Case Report

Primary renal well-differentiated neuroendocrine tumors with lymph node metastasis: A case report and literature review

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Abbreviations & Acronyms
CT = computed tomography
NEC = neuroendocrine carcinoma
NET = neuroendocrine tumors
RCC = renal cell carcinoma
WD = well-differentiated
WDNETs = well-differentiated neuroendocrine tumors

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Introduction: Well-differentiated neuroendocrine tumors of the kidney are rare and generally less aggressive than renal cell carcinoma, although metastasis is still present at the time of diagnosis. Surgical resection remains the preferred treatment, even in cases with lymph node metastases.

Case presentation: We present the case of a 38-year-old female with a right renal WDNET and lymph node metastasis who underwent laparoscopic radical nephrectomy with lymphadenectomy. Pathological examination confirmed metastasis in 9 out of 11 lymph nodes. Immunohistochemistry results were positive for synaptophysin and chromogranin, with a Ki-67 index of less than 10%. No recurrence was observed after 36 months.

Conclusion: Well-differentiated neuroendocrine tumors are rare, with non-specific clinical and imaging characteristics, requiring immunohistochemical analysis for diagnosis. Surgical resection is the treatment of choice, and long-term follow-up is essential.

Key words: kidney neoplasms, lymph node excision, lymphatic metastasis, nephrectomy, neuroendocrine tumors.

Keynote message

Well-differentiated neuroendocrine tumors of the kidney are rare and usually low in malignancy, but they can present with metastasis, particularly to lymph nodes. Surgical resection is the preferred treatment, and strict postoperative monitoring is crucial due to the high risk of recurrence.

Introduction

NETs originate from neuroendocrine cells and peptidergic neurons, commonly located in the respiratory and gastrointestinal systems.[1] WDNETs are rare, making up less than 1% of all NET cases, and are linked to a more favorable prognosis compared to NEC.[2] For patients with WDNETs, even those with lymph node metastases, surgical resection is preferred.[3] In September 2021, our department diagnosed a case of WDNETs of the kidney with lymph node metastasis, with no recurrence observed after 36 months of follow-up. This case report retrospectively reviewed the patient's medical records, diagnosis, and treatment, integrating findings with a literature review to provide insights into WDNETs.

Case presentation

A 38-year-old female presented with a 10-day history of intermittent right flank pain. Physical examination revealed no significant abnormalities and gross hematuria was absent. There were no abnormal findings observed in the laboratory examinations. CT scan with contrast enhancement in the venous phase demonstrated a well-defined, mildly enhancing mass in the right kidney measuring approximately 87 × 98 mm. Additionally, a single enlarged lymph node measuring 40 × 17 mm was identified (Fig. 1). Vascular assessment showed that the right renal arteries, branches, renal vein, and inferior vena cava were all normal. Following the preoperative assessment, a diagnosis of a right renal tumor, with a potential diagnosis of

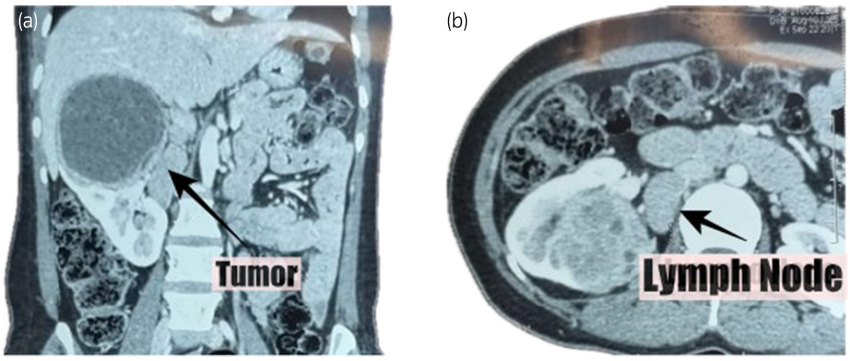

Fig. 1 Results of abdominal computed tomography. (a) A well-circumscribed and slightly heterogeneous enhancing mass in the venous phase. (b) A single enlarged lymph node measuring 40 × 17 mm was identified.

RCC and suspected lymph node metastasis, was established. In light of the suspicion of RCC and the potential for surgical intervention, a preoperative biopsy was not performed.

Following this, a right retroperitoneal laparoscopic radical nephrectomy was conducted, during which the enlarged lymph node at the renal hilum was excised (Fig. 2). Lymphadenectomy was performed using a template that included the renal hilar, paracaval, and precaval lymph nodes.

Gross inspection of the resected kidney displayed a tan-brown, hemorrhagic, and nodular mass that involved the renal sinus and extended into the renal vein (Fig. 3). Pathological examination 9 out of the 11 resected lymph nodes confirmed metastatic involvement including the enlarged lymph node located in the renal hilum. Microscopically it comprises ribbon and trabeculae of uniform tumor cells with 3 mitoses/10HPF. Immunohistochemical analysis was negative for PAX8 and RCC but positive for synaptophysin and chromogranin, with a Ki-67 index below 10% (Fig. 4). The final diagnosis was established as pT3aN1 WDNET of the kidney. At 36 months after surgery, follow-up CT scan showed no evidence of recurrent tumor. The patient continues to be monitored with regular follow-up visits every 3–6 months.

Discussion

NETs are exceedingly rare within the urinary system, with renal-origin NETs being even more uncommon.[4] Previously, NETs were commonly referred to as carcinoid tumors.

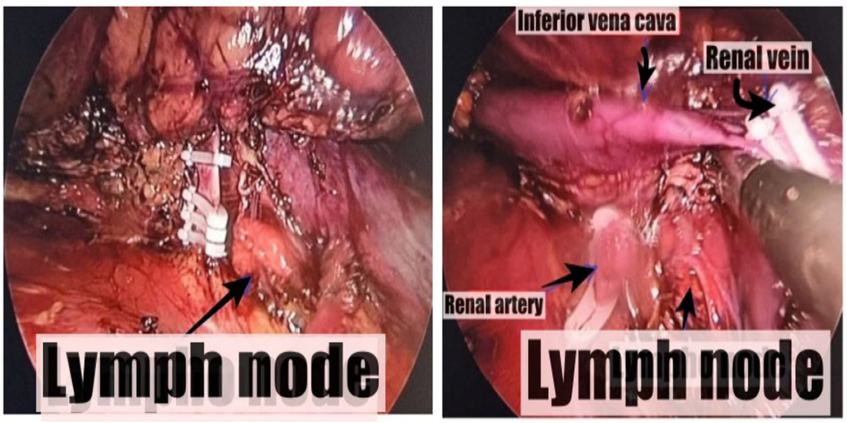

Fig. 2 Images of lymph node excision performed via laparoscopic surgery through a retroperitoneal approach, including relevant anatomical landmarks.

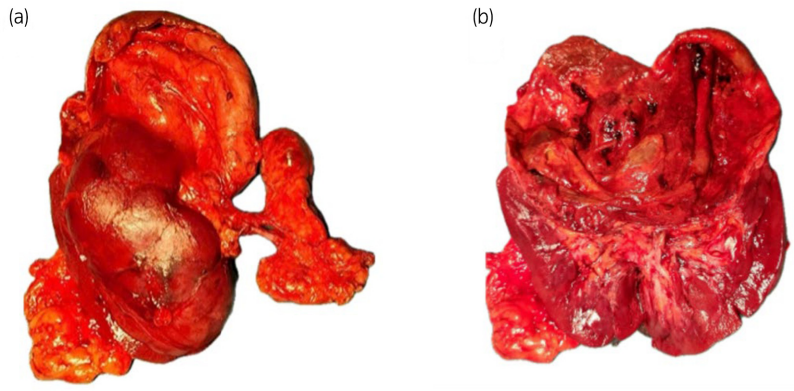

Fig. 3 Gross examination of the tumor specimen. (a) A well-circumscribed, oval mass with an approximate size of 87 × 98 × 40 mm. (b) The cut surface of the tumor with a complete capsule.

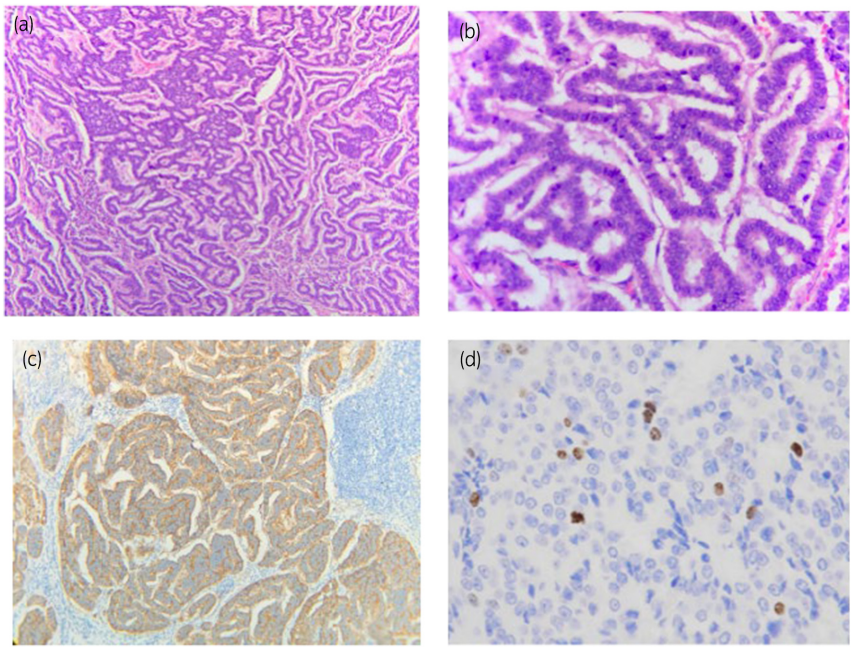

Fig. 4 Histologic features in lymph node metastasis. Microscopically it comprises ribbon and trabeculae of uniform tumor cells (a ×40, b ×200); Synaptophysin showed diffuse positive staining (c); Ki-67 index 5%–7% (d).

However, since the WHO 2016 classification, this term is no longer recommended. Accordingly, urinary system NETs are categorized into WDNETs, large-cell NEC, small-cell NEC, and paraganglioma. WDNET is characterized by a histopathological profile featuring minimal necrosis and a low mitotic count, in contrast to large-cell NEC and small-cell NEC, which exhibit extensive necrosis and a high frequency of mitotic figures.[5]

The characteristics of renal NETs do not differ from the clinical features of other types of renal tumors. Approximately 25%–30% of cases are diagnosed incidentally.[6] Other common symptoms include flank pain, abdominal pain, abdominal mass, and hematuria. Although renal NETs are neuroendocrine tumors, the occurrence of carcinoid syndrome in renal NETs is rare.[7]

Common preoperative imaging characteristics include no or minimal enhancement, heterogeneity, and calcifications observed in 75%, 60%, and 26% of reported cases, respectively; however, there is no definitive sign to differentiate NETs from other renal tumors before surgery.[8]

Diagnosing WDNET necessitates both pathological and immunohistochemical examinations, as most WDNETs present as solid masses with distinct margins and typically exhibit grayish-white or grayish-brown areas,[10] with hemorrhage and necrosis being uncommon.[9] The characteristics of minimal necrosis and low mitotic activity help differentiate WDNET from NEC.[5] These tumors express specific neuroendocrine markers, including Syn, CD56, and CGA, which provide high specificity and sensitivity for the diagnosis of WDNETs.[11]

Although WDNETs of the kidney are generally less aggressive than RCC, metastasis remains common, with approximately 50%–60% of cases exhibiting metastatic disease—often identified during initial evaluation[12]— primarily to regional lymph nodes and the liver, but also to other sites such as the lungs, breast, and thyroid,[13] with the likelihood of metastasis correlating with tumor size.[14]

Radical nephrectomy is the main treatment for localized WDNETs of the kidney, with partial nephrectomy as an alternative, but there is no evidence of its superiority.[13] Furthermore, patients with regional lymph node metastasis who underwent radical nephrectomy combined with lymph node resection had a disease-free survival rate of 47% at 43 months,[11] and those with inferior vena cava tumor thrombus can also achieve long-term survival through radical nephrectomy and tumor thrombus removal.[15]

Metastatic renal carcinoid tumors are resistant to chemotherapy,[16,17] with single-agent therapies like 5FU, cisplatin, and doxorubicin achieving about a 20% response rate.[18]

Due to the risk of metastatic disease persisting even 5 years after diagnosis, long-term follow-up after surgery is recommended, which should include physical examinations, laboratory tests, serum chromogranin A-level assessments, and imaging every 3–6 months.[8]

Conclusion

WDNETs of the kidney are rare and often present with nonspecific clinical and imaging features. Diagnosis is confirmed through immunohistochemical analysis. These tumors generally exhibit low malignancy and have a favorable prognosis, making surgical resection the preferred treatment even in cases with lymph node metastases. However, some patients may experience recurrence and metastasis after surgery, necessitating strict postoperative follow-up similar to that for renal NETs.

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Author contributions

Huy-Hoang Nguyen: Conceptualization; investigation; writing – review and editing. Hoang-Giang Phan: Writing – review and editing. Duc-Thuong Ho: Writing – review and editing. Van-Hung Le: Writing – original draft; conceptualization.

Conflict of interest

The authors declare no conflicts of interest regarding the publication of this article.

Approval of the research protocol by an Institutional Reviewer Board

Not applicable.

Informed consent

Written informed consent for publication was obtained from the patient.

Registry and the Registration No. of the study/trial

Not applicable.

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