Clinical Case Report

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Adult renal neuroblastoma

A case report and literature review

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Abstract

Rationale: Adult renal neuroblastoma (NB) is extremely rare, and there have been only a few cases previously described in the literature. We report a case of adult renal NB and summarize the clinical and imaging features of the reported cases.

Patient concerns: A 41-year-old female was admitted to our hospital with a chief complaint of gross hematuria that had persisted for a month. Nonenhanced computed tomography (CT) revealed a hypodense right renal mass without calcification. Enhanced CT showed an infiltrative, heterogeneously enhancing right renal mass with retrocaval lymphadenopathy and right renal vein thrombus. Magnetic resonance imaging (MRI) revealed that the right renal mass was isointense relative to the renal parenchyma on nonenhanced T1-weighted images; it showed mixed hypointensity and hyperintensity on T2-weighted images, and heterogeneous enhancement with a hyperintense rim on fat-saturated, enhanced T1W images. The initial impression was renal cell carcinoma (RCC).

Diagnoses: Adult renal neuroblastoma.

Interventions: Right nephroureterectomy with lymph node dissection was performed. The pathology and immunohistochemistry confirmed the diagnosis of renal NB with retrocaval lymphadenopathy and retroperitoneal metastasis.

Outcomes: After surgery, the patient received 6 courses of chemotherapy, and no recurrence was observed during a 24-month follow-up period.

Lessons: The clinical picture of adult renal NB is that of a 44-year-old woman, presenting with an abdominal or renal mass about 13cm in size, accompanied by hypertension, hematuria, or pain. In contrast to CT features described in previous literature, no tumor calcification is mentioned in these adult renal NB cases. It is difficult to differentiate renal NB from RCC based on CT or MRI. However, biopsy, urinary catecholamine levels, and metaiodobenzylguanidine (MIBG) scan may aid in presurgical diagnosis.

Abbreviations: CT = computed tomography, FDG-PET = ^{18}F-fluorodeoxyglucose positron emission tomography, INSS = International Neuroblastoma Staging System, MIBG = metaiodobenzylguanidine, MRI = magnetic resonance imaging, NB = neuroblastoma, RCC = renal cell carcinoma.

Keywords: adult renal neuroblastoma, computed tomography, magnetic resonance imaging, pediatric renal neuroblastoma, renal cell carcinoma

1. Introduction

Neuroblastoma (NB) is typically a tumor of early childhood; more than 90% of cases occur in individuals younger than 10 years of age, and adults are rarely affected.[1] Adult renal NB is even rarer, and only 7 cases have been reported in the previous literature.[2–7] We report a case of adult renal NB and summarize the clinical and imaging features of the reported cases.

2. Case report

A previously healthy 41-year-old female visited our outpatient department in December 2015 with a chief complaint of gross hematuria that had persisted for a month. The physical examination did not show any abnormality. Urine cytology did not reveal malignancy. The patient had no history of hypertension. Non-enhanced computed tomography (CT) (Somatom Sensation 64; Siemens Health Care, Forchheim, Germany) revealed an infiltrative right renal mass ($7.8 \times 7.5 \times 5.2$ cm) isodense to the renal parenchyma, and no presence of calcification. The right renal mass showed heterogeneous enhancement and extracapsular extension into the perirenal space on enhanced images. Confluent retrocaval lymphadenopathy was also observed. A tumor thrombus was noted in the right renal vein (Fig. 1). Magnetic resonance imaging (MRI) (MAGNETOM Verio, Siemens Healthcare, Erlangen, Germany) revealed that the right renal mass was isointense relative to the renal parenchyma on nonenhanced T1W images (T1WI); it showed mixed hypointensity and hyperintensity relative to the renal parenchyma on T2W images (T2WI), and heterogeneous enhancement with a hyperintense rim on fat-saturated, enhanced T1W images (Fig. 2). The initial impression was renal cell

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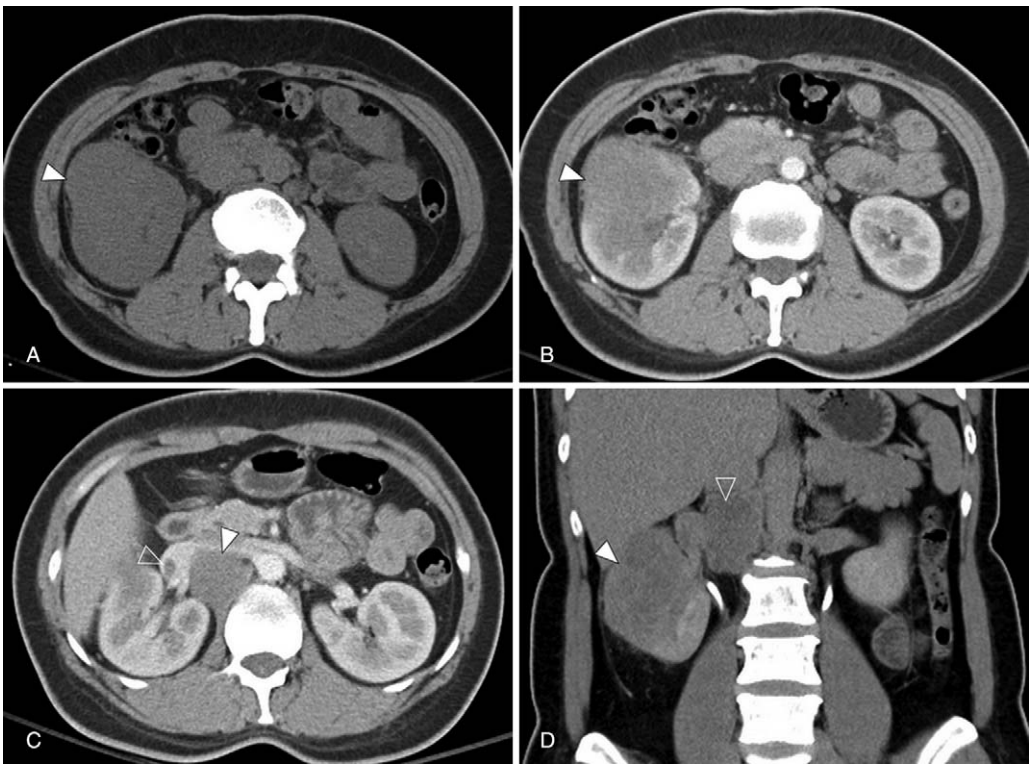

Figure 1. Computed tomography of the abdomen. (A) Axial nonenhanced image reveals isodense right renal mass without calcification (arrowhead). (B) Axial enhanced image reveals right infiltrative renal mass with heterogeneous enhancement (arrowhead). (C) Axial enhanced image shows tumor thrombus in right renal vein (open arrowhead). There is confluent lymphadenopathy in retrocaval region (arrowhead). (D) Coronal delayed-phase image reveals the right renal mass (arrowhead) and retrocaval lymphadenopathy (open arrowhead).

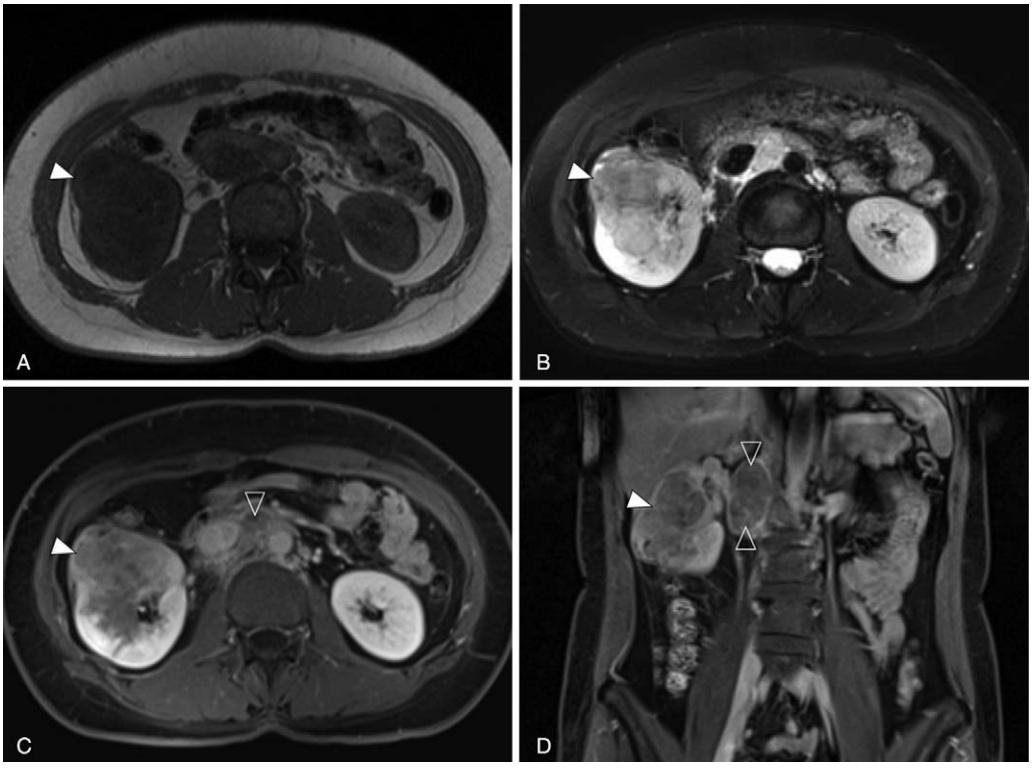

Figure 2. Magnetic resonance imaging of the abdomen. (A) Axial nonenhanced T1-weighted image reveals the right renal mass isointense to renal parenchyma (arrowhead). (B) Axial T2-weighted image reveals the right renal tumor has heterogeneous, mixed hypointensity, and hyperintensity (arrowhead). (C, D) Axial enhanced, fat-saturated, T1-weighted image shows the right renal mass (arrowheads), and lymphadenopathy (open arrowheads) have heterogeneous enhancement and hyperintense rim.

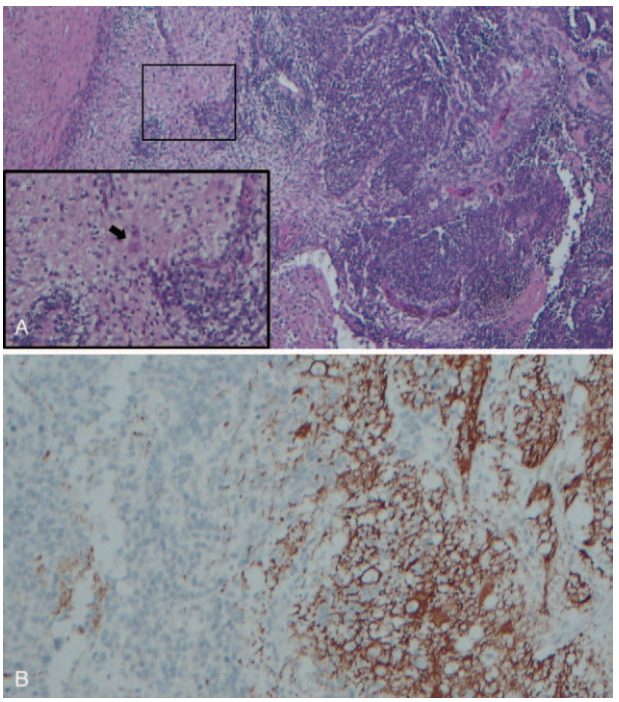

Figure 3. Pathology and immunohistochemistry of renal mass. (A) Undifferentiated cells in fibrillary background with neural tubule-like structures forming (H&E, ×200). Ganglionic differentiation (arrow) was also focally identified (enlarged in left lower corner of figure, ×400). (B) Synaptophysin antibodies highlighted fibrillar background of tumor (×200).

carcinoma (RCC) with renal vein thrombus and regional lymphadenopathy. Urinary catecholamine levels were not measured.

Right nephroureterectomy with lymph node dissection was performed. The pathology revealed a renal mass with a grayish white, soft texture, and vascular invasion. The enlarged retrocaval lymph nodes were attached to the adrenal gland without invasion. Metastasis in the retroperitoneum was also noted. Microscopically, the tumor was chiefly composed of undifferentiated cells in a fibrillary background. Focal immature neuroepithelial (neural tube-like structures) and ganglionic differentiation was observed (Fig. 3A). The differential diagnosis included nephroblastoma (Wilms tumor), Ewing sarcoma, NB, and primary or metastatic germ cell tumor with predominant immature neuroepithelial element with sarcomatous differentiation. Immunohistochemically, undifferentiated tumor cells were negative for CD45, PAX8, GATA3, CD99, and WT1. The fibrillary background and ganglion cells showed expression of synaptophysin (Fig. 3B), chromogranin A, and neuropil, allowing exclusion of the possibilities of Wilms tumor and Ewing sarcoma. Therefore, NB was the most suitable diagnosis.

After surgery, 6 courses of chemotherapy with cisplatin (60 mg/m^2 on day 1), doxorubicin (30 mg/m^2 on day 2), etoposide (80 mg/m^2 on days 2, 5), and cyclophosphamide (750 mg/m^2 on days 3, 4) were administered. No evidence of recurrence was observed during a 24-month follow-up period.

The case report has been approved by the Chang Gung Medical Foundation Institutional Review Boards (IRB, http://links.lww.com/MD/C187), Taipei, Taiwan. The patient consent was waivered by the IRB, http://links.lww.com/MD/C187.

3. Discussion

NB is a rare tumor in the adult population. Intrarenal NB is extremely rare. We collected all published cases (n = 8) of adult renal NB in Table 1, and summarized features of these cases are shown in Table 2. While only a few case reports exist, adult renal NB displays a female (75%) and right-sided (62.5%) predominance. The onset of age is about 44.00 ± 18.12 years. The maximal diameter of the mass is 12.94 ± 8.12 cm. Initial symptoms include: hematuria, abdominal mass, renal mass, pain, and hypertension. The sites of distant metastasis are liver, bone, lung, and pelvic lymph nodes.

According to the International Neuroblastoma Staging System (INSS), half of the cases were stage 4 at initial presentation (n = 4). In 4 cases (57.14%; case 7 had no report of outcome), long-term disease-free survival (18 months–5 years) was achieved, including 3 cases of stage 1 and 1 case of stage 4 disease.

Fan[8] reported that the features of pediatric renal NB include: male predominance; average age of onset of 17 months; typical presentation with an abdominal mass and hypertension; and possibly elevated urinary catecholamine levels. Table 3 shows a comparison of features between adult and pediatric renal NB.

Image features of adult renal NB have been described in previous reports. The CT findings include: isodense renal mass without calcification on nonenhanced CT; heterogeneously enhancing mass with central necrosis after contrast medium injection, associated with perirenal invasion, regional lymphadenopathy, or renal vein thrombosis. The MRI findings include: isointense to hypointense renal mass on T1WI; heterogeneous, mixed hypointense and hyperintense renal mass on T2WI; and heterogenous enhancement with a hyperintense rim. Lonergan et al[9] reported that approximately 80% to 90% of NBs demonstrate calcification on CT scans; however, none of the adult renal NB cases reported demonstrated renal calcification. According to these findings, it is difficult to differentiate renal NB from RCC based on CT or MRI features.

Other modalities, however, may be helpful in the differentiation of NB. Ninety percent of NB cases show elevated blood or urinary catecholamine levels. Catecholamine metabolites such as vanillylmandelic acid, homovanillic acid, and dopamine can aid in the diagnosis of NB and have been used in clinical diagnosis and early detection.[10] However, most patients with adult renal NB did not receive these tests because the lesions were mistaken for RCC.

Fine needle aspiration cytology and core needle biopsy can provide accurate diagnosis prior to surgery. Frostad et al[11] reported that fine needle aspiration cytology with immunohistochemistry, in combination with elevated urinary catecholamine levels, can offer an accurate diagnosis of neuroblastic tumors in children. Mandelia et al[12] stated that fine needle aspiration cytology of NB can provide sufficient material for molecular genetic analyses. Mullassery et al[13] reported that core biopsy with an 18G needle appeared to provide adequate tissue sampling for diagnosis, risk classification, and tumor staging.

Metaiodobenzylguanidine (MIBG) is structurally similar to norepinephrine, and can be used for localization of neural crest tumors. The specificity of MIBG scintigraphy for NB detection approaches 100%, and the sensitivity has been reported to be 90% to 95%.[14] MIBG scintigraphy was reported to be more specific and superior to ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET). Thus, the primary role of FDG-PET lies in identifying those NBs that do not demonstrate MIBG uptake. However, approaches using newer tracers, such as

Table 1

All published cases of adult renal neuroblastoma and present case.

	Age	Sex	Tumor location	Tumor size, cm	INSS stage	Symptoms	Imaging findings	Distant metastasis	Treatment	Outcome
Case 1, Baumgartner et al[2]	56	F	Left upper	N/A	4	Back pain, weakness of both lower extremities	IVP: distortion of upper pole calyces ANGIO: cystic, relative avascular mass with irregular tumor vessels, no calcification, persistent tumor stain	Lung, liver, bone	Surgery	Patient died on 4th postoperative day owing to platelet deficiency.
Case 2, Gohji et al[3]	35	M	Right lower	$15 \times 11 \times 10$	1	Abdominal mass	IVP: mass in the lower pole of the right kidney ANGIO: arteriovenous fistula, tumor stain and irregular neovascularity CT: mass with a scattered lower density area	N	Surgery, R/T	No recurrence at 5 year follow-up
Case 3, Gohji et al[3]	29	M	Right upper	$28 \times 25 \times 20$	2a	Back pain, abdominal mass	IVP, ANGIO, CT: compatible with renal cell carcinoma	N	Surgery (incomplete), C/T	Patient's condition had been gradually worsening
Case 4, Bayrak et al[4]	37	F	Right lower	$6 \times 6 \times 6$	1	Renal mass	US: renal mass CT: heterogeneous, centrally necrotic renal mass	N	Surgery	No recurrence (30 months after surgery)
Case 5, Tiu et al[5]	79	F	Left lower	$7 \times 6.5 \times 6$	1	Painless hematuria, hypertension	CT: heterogeneously hypodense renal mass with central necrosis and perirenal invasion after contrast enhancement	N	Surgery	No recurrence (18 months after surgery)
Case 6, Liu et al[6]	22	F	Left upper	$8.2 \times 7.3 \times 3.1$	4	Abdominal and joint pain	CT: heterogeneous, centrally necrotic renal mass, enlarged retroperitoneal lymph nodes	Liver, bone	Surgery, R/T	No local recurrence. Progression of metastasis (9 months after surgery)
Case 7, Jain et al[7]	53	F	Right	$12.6 \times 18.6 \times 11.5$	4	Renal mass, hypertension	F^{18}-FDG and ^{68}Ga-dotanoc PET/CT: tracer uptake at right renal region and pelvic lymph nodes	Pelvic lymph nodes	Surgery	N/A
Case 8 Present case	41	F	Right lower	$7.8 \times 7.5 \times 5.2$	4	Gross hematuria	NECT: infiltrative renal mass (30.6 $\pm$10.5 HU) isodense to renal parenchyma, no calcification CECT: heterogeneously enhancing mass hypodense to renal parenchyma (46.6$\pm$10.1 HU on corticomedullary phase; 55.1$\pm$11.9 HU on venous phase; 54.5$\pm$11.2 HU on delayed phase), confluent lymphadenopathy in retrocaval region, thrombus in right renal vein MRI: T1W hypointense, T2W heterogeneous, mixed hypointense and hyperintense renal mass. The renal mass and lymphadenopathy show heterogeneous hypointensity to renal parenchyma with rim enhancement on enhanced images, right renal vein thrombus	Retroperitoneum	Surgery, C/T	No recurrence (24 months after surgery)

^{68}Ga-dotanoc = ^{68}Ga-labeled [1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid]-1-Nal3-octreotide, ANGIO = angiography, C/T = chemotherapy, CECT = contrast-enhanced computed tomography, CT = computed tomography, F = female, F^{18}-FDG = ^{18}F-fluorodeoxyglucose, HU = Hounsfield unit, INSS = International Neuroblastoma Staging System, IVP = intravenous pyelogram, M = male, MRI = magnetic resonance imaging, N/A = non-available, NECT = nonenhanced computed tomography, R/T = radiotherapy, T1W = T1 weighted, T2W = T2 weighted, US = ultrasound.

Table 2

Summary table of reported cases of adult renal neuroblastoma (n = 8).

Sex	Female = 6 (75%)
Age	44.00 ± 18.12 years
Location	Right side = 5 (62.5%)
Maximal diameter	12.94 ± 8.12 cm
Symptoms	Hematuria = 2 (25%)
	Abdominal mass = 2 (25%)
	Renal mass = 2 (25%)
	Pain = 3 (37.5%)
	Hypertension = 2 (25%)
INSS stage at initial presentation	Stage 1 = 3 (37.5%)
	Stage 2a = 1 (12.5%)
	Stage 4 = 4 (50%)
Distant metastasis	4 cases (50%)
	Liver, bone = 2 (25%)
	Lung = 1 (12.5%)
	Pelvic lymph nodes = 1 (12.5%)
	Retroperitoneum = 1 (12.5%)
Long-term disease-free survival	4 in 7 patients (18 months–5 years)

Table 3

Comparison between pediatric and adult renal neuroblastoma.

	Adult	Pediatric
Sex	Female predominant	Male predominant
Mean age	44 years (22–79 years)	17 months (3–39 months)
Symptoms	Hematuria, abdominal mass, renal mass, pain, hypertension	Abdominal mass, hypertension with or without urinary catecholamine levels
Often mistaken as	Renal cell carcinoma	Wilms tumor

^{11}carbon labeled hydroxyephedrine and ^{11}C-epinephrine PET, have also been studied.[15]

4. Conclusion

Adult renal NB is extremely rare, and we summarize the clinical and imaging features based on the cases reported in the literature. The clinical picture of adult renal NB is that of a woman of 44 years of age, presenting with an abdominal or renal mass about 13 cm in size, accompanied by hypertension, hematuria, or pain. In contrast to the CT features reported in the previous literature, no tumor calcification was observed in these adult renal NB cases. It is difficult to differentiate renal NB from RCC based on presurgical CT or MRI. However, biopsy, urinary catecholamine levels, and MIBG scan may aid in the diagnosis prior to surgery.

Author contributions

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Writing – review & editing: C.-W. Yen, H.-C. Chuang, L.-S. Hsu, M.-L. Chen, W.-H. Lin, W.-Y. Lin.

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