

Primary Renal Neuroblastoma in Adults

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CASE PRESENTATION

A 79-year-old woman was admitted to the hospital with a closed intertrochanteric femoral neck fracture after a fall and underwent dynamic hip screw fixation. Postoperatively, she developed painless hematuria but was hemodynamically stable. She had no significant medical history, apart from hypertension, which had been managed with antihypertensive medications for the previous 20 years. Her blood test and urine cytology results did not show any obvious abnormality. However, computed tomography of the abdomen and pelvis showed an enhancing mass measuring $5.4 \times 6.1 \times 6.0$ cm in the lower pole of the left kidney (Fig. 1). She underwent additional staging examinations with computed tomography of the chest and a bone scan, the findings of which were unremarkable.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of the renal mass included primary malignant tumors (renal cell carcinoma, urothelial carcinoma, lymphoma), metastatic disease, benign mass or cyst, and infection (xanthogranulomatous pyelonephritis). Renal cell carcinoma is the most common cause of a malignant solid renal mass in the elderly; therefore, this was at the top of our differential diagnosis list. Her presentation of hematuria raised the possibility of urothelial carcinoma of the renal pelvis; however, because she was a nonsmoker with negative cytology findings, this was unlikely.

The patient was counseled on the management options for a clinical stage T1b renal mass, which included partial nephrectomy and radical nephrectomy. Given the complexity of the large solid renal mass and the high likelihood of it being malignant, she underwent elective laparoscopic left radical nephrectomy. After an

uneventful postoperative recovery, she was discharged on day 3. At 18 months of follow-up, she showed no evidence of recurrence or metastatic disease on the computed tomography scan of the chest, abdomen, and pelvis.

PATHOLOGY ASSESSMENT

Presented by Ewan Miller, M.D.

Macroscopically, the kidney was distorted by a $70 \times 65 \times 60$ -mm mass in the region of the mid and lower poles, with a yellow, focally hemorrhagic cut surface (Fig. 2A). Focal infiltration of perinephric fat was present. Microscopically, the tumor cells were arranged in nests and sheets with a rosette formation and neuropil present (Fig. 2B), with an infiltrative growth pattern. The cells contained small, uniform, hyperchromatic nuclei with coarse chromatin. Occasional, larger, ganglion-like cells were present, and focal anaplasia was seen. The tumor cells stained strongly positive for chromogranin, synaptophysin, neurofilament, and CD56 (Fig. 2C, D). There was focal dot positivity for cytokeratin. Staining for vimentin, WT1, NB, desmin, actin, S-100, glial fibrillary acidic protein, epithelial membrane antigen, and CD99 were negative. Cytogenetic analysis showed no evidence of hyperdiploidy or amplification of MYCN. These findings are consistent with adult renal neuroblastoma. Neuroblastomas are typically positive for neural markers (eg, chromogranin, synaptophysin, neurofilament, and CD56) and negative for CD99 and myogenic markers. Other entities considered in the differential diagnosis included primitive neuroectodermal tumor, which is typically positive for CD99, and ectomesenchymoma, which is usually negative for muscle markers and lacks rosette-like structures.

DISCUSSION

Presented by Albert Tiu, M.D. and Peter Aslan, M.D.

Neuroblastoma is the second most common solid pediatric malignancy, with >90% of tumors diagnosed in children <10 years old.¹ The incidence in those aged ≥ 20 years has been reported to be 0.12 cases/1 million.² Neuroblastoma occurs in the sympathetic nervous system and principally affects the adrenal glands and retroperitoneum, with a similar pattern of distribution in children and adults. The presentation of the neuroblastoma can be asymptomatic and varies depending on the tumor size and site, involvement of the

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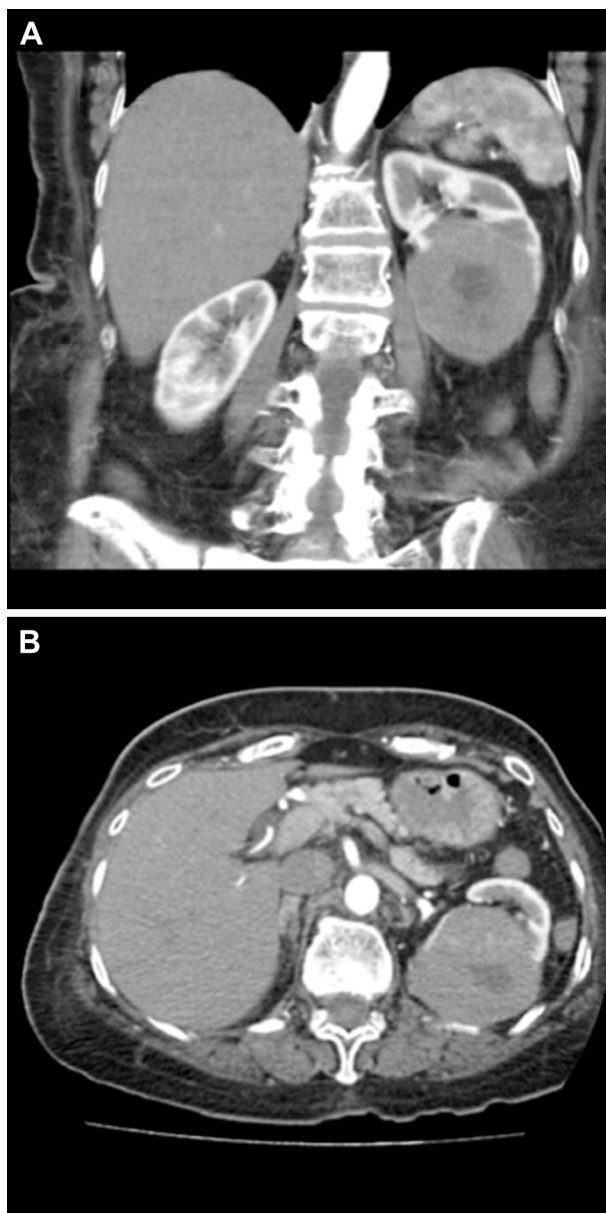


Figure 1. Computed tomography scan of abdomen and pelvis. **(A)** Coronal image showing heterogeneous mass occupying two thirds of left kidney. **(B)** Axial image showing heterogeneous mass at left kidney.

adjacent organs, and the presence of metastatic sites. Elevated urinary catecholamine metabolites and positive meta-iodobenzylguanidine scintigraphy can aid in the diagnosis of neuroblastoma. Oral and intravenous-based contrast-enhanced computed tomography of the abdomen should be performed to localize the tumor accurately, provide anatomic information, and determine contrast enhancement. Magnetic resonance imaging can be used in cases of locally advanced malignancy, possible venous involvement, renal insufficiency, and an allergy to intravenous contrast.³

Primary renal neuroblastoma in adults is extremely rare and can potentially cause diagnostic dilemmas. To our

knowledge, only 5 cases have been reported in English-language published studies.⁴⁻⁷ The rare nature of this tumor, especially in adults, has limited its study; thus, little is known about the treatment recommendations. The treatment modalities for children have included surgery, chemotherapy, and radiotherapy. Treatment options have varied, depending on the tumor stage, patient age, and biologic prognostic factors. Patients can be stratified into favorable and unfavorable risk groups according to the histopathologic characteristics. The factors known to have a positive prognosis in children include age <1 year, a low disease stage, a lack of MYCN amplification, and hyperdiploidy.⁸⁻¹⁰ Children with stage I disease will have a disease-free survival rate >90% with surgical resection alone. Adjuvant therapy (chemotherapy with or without radiotherapy) is indicated for patients with recurrence or higher stage tumors with MYCN amplification and/or unfavorable histologic features.¹¹

The presented patient subsequently underwent radio-nuclear meta-iodobenzylguanidine imaging to identify any evidence of multifocal disease. The findings were negative, and the diagnosis of stage I primary renal neuroblastoma was confirmed, in accordance with the International Neuroblastoma Staging System.¹²

Because of the lack of studies and experience, the treatment of neuroblastoma in adults has generally followed pediatric protocols. Complete surgical resection is the most effective therapy for localized disease. The role of chemotherapy for neuroendocrine tumors has been difficult to assess owing to the rarity of the disease and variations in the biologic characteristics. Adjuvant chemotherapy is recommended for patients with locally advanced neuroblastoma. The most common agents used, alone or combined, include alkylating agents (cyclophosphamide/ifosfamide), platinum-based agents (cisplatin/carboplatin), etoposide, and Adriamycin.¹³ Local radiotherapy could be indicated for patients who have microscopic residual disease. Nevertheless, it has been reported that neuroblastoma has a worse long-term prognosis for adolescence or adults than for children, regardless of stage or site.¹⁴ Despite the poor outcome, adults with stage I-III (localized or regional) disease have a better prognosis with a longer interval between the diagnosis and recurrence than patients with stage IV (disseminated) disease at diagnosis.¹

The present case has demonstrated the diagnostic dilemma faced by clinicians when managing obscure and virtually unheard of pathologic entities in adult populations. The present patient represents the oldest case of primary renal neuroblastoma we were able to identify in the English-language studies. The present case emphasizes the need for a clear histopathologic diagnosis to establish the appropriate investigations, treatment options, and routine follow-up protocol.

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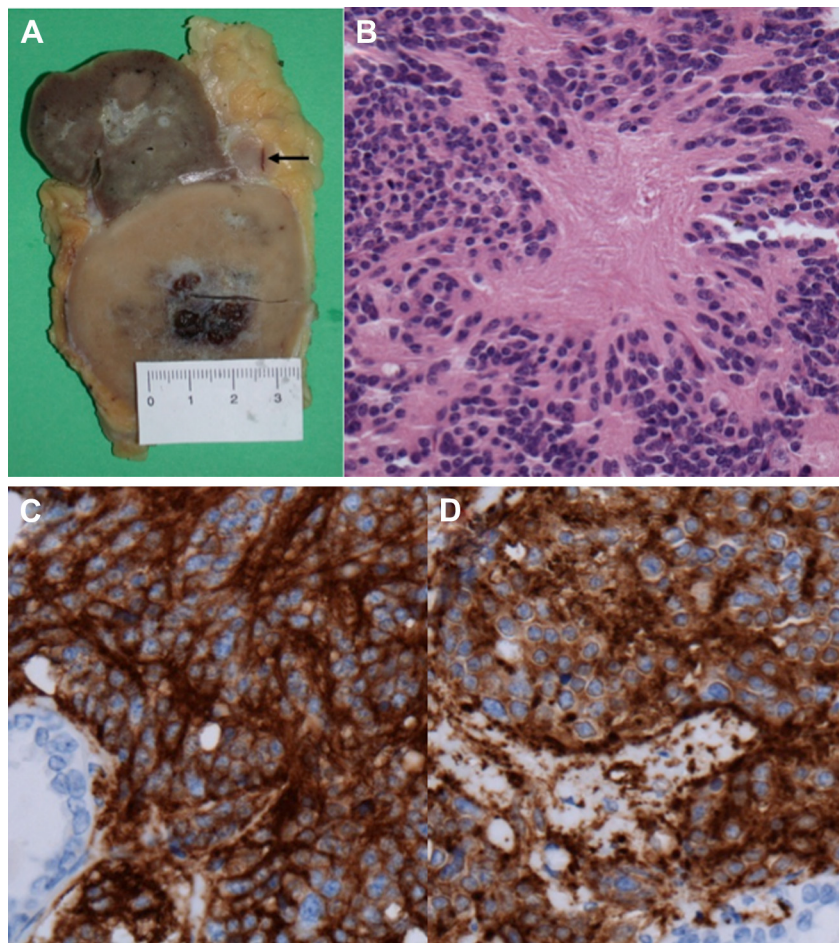


Figure 2. (A) Macroscopic section of left kidney specimen demonstrating well-circumscribed tan mass replacing the lower pole, with central hemorrhage. Focal extension of the tumor into perinephric fat (arrow) is present. (B) Hematoxylin-eosin staining showing tumor had formed well-defined rosettes with fibrillary neuropil. (C) Strong positive staining for CD56 with an adjacent negatively staining renal tubule. (D) Strong positive staining for synaptophysin. (Color version available online.)

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