Case Report

Atypical CT findings of renal neuroblastoma: a case report

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Background: The neuroblastoma (NB) is a highly malignant tumor of the ectoderm of sympathetic nerve cells and one of the most common malignant tumors in children, which can occur in any part of the sympathetic nerve plexus distribution, however it is less common in the kidney.

Case Description: Here we present a case of a 4-year-old boy who came to our hospital for medical help because of "abdominal distension for 1 day". Abdominal computed tomography (CT) revealed a huge retroperitoneal soft tissue mass with unclear boundaries with kidneys and adrenal glands, and low-density cystic necrosis areas were seen in the tumor. Contrast-enhanced scan showed that the mass showed mild heterogeneous enhancement. Based on these findings in the patient, he was initially considered to have Wilms tumor, but was finally pathologically confirmed as renal NB. The purpose of this article is to provide the clinicopathological features and CT manifestations of renal NB, and to discuss its differential diagnosis with other renal tumors, in order to better provide clinicians with a better understanding of the rare solid tumor. The renal NB is usually a large lobulated soft tissue mass with unclear boundary and incomplete capsule, which is prone to hemorrhage, necrosis, cystic degeneration and calcification. On CT, the mass is usually isodensity or slightly hypodense, and the cystic degeneration and necrosis area is hypodense, and on contrast-enhanced scan, it can be mildly to significantly enhanced, but the cystic degeneration and necrosis area have no enhancement.

Conclusions: The CT findings of our case were atypical and overlapped with those of Wilms, so our case suggests that renal NB should be considered as one of the differential diagnoses of Wilms, the most common malignancy of the kidney in children.

Keywords: Renal; neuroblastoma (NB); nephroblastoma; computed tomography (CT); case report

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Introduction

Neuroblastoma (NB) is a highly malignant tumor of the ectoderm of sympathetic nerve cells, often occurring in sympathetic nerve tissues and originating from neural crest cells. It is one of the most common malignant tumors in children, accounting for approximately 10% (1). More than 70% of NBs occur in children under 5 years old, and the incidence is higher in males. Furthermore, it can occur in any part of the sympathetic nerve plexus distribution; about 65% of NBs are located in the abdomen, of which approximately 70% are located in the adrenal gland. Most of the remaining 30% of cases originate from the sympathetic trunk and the anterior sacral area near the spine, and occasionally from the abdominal trunk or the para-aorta (2), and is less common in the kidney. Radiological examinations [e.g., ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI) examinations] play a significant role in the diagnosis of renal NB, the typical CT signs of renal NB are large or huge lobulated soft tissue mass in the retroperitoneum, with blurred borders,

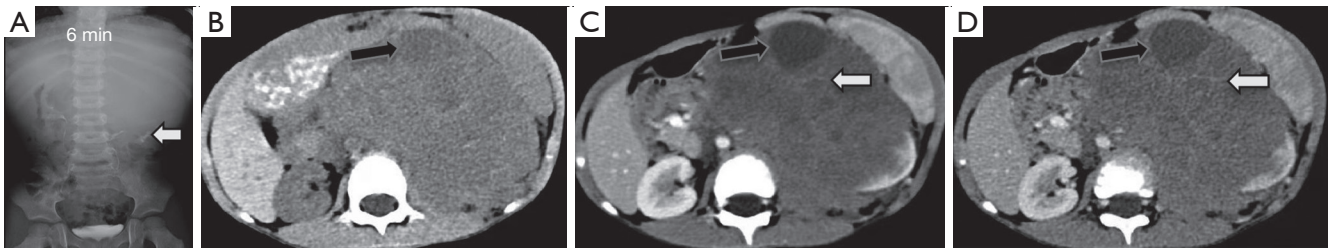

Figure 1 Abdominal CT scan image of patient before treatment. (A) Intravenous urography showed that the left kidney shadow increased, the density increased, and the left renal pelvis, kidney, and upper part of the ureter were compressed to the lower part (arrow). (B) CT unenhanced scan: a large soft tissue mass (about 25 cm × 18 cm × 21 cm) was observed in the left retroperitoneum, with uneven density and unclear boundaries between the lesion and the left kidney and adrenal gland. A low-density cystic lesion (black arrow) was also observed in the tumor. (C) Contrast-enhanced cortical phase: the lesion presented mild heterogeneous enhancement. Vessels are visible in the mass (white arrow), and there is no enhancement in the necrotic area of the cyst (black arrow). The pancreas, spleen, and surrounding intestine were significantly compressed and shifted to the right. (D) Medullary phase of enhanced scan: the lesion exhibited continuously inhomogeneous enhancement and was clearly demarcated from the remaining renal parenchyma. Vessels are more visible in the mass (white arrows), and there is still no enhancement in the necrotic area (black arrows). CT, computed tomography.

incomplete capsule, infiltration into the surrounding area, easy to surround and bury renal blood vessels, which is prone to necrosis, hemorrhage, cystic degeneration, and calcification, and the incidence of calcification is about 70%, mostly sandy or massive calcification (3,4). Herein, we report a case of renal NB with atypical CT findings, the purpose of which is to improve the understanding of the disease and the level of imaging diagnosis for further precise clinical treatment. We present the following article in accordance with the CARE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-22-205/rc).

Case presentation

A 4-year-old male child came to our hospital for medical attention due to "abdominal distension for 1 day". Physical examination revealed swelling on the left side of the abdomen, a locally palpable mass, and percussive pain in the left kidney area, with no other signs of discomfort. Laboratory tests and tumor markers were negative. Intravenous urography showed an enlarged left renal shadow, suggesting the high possibility of a mass (*Figure 1A*). Abdominal CT examination revealed a large soft tissue mass of uneven density in the left retroperitoneum, that was poorly demarcated from the left kidney and was considered to be a nephroblastoma (*Figure 1B-1D*).

Subsequently, the patient underwent surgery to remove the tumor. During the operation, a huge tumor (about 26 cm × 20 cm × 22 cm) was observed in the upper pole of the left kidney, with local cystic degeneration. The tumor was soft, adhered to the surrounding tissues, invaded the renal capsule, and involved the renal pelvis. Intraoperatively, the tumor tissue was sent for frozen sectioning, which indicated that the tumor was malignant, so left renal radical resection was immediately performed. The left renal pedicle vessel was severed, and the left kidney and tumor tissue were removed. Postoperative immunopathology is shown in *Figure 2*. The neoplastic cells were round or ovoid and were fused into fragments with ill-defined boundaries and hyperchromatic nuclei. Immunohistochemical staining of the tumor cells showed positive expression of vimentin, neuron-specific enolase (NSE), KI-67, neural cell adhesion molecules (CD56), and synaptophysin (Syn), and negative expression of cytokeratin (CK), desmin, epithelial membrane antibody (EMA), WT-1, CD99, lymphocyte common antigen (LCA), and neurofilament protein (NF), etc. According to the above microscopic characteristics, a pathologic diagnosis of left renal NB (grade IV) was made, with no tumor involvement at the broken end of the ureter. In addition, further genetic examination showed that the neuron-specific enolase was increased (with a value of 33.6 ng/mL), and the *N-MYC* gene was amplified, but the vanilla bitter almond value was normal.

Postoperatively, the patient achieved complete remission after receiving eight courses of chemotherapy with mesna, cyclophosphamide, and irinotecan hydrochloride. Two years later, the patient consciously came to our hospital for back

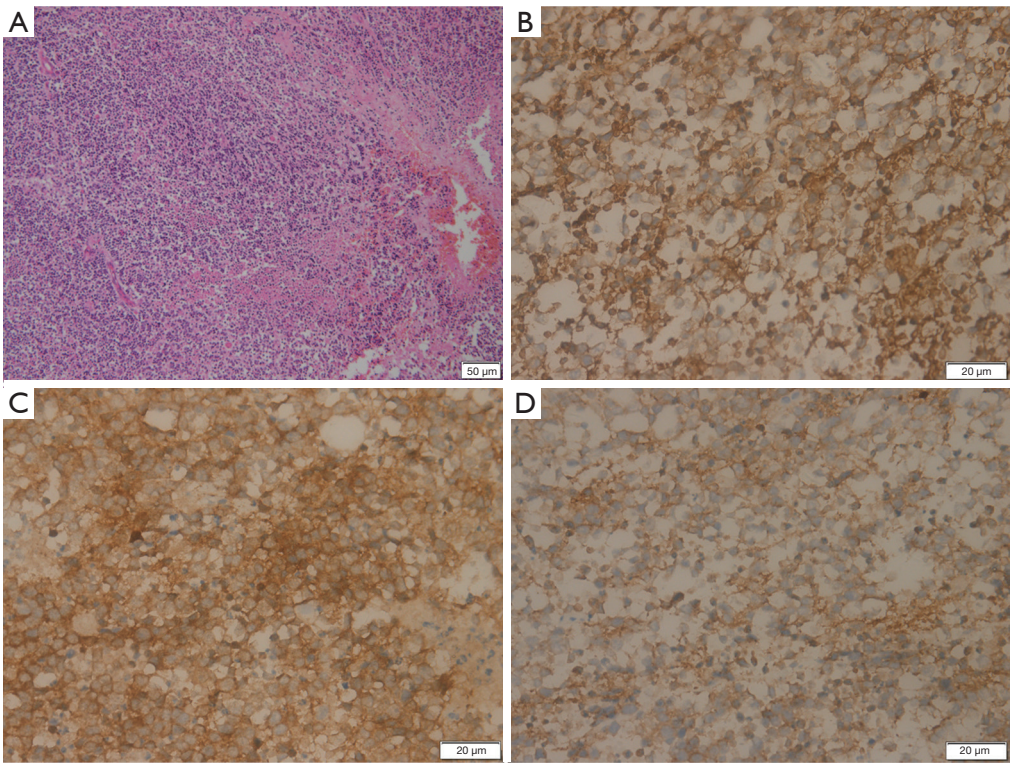

Figure 2 Histopathological features and immunohistochemical staining of renal neuroblastoma. Hematoxylin-eosin staining: pathological sections showed small round or oval tumor cells with uniform diffuse distribution (A). Immunohistochemical staining with antigen demonstrated positive expression for CD56 (B), NSE (C), and Syn (D). CD56, neural cell adhesion molecules; NSE, neuron-specific enolase; Syn, synaptophysin.

pain on the left side, and positron emission tomography (PET)/CT showed metastases in the left retroperitoneum (PET/CT images are shown in *Figure 3*), and the patient was lost to follow-up after 1 year.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Oral and written informed consent was obtained from the patient's legal guardian for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

The incidence of renal malignancy in children gradually increases with age (5), with the most common being Wilms tumor, accounting for up to 90% (6). Other primary renal tumors are relatively rare. The pathogenesis of NB originating in the kidney is still unclear, and most scholars believe that it is more likely to originate from the adrenal medulla or the sympathetic ganglion in the kidney. Renal NB usually has no clinical symptoms in the early stage; as the disease progresses, the tumor may press on the surrounding intestinal structure and induce an intestinal reaction. When the tumor invades the hilum, the patient may present painless hematuria and other non-specific manifestations. NB is a neuroendocrine tumor, which is composed of small round or oval cells of uniform size (observable under light microscopy), with large hyperchromatic nuclei. Tumor cells may be arranged in a daisy-shaped nest or rosette configuration.

The immunohistochemical results of our patient were consistent with tumor markers expressed specifically by neuroendocrine tumors, such as NSE, chromogranin A (CgA), and Syn (7). Previous studies (3,4) have suggested that typical CT signs of renal NB include large or huge lobulated soft tissue masses in the retroperitoneum, with

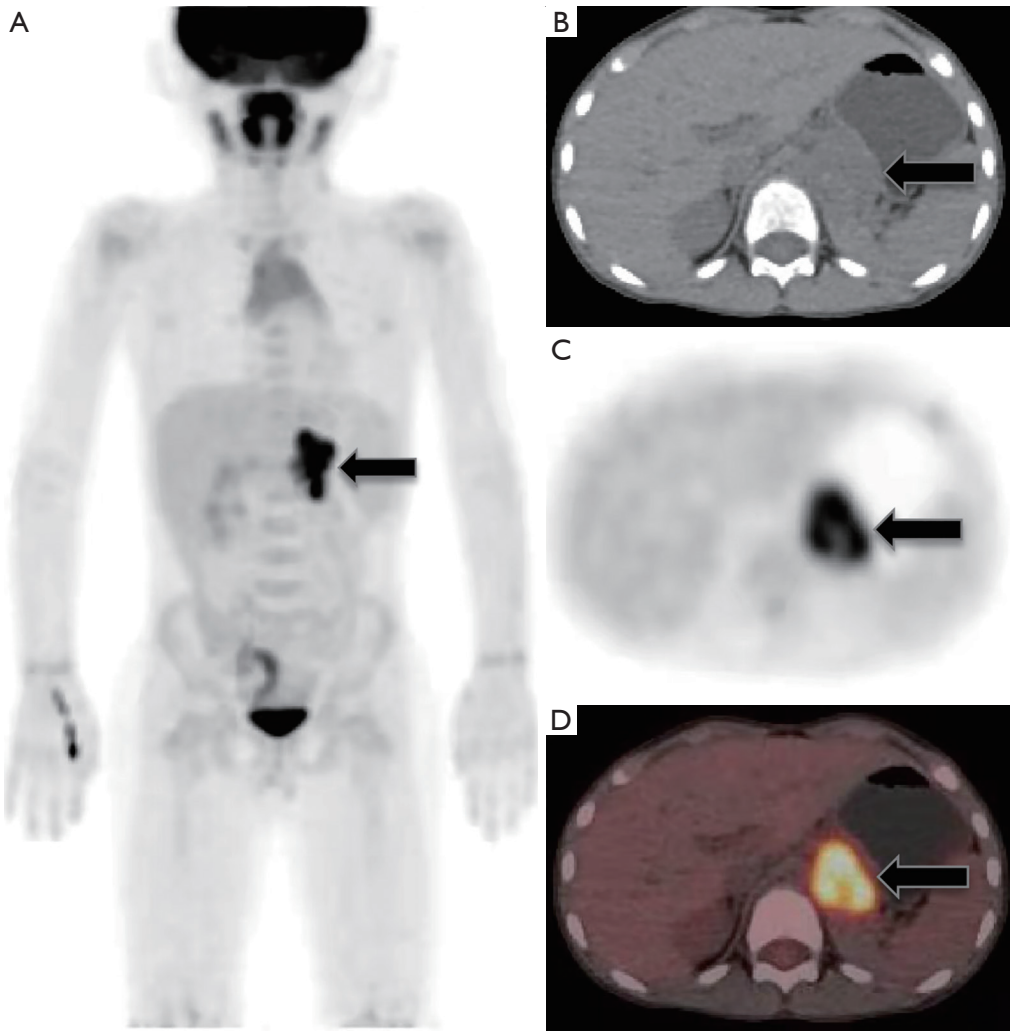

Figure 3 PET/CT examination of the patient at 2 years postoperatively showed that there was a soft tissue mass with high metabolism in the left retroperitoneum. (A) Maximum intensity projection; (B) axial CT; (C) axial PET; (D) axial PET/CT fusion. The black arrows show metastases in the left retroperitoneum. PET, positron emission tomography; CT, computed tomography.

fuzzy boundaries and an incomplete capsule, which infiltrate into the surrounding area and are easy to surround and bury renal vessels. Moreover, these masses are prone to necrosis, hemorrhage, cystic degeneration, and calcification, of which the incidence of calcification is about 2/3, and is usually sandy or massive calcification. In this case, Contrast-enhanced CT showed mild to obvious enhancement of the tumor, but no enhancement in the cystic degeneration and necrotic areas. We also found that the tumor tissue easily crossed the midline and invaded the abdominal aorta and inferior vena cava, pushing them forward. The CT findings of this patient showed no obvious calcification; therefore, the radiologist's primary diagnosis was misdiagnosed as nephroblastoma.

NB develops rapidly and has a high degree of malignancy, which is easily transferred to the bone marrow, bone, lung, brain, and other organs in the early stage. Approximately 60% of children have metastasis at the time of diagnosis, which seriously threatens their lives. According to the characteristics of the primary tumor, lymph node involvement, invasion of adjacent structures, and the presence or absence of metastatic disease, the International Neuroblastoma Staging System (INSS) has proposed multiple treatments for NB (8). However, since renal NB is

not common clinically, and clinicians are still lack research and experience, the current treatment regimen for renal NB in children generally follows that of nephroblastoma, which is the most common renal tumor in children. Surgical resection is the most effective treatment method, but in patients with late stage disease, the possibility of complete surgical resection is often reduced due to the close connection between tumor tissues and blood vessels or tumor growth around blood vessels, thus affecting the prognosis.

The role of chemotherapy in neuroendocrine tumors has been difficult to evaluate due to the rarity and biological variability of neuroendocrine tumors. Some scholars have suggested adjuvant chemotherapy for patients with locally advanced NB. The most commonly used chemotherapy drugs include cyclophosphamide, ifosfamide, cisplatin, carboplatin, etoposide, and adriamycin, etc. However, their clinical efficacy is not significant, and therefore, the survival rate of children can only be improved through early diagnosis and treatment (6,7,9,10). Our patient was at an advanced stage at the time of hospitalization; thus, despite receiving surgical resection and postoperative chemotherapy [fluorine-18 fluorodeoxyglucose (^{18}F-FDG)], PET/CT imaging of the systemic tumor showed multiple retroperitoneal lymph node metastases 3 months after surgery, and the patient was lost to follow-up after 1 year.

Based on the above description, we analyzed the reasons why this patient was misdiagnosed as nephroblastoma before surgery: (I) nephroblastoma is the most common renal malignant tumor in children, and primary NB in the kidney is relatively rare, and thus fails to attract sufficient attention from surgeons and radiologists; (II) the CT findings of this patient were atypical, and there was no relatively specific calcification in the diagnosis of NB, and there was also less calcification in the diagnosis of nephroblastoma; and (III) NB can produce catecholamines, so most patients have significantly increased vanillylmandelic acid (VMA) in the blood and urine; however, in this case, the indicators in laboratory tests were within the normal range.

CT plays an important role in discovering renal tumors, determining the relationship between tumors and surrounding tissues, and characterizing tumors. Contrast-enhanced scanning can help determine tumor boundaries and help in qualitative diagnosis (11). According to the clinical features and CT manifestations of renal masses in children, renal NB should be differentiated from the following tumors: (I) Wilms, which is the most common renal malignancy in children. CT findings show mixed density masses from the renal parenchyma, with a few cases of hemorrhage and calcification. The calcification rate is much lower than that of NB (12,13). Also, CE-CT shows uneven enhancement of the tumor soft tissue, and "crescent" enhancement is a typical enhancement feature of Wilms. When the tumor is large, it could cross the midline and compress the surrounding great vessels, leading to its displacement under pressure, but this tumor does not wrap around the great vessels, which distinguishes it from renal NB. (II) Clear cell carcinoma of the kidney, which usually occurs in adults and may also exhibit cystic degeneration, necrosis, bleeding, or calcification. CE-CT shows significant enhancement at the renal cortical phase, while the enhancement degree of lesions at the medullary phase and delayed scan decrease rapidly, presenting a typical "fast in and fast out" performance (14,15), which differs from the progressive enhancement of renal NB. (III) Ewing's sarcoma, which is another malignant tumor with a low incidence in the kidney, and is usually characterized by a single large, ill-defined, irregular soft-tissue mass in the kidney on CT. This mass tends to be invasive and prone to necrosis, cystic degeneration, and hemorrhage, so its density is often uneven. CE-CT shows that the enhancement degree of the tumor parenchyma is different, mainly in the form of separation, flower ring, and honeycomb, which has certain characteristics (16,17). (IV) Renal clear cell sarcoma, which has a relatively low incidence, but is more common in children. CT shows a large soft tissue mass in the kidney that is prone to hemorrhage, cystic degeneration, and necrosis. Calcification is relatively rare. CE-CT shows obvious enhancement and characteristic enhancement changes of plaques and stripes in the tumor (18). In addition, primary NB of the kidney needs to be distinguished from renal invasion by retroperitoneal tumor.

Conclusions

NB originating in the kidney is rare, and its clinical characteristics are not specific. When the CT features of renal NB are atypical, it is easily misdiagnosed as nephroblastoma. NB has a very high degree of malignancy, and even after surgical resection, the tumor is prone to relapse and distant metastasis. Therefore, understanding the characteristics of this disease is of great clinical significance for the diagnosis and early intervention in this disease. The final diagnosis of renal NB should be combined with pathology and immunohistochemistry results.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-22-205/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-22-205/coif). YT reports that the study was funded by National Science and Technology Foundation of Zunyi City [No. HZ(2021)109]. PW reports that the study was funded by Zunyi Medical College Research Start Fund (2018ZYFY03). JC reports that this study was funded by National Natural Science Foundation of the Peoples Republic of China, NSFC (grant number: 81571712). The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Oral and written informed consent was obtained from the patient's legal guardian for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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