Case Report

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Paraneoplastic limbic encephalitis cured with nephron-sparing surgery in a patient with clear cell renal cell carcinoma: a case report

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Abstract

Paraneoplastic limbic encephalitis (PLE) in association with clear cell renal cell carcinoma has never been reported in China. We herein describe a 54-year-old man with a 1-week history of headache and a 3-day history of psychiatric symptoms. Slight nuchal rigidity was found by physical examination. Imaging studies of the head were normal. Blood and cerebrospinal fluid antibody testing were both positive for N-methyl-D-aspartic acid antibodies. Subsequent contrast-enhanced computed tomography revealed a 5.2- × 4.2-cm left kidney mass with intense enhancement. Emergent laparoscopic nephron-sparing surgery was successfully performed. Immunohistochemistry revealed clear cell renal cell carcinoma. The patient's status improved after the surgery, and he was discharged after 1 month of hospitalization. At the 6-month follow-up, magnetic resonance imaging showed no recurrence, and the patient was living independently. This case indicates the potential effect of nephron-sparing surgery in the treatment of PLE. Tumor screening should be performed early in patients with suspected PLE. Early surgical resection of the primary tumor can improve patients' prognosis.

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Introduction

Paraneoplastic limbic encephalitis (PLE) is a rare neuropsychiatric condition related to malignancies without direct neoplastic invasion into the nervous system (<1%).[1] Corsellis et al.[2] first found that PLE is associated with malignant tumors in 1968. The syndrome of PLE is typically characterized by an altered mental status, subacute cognitive dysfunction, memory impairment, sleep disturbances, seizures, and psychiatric features that include depression, anxiety, and hallucinations. The diagnosis of PLE should be based on the presence of cancer and a classical neurological syndrome with well-characterized onconeural antibodies.[3] Therefore, the diagnosis is often difficult; PLE is usually diagnosed in the weeks to months following a diagnosis of neoplasia because similar symptoms are caused by many other diseases. Signs of a neurologic disorder may also be the first manifestation of an unrecognized malignancy.[4]

An association between limbic encephalitis and renal cell carcinoma is extremely rare. Two cases of limbic encephalopathy related to renal cell carcinoma were first diagnosed at autopsy.[5] Subsequently, Bell et al.[6] and Harrison et al.[7] each reported one case of renal cell carcinoma that was associated with limbic encephalitis and cured with radical nephrectomy. We herein describe a patient with renal cell carcinoma in whom the clinical progression of PLE was reversed using nephron-sparing surgery. To our knowledge, this is the first case of PLE cured with nephron-sparing surgery in China.

Case report

A 54-year-old man presented with a 1-week history of headache and a 3-day history of mental disorder. The headache manifested in the whole head with mild to moderate distending pain. The mental disorder included dysphoria, excitement, and speaking gibberish. Slight nuchal rigidity was found by physical examination. Imaging studies of the head were normal. Two cerebrospinal fluid examinations indicated a normal pressure, glucose level and chloride level. After 1 week of treatment with antivirals and nutritional, neurologic, and immunomodulatory treatments, the symptoms worsened. Blood and cerebrospinal fluid antibody testing were both positive for N-methyl-D-aspartic acid (NMDA) antibodies. The possibility of PLE was suspected. Therefore, a computed tomography scan was performed to assess for an occult tumor. Computed tomography revealed a 5.2- $\times$ 4.2-cm left kidney mass with intense enhancement (Figure 1). Emergent laparoscopic nephron-sparing surgery was successfully performed. Pathological examination showed Fuhrman grade 2 clear cell renal cell carcinoma measuring $5.5 \times 5.0 \times 4.0$ cm (Figure 2). The symptoms of PLE gradually improved, and the patient was discharged after 1 month. At the 6-month follow-up,

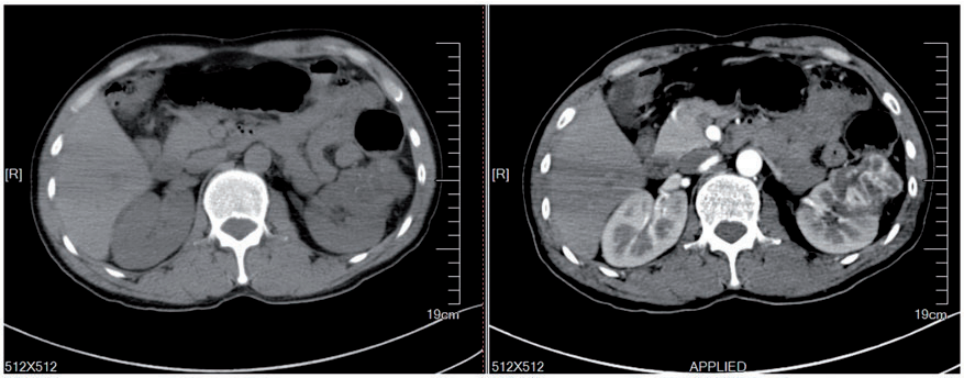

Figure 1. Computed tomography image showing renal cell carcinoma in the left kidney.

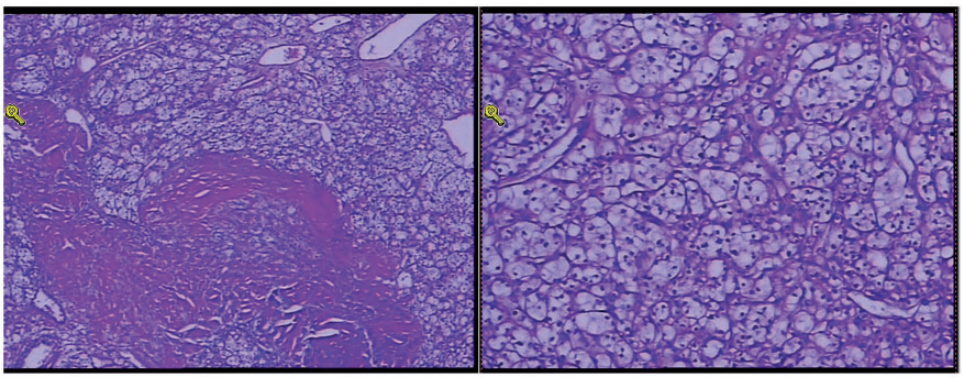

Figure 2. Hematoxylin and eosin-stained sections showing clear cell renal cell carcinoma.

no recurrence was found and the patient was living independently.

Discussion

The malignancies most frequently related to PLE are small cell lung cancer and testicular cancer.[8] An association between PLE and renal cell carcinoma is extremely rare. To our knowledge, our report describes the first case of PLE cured with nephron-sparing surgery in a Chinese patient with renal cell carcinoma. As many as 10% to 40% of patients with renal cell carcinoma have paraneoplastic syndromes.[9] However, endocrine or neuroendocrine effects rather than neurologic symptoms are often present in these patients. These paraneoplastic syndromes include high blood pressure, anemia, fever, weight loss, cachexia, polycythemia, abnormal liver function, hypercalcemia, high blood sugar, rapid blood sedimentation, neuromuscular disease, amyloidosis, excessive breast disease, and coagulopathies. The occurrence rate of central and peripheral nervous syndromes is only 0.5% to 1.0% in patients with renal cell carcinoma.[10] These syndromes are not

associated with the tumor stage. These neurological syndromes are frequently the main complaint associated with a potential tumor, and the physician's awareness of these syndromes may contribute to the early diagnosis of cancer.[11]

Limbic encephalitis is a type of inflammation in the limbic system, which is involved in motivation, memory behavior, and emotion. The etiology and mechanism of PLE remain unclear, but the main theory is an autoimmune mechanism. Antigens located in the central nervous system may be similar to antigens detected ectopically in malignancies. An assay of antibodies to onconeural antigens in the serum or cerebrospinal fluid may help to diagnose PLE. However, negative classic antibody and cerebrospinal fluid results do not rule out the diagnosis of PLE. Studies have shown that only approximately 60% of patients are positive for antibodies.[12] Antibody-positive patients can be initially divided into two groups. The first group comprises patients with antibodies to intracellular neural antigens (including antibodies to Hu, Ma2, and amphiphysin). The second group comprises patients with antibodies to neural cell membrane antigens (including antibodies to NMDA receptors and voltage-gated potassium channels). There are also reports of PLE associated with other antibodies that cannot be classified into these two groups.[13] The detection of specific antibodies takes time, but it is helpful for diagnosis and treatment. Compared with disorders involving antibodies to intracellular antigens, immunotherapy has a stronger curative effect on disorders involving antibodies to neural cell membrane antigens.[14] Additionally, if the clinician highly suspects PLE, imaging examination of the thorax, abdomen, and pelvis should be done early. Initial imaging findings are often normal, in which case a positron emission tomography scan may be useful.[15] Treatment of PLE consists of tumor resection and immunotherapy involving steroids, intravenous immunoglobulin, or plasma exchange. The present case indicates that if PLE is diagnosed early, emergent nephron-sparing surgery for renal cell carcinoma can effectively treat the limbic encephalitis.

To the best of our knowledge, this is the first case in which PLE was cured using nephron-sparing surgery for clear cell renal cell carcinoma in China. This case indicates the potential effect of nephron-sparing surgery in the treatment of PLE. Doctors should improve their understanding of this disease. Tumor screening should be performed early in patients suspected to have PLE. Early surgical resection of the primary tumor can improve patients' prognosis.

Abbreviations

PLE, paraneoplastic limbic encephalitis; NMDA, N-methyl-D-aspartic acid.

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Authors' contributions

Data collection: Lai, Xie.
Data analysis: Zhu, Deng.
Manuscript writing: Zhu, Deng.
Manuscript interpretation and editing: Tan, Zhu.
All authors read and approved the final manuscript.

Availability of data and material

The data are contained within the manuscript, and any missing details will be available from the corresponding author on reasonable request.

Consent for publication

The patient provided written informed consent for his case report to be published.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Ethics approval and consent to participate

This report was approved by the Ethics Committee of The Affiliated Ganzhou Hospital of Nanchang University (201702654), and the patient provided informed consent.

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