To the Editor: A 63-year-old man was transferred to the Department of Neurology for changes in personality and social withdrawal on March 03, 2015. He appeared to be unwilling to talk to his family, whereas he had previously been social and caring. He exhibited unusual behavior, dressing his clothes inside out, and impulsively eating foods. He also had excessive daytime sleepiness. However, the patient himself was unaware of this behavior. He was suspected as having herpes simplex encephalitis in the local hospital and was then administered acyclovir intravenously for 21 days. The patient’s condition did not improve.

The patient was healthy, except for cerebral infarction 15 years ago, which resulted in mildly weakened muscle strength of the right lower limb. He regularly takes indapamide 2.5 mg q.d. and controls blood pressure at 140–150/80–90 mmHg (1 mmHg = 0.133 kPa). He had no history of allergies, mental disorders, trauma, and surgery. He had a 500 pack-year history of cigarette smoking but had quit 15 years earlier. He drank 65 g of alcohol/day but also quit 15 years ago. There was no known relevant family history.

His vital signs were normal on a physical examination. No lesions were noted on the mouth or oropharynx. A tough and movable mass in diameter). Examination of the cardiac, pulmonary, and abdominal systems was unremarkable.

A neurological examination showed that the patient was alert, with normal orientation and comprehension. His speech was fluent without paraphasias, but he had a lack of motivation. He could perform serial subtractions of the numbers 7 from 100. He could register and repeat the names of three objects, but he recalled none of them after 3 min. His pupils were equal in size, symmetric, and reactive to light and accommodation. Examinations of the cranial nerves showed that they were almost normal. Strength and reactive to light and accommodation. Examinations of the cranial nerves showed that they were almost normal. Strength and coordination examinations were normal. A mini-mental state examination showed 20 points, which suggested moderate dementia. The memory quotient score was 48 points, which indicated severe memory impairment.

Magnetic resonance imaging (MRI) of the head on March 4 showed abnormal signals in the bilateral hippocampus of temporal lobes, medial frontal gyrus, hypothalamus, basal ganglia region, posterior limb of the internal capsule, and corpus callosum on T2-weighted [Figure 1a] and fluid attenuated inversion recovery imaging. There was slight abnormal contrast-enhancement in MRI with gadolinium enhancement. Magnetic resonance spectroscopy showed an increased lactic acid peak and a slightly low NAA/creatine value. An electroencephalogram was mild to moderately abnormal, showing diffuse slow activity without epileptiform discharges.

A lumbar puncture was performed on March 9. Additional laboratory reports showed abnormal results for electrolyte levels, renal function, and paraneoplastic antibodies, anti-Hu (+) and anti-PNMA2 (+). A smear of the cerebrospinal fluid showed no bacteria, fungi, or tumor cells. The patient had hyponatremia without edema. Because serum osmolality was low and urine osmolality was greater than serum osmolality, the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) was diagnosed. We treated him with restriction of fluid (1000–1500 ml/d) and oral sodium chloride powder (2 g, t.i.d.).

Cervical ultrasound showed no abnormalities of the thyroid. Multiple solid nodules were observed on the left side of the carotid artery, and the largest was 3.7 cm x 2.2 cm, with a smooth margin, regular shape, uneven echo, and high blood flow signal. Chest computed tomography (CT) showed distention in the edge of the right vocal cords. CT of the abdomen was normal.

Department of Thoracic Surgery performed a biopsy of the left cervical mass on March 10. A positron-emission tomography/CT (PET/CT) scan on March 11 showed a hypermetabolic (remarkable F-18 fluorodeoxyglucose uptake) soft tissue mass image in the right posterior limb of the internal capsule, and corpus callosum on T2-weighted [Figure 1a] and fluid attenuated inversion recovery imaging. There was slight abnormal contrast-enhancement in MRI with gadolinium enhancement. Magnetic resonance spectroscopy showed an increased lactic acid peak and a slightly low NAA/creatine value. An electroencephalogram was mild to moderately abnormal, showing diffuse slow activity without epileptiform discharges.

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posterior wall of the hypopharynx (2.5 cm × 2.6 cm) involving the glottis. Simultaneously, a whole-body PET/CT examination ruled out other related carcinomas, such as small cell lung cancer and testicular tumor.

Histologically, the tumor was mainly composed of nests of epithelioid cells with oval, enlarged nuclei and a slight cytoplasm, with the scattered distribution of lymphocytes. Some syncytial cells were enlarged and cytologically atypical. Vesicular nuclei were commonly seen with a distinct nucleolus and mitotic figures [Figure 1b]. According to immunohistochemical analysis, the tumor cells were positive for the epithelial markers cytokeratin 5 (CK5) and CK8. The neuroendocrine markers chromogranin, syntophysin, and neuron-specific enolase were negative. The squamous cell marker P63 was partially positive. Transcription of Epstein–Barr virus-encoded nonpolyadenylated RNAs is present in most nasopharyngeal carcinomas (NPCs),[1] but it was negative in our patient. In spite of this, the pathological findings are most consistent with metastatic NPC.

SIADH, as a manifestation of paraneoplastic syndrome, mainly occurs because the tumor secretes substances that mimic normal hormones. Nonetheless, in our case, the neuroendocrine markers were negative. Therefore, SIADH of our patient may be explained by immune-mediated dysfunction of the hypothalamus. In addition, limbic encephalitis, as a paraneoplastic neurological disorder, is immune-mediated. The mechanism entails tumor antigen expression being identical to the neural antigen that is normally expressed in the nervous system. However, the immune system identifies the normal neural antigen as foreign and mounts an immune attack.[2]

In conclusion, neurological symptoms may precede the clinical manifestation of primary NPC or metastases, such as swelling of the lymph nodes in the neck. When paraneoplastic limbic encephalitis occurs, NPC should not be ignored while evidence of Epstein–Barr virus has not been found. This case underscores the importance of a comprehensive assessment and a well-grounded diagnosis of diseases.

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Conflicts of interest
There are no conflicts of interest.

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