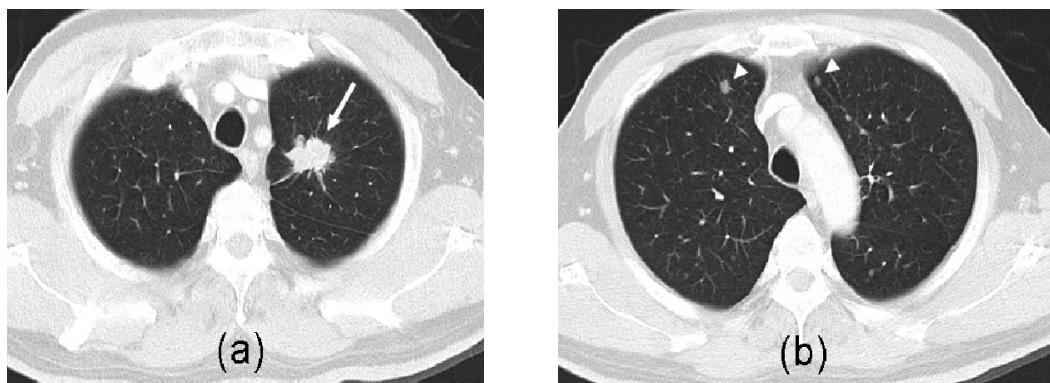


Fig. 3. CT scan of the chest. (a) A speculated nodule (arrow) in the left upper lobe, 2.8 cm \times 1.9 cm in size. (b) Innumerable nodular lesions in both lungs (arrow heads).

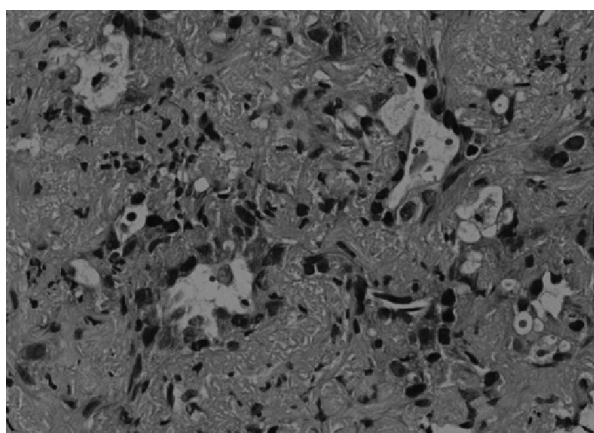


Fig. 4. Section shows adenocarcinoma composed of tumor cells with hyperchromatic nuclei and pale cytoplasm arranged in a glandular pattern (hematoxylin & eosin, 200 \times)

and correction of symptoms upon exogenous ADH administration are the clinical hallmarks of central DI. Among patients with central DI, 10% to 20% have pituitary metastases [1]. CT scans cannot detect pituitary abnormalities in many patients; however, MRI scans are an effective tool to identify pituitary metastases [12]. In MRI of the pituitary tumor, T1-weighted images do not show the normal physiological bright spot for the posterior lobe, and post-gadolinium (Gd) imaging reveals abnormal enhancement in the posterior lobe [13]. On the

basis of factors such as patient age of more than 50 years, rapid onset or progression of symptoms, presence of cranial nerve palsy, history of malignancy, and failure of bromocriptine treatment, clinicians can differentiate pituitary metastases from pituitary adenomas [6, 14].

Administration of exogenous ADH usually improves the symptoms of central DI. However, most patients require lifelong administration because of the destructive, irreversible nature of the pituitary lesions. Resolution of central DI after brain radiotherapy has been observed in a few cases [12, 15-16]. Piedra *et al.* also reported a patient in whom the DI medication could be reduced 3 months after gamma knife surgery for a solitary metastasis in the pituitary stalk [17]. Early radiotherapy or surgical decompression do not change the overall poor prognosis associated with pituitary metastases. However, they may improve the quality and quantity of life of symptomatic patients [10].

In conclusion, if a patient initially presents with central DI but no other CNS symptoms, physicians should consider metastatic disease from lung cancer.

References

1. Kimmel DW, O'Neill BP. Systemic cancer presenting as diabetes insipidus. *Cancer* 1983; 52(12): 2355-8.
2. Teeares RJ, Silverman EM. Clinicopathologic review of 88 cases of carcinoma metastatic to the pituitary gland. *Cancer* 1975; 36(1): 216-20.
3. Krol TC, Wood WS. Bronchogenic carcinoma and diabetes insipidus: Case report and review. *Cancer* 1982; 49(3): 596-9.
4. Dabrowski A, Okrzeja Z. Diabetes insipidus as the initial symptom in bronchial carcinoma. *Wiad Lek* 1972; 25(12): 1093-5. [In Polish, English abstract]
5. Sosovec V, Stopek D. Diabetes insipidus as a first clinical manifestation of inconspicuous bronchogenic carcinoma. *Vnitr Lek* 1972; 18(8): 806-10. [In Slovak, English abstract]
6. Reddy P, Kalemkerian GP. Unusual presentations of lung cancer: Case 1. Diabetes insipidus as the initial manifestation of non-small-cell lung cancer. *J Clin Oncol* 2002; 20(23): 4597-8.
7. Robertson, GL. Disorders of neurohypophysis. In: E Braunwald, AS Fauci, DL Kasper, *et al.* editors. *Harrison's Principles of Internal Medicine*, 16th ed. New York: McGraw-Hill; 2005: 2099-100.
8. Chiang MF, Brock M, Patt S. Pituitary metastases. *Neurochirurgia* 1990; 33: 127-31.
9. Asberg TM Jr, Kay M, Sternau L. Metastatic tumors to the pituitary. *Am J Ophthalmol* 1995; 119: 779-85.
10. Morita A, Meyer FB, Laws ER. Symptomatic pituitary metastases. *J Neurosurg* 1998; 89: 69-73.
11. Branch CL, Laws ER. Metastatic tumors of the sella turcica masquerading as primary pituitary tumors. *J Clin Endocrinol Metab* 1987; 65(3): 469-74.
12. Matsuda R, Chiba E, Kawana I, *et al.* Central diabetes insipidus caused by pituitary metastasis of lung cancer. *Intern Med* 1995; 34(9): 913-8.
13. Koshimoto Y, Maeda M, H Naiki, *et al.* MR of pituitary metastasis in a patient with diabetes insipidus. *Am J Neuroradiol* 1995; 16(4 Suppl): 971-4.
14. Guillén-Ponce C, Garrido-López MP, Molina-Garrido MJ, *et al.* Panhypopituitarism as the first manifestation of a lung cancer. *Clin Transl Oncol* 2007; 9(1): 53-5.
15. Yap HY, Tashima CK, Blumenschein GR, *et al.* Diabetes insipidus and breast cancer. *Arch Intern Med* 1979; 139: 1009-11.
16. Nosedá A, Louis O, Mockel J, *et al.* Diabetes insipidus from metastatic oat cell carcinoma: Recovery after brain irradiation. *Am J Med Sci* 1985; 289(1): 27-30.
17. Piedra MP, Brown PD, Carpenter PC, *et al.* Resolution of diabetes insipidus following gamma knife surgery for a solitary metastasis to the pituitary stalk. *J Neurosurg* 2004; 101(6): 1053-6.

中樞性尿崩症：肺癌一不尋常的最初表現

楊思雋 林建中 曾進忠* 張漢煜

肺癌最初以中樞性尿崩症為表現的實為罕見。這些患者通常合併有其它中樞神經系統的症狀。我們在此報告一個病例：一位五十四歲的男性，主訴多尿已三個月，住院接受理學及神經學檢查皆正常。經限水試驗（water deprivation test）證實是中樞性尿崩症（central diabetes insipidus）。腦部核磁共振影像發現多處轉移性病灶，包括一位於腦垂腺後葉的病變。胸部X光片看到一左上肺葉結節。電腦斷層導引細針切片術證實它是肺腺癌。之後患者接受desmopressin鼻噴劑，數碼導航刀暨全腦部放射線治療及化學治療。多尿的症狀明顯地改善而且無相關的併發症。我們藉由這樣的病例報告，對於最初表現僅是中樞性尿崩症的患者，即使無中樞神經系統的症狀，臨床醫師亦須考慮腦部轉移的癌症，尤其是肺癌的可能性。*(胸腔醫學 2010; 25: 305-310)*

關鍵詞：尿崩症，肺癌，腦垂腺轉移

成功大學附設醫院內科部 胸腔內科，*腎臟科

索取抽印本請聯絡：林建中醫師，成功大學附設醫院內科部 胸腔內科，704台南市北區勝利路138號