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Renal ganglioneuromas in a pediatric patient: Case report and review of the literature

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ABSTRACT

Ganglioneuromas are rare benign tumors originating from the sympathetic nervous system and neural crest cells. A 4-year-old girl presented with numerous urinary tract infections. Ultrasound and computed tomography revealed a large mass within the right kidney. A right nephrectomy and sampling of surrounding lymph nodes were performed. Pathology confirmed that the mass was a mature ganglioneuroma. The patient remains disease-free, more than 2 years after surgery. We present this rare case of renal ganglioneuroma as well as a review of the literature.

Renal ganglioneuroma is a rare form of benign tumor involving neural crest cells and kidney tissues [1]. Most often these tumors arise from the retroperitoneum and thoracic cavity and are not metabolically active [2,3]. These tumors are made primarily of sympathetic ganglion cells, Schwannian stroma, fibrous tissue and nerve fibers [4,5]. While most cases arise in adults, we present a case of a 4-year-old girl with an incidental finding of a right renal mass after ultrasound examination due to frequent urinary tract infections [4].

1. Case report

A 4-year-old female presented to us had a history of recurrent urinary tract infections and underwent an ultrasound which revealed a right renal mass. Preoperative workup included both urine metanephrines (which were negative) and computed tomography (CT). The CT scan revealed a large mass in the right kidney, with surrounding hydronephrosis, measuring 6.3 cm × 5.5 cm at its widest (Fig. 1a). The right renal artery appeared to connect to the mass and there was a prominent draining vein from the mass to the inferior vena cava. The scan also showed a smaller calcified nodule lying adjacent to the right adrenal gland measuring approximately 27 mm × 9 mm and a tiny lesion lying ventral to the IVC (Fig. 1b). The left kidney and both adrenal glands were normal along with the liver, spleen, gallbladder, pancreas, bowel and bones. The differential diagnosis included Wilms tumor (given the location and her age), neuroblastoma (due to the punctate calcifications), meconium peritonitis (also due to the calcifications), and a primary renal neoplasm (due to the tumor involving the right renal vein and renal artery).

The patient underwent a laparotomy, right radical nephrectomy and biopsies of enlarged periaortic and paracaval node with sparing of the adrenal gland. Intraoperatively, a large, hard, calcified mass was noted occupying most of the medial half of the kidney. While some nodes were completely resected, some were adherent to the IVC which prevented complete resection, therefore frozen biopsies were taken instead. Final pathology confirmed the tumor to be a stage 3 maturing/mature intrarenal ganglioneuroma. Histological examination of the three biopsied nodules revealed that two contained ganglioneuroma tissue, including mature ganglion cells, Schwann cells and fibrous tissue (Fig. 2), and were either separate tumor nodules or lymph nodes nearly completely overtaken by ganglioneuroma. A second pathology opinion was obtained from the Children's Oncology Group Renal Tumor Pathology Center (Chicago, Ilinois, USA) and they concurred with the above diagnosis. Given the benign nature of the tumor, no further adjuvant treatment was required.

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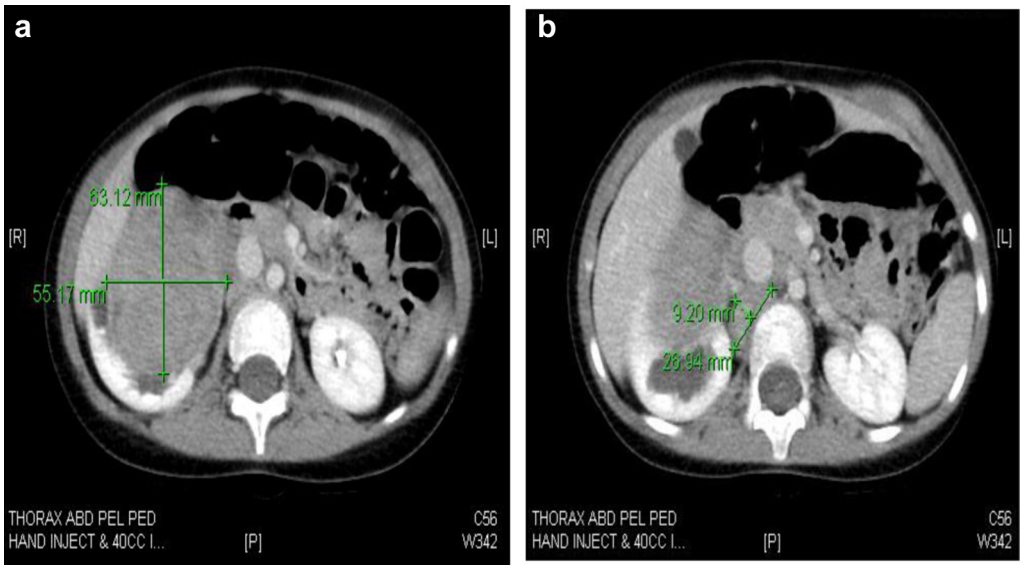

Fig. 1. (a): CT image showing a large, retroperitoneal solid mass (6.3 cm × 5.5 cm) occupying most of the right kidney. The dimensions of the mass are highlighted by the green lines. Note is also made of hydroneprhosis of the upper pole. (b) Another CT image showing a smaller extra renal nodule of soft tissue with punctate calcifications lying adjacent to the right adrenal gland measuring 2.7 cm × 0.9 cm (the dimensions of the mass are highlighted with green lines).

The patient has now been followed closely in our pediatric oncology clinic for over 2 years, with abdominal ultrasounds every 3 months and urinary catecholamines. She remains disease-free, with no evidence of tumor recurrence.

2. Discussion

Ganglioneuromas, neuroblastomas and ganglioneuroblastomas are referred collectively as neuroblastic tumors originating from the sympathetic nervous system and neural crest cells [5]. Ganglioneuromas are the most differentiated, least severe tumors and often occur in older patients with evidence showing more occurrences in females over men (0.77–0.72 female:male) [5–7].

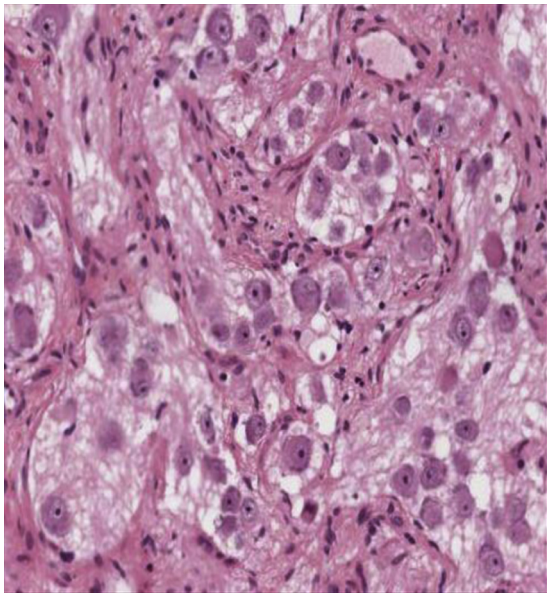

Fig. 2. Sections show loosely arranged groups of maturing and fully mature ganglion cells with surrounding Schwannian stroma. No neuroblasts present (Hematoxylin and eosin stain, 400× magnification).

Unlike neuroblastomas and ganglioneuroblastomas, ganglioneuromas usually show little metabolic activity, with only 37% of ganglioneuromas causing increased catecholamine and urine levels (vs. 90–95% of neuroblastomas and ganglioneuroblastomas) [3,5]. However, there is a correlation between increased ganglioneuroma size and levels of catecholamine metabolites, namely vanillylmandelic acid (VMA) and homovanillic acid (HVA), showing that large ganglioneuromas are significantly more likely to have increased HVA and VMA levels [7]. Our patient did have increased urine HVA levels (21.6 umol/mmol creatinine (normal 0–14)) but normal urinary VMA levels (3.4 umol/mmol creatinine (normal 0–4.5)). Lucas et al. revealed that no patients with small ganglioneuromas had increased HVA or VMA levels [6]. CT and magnetic resonance imaging are also unable to differentiate between these tumors; the only method for diagnosis of ganglioneuroma is through histopathological analysis [3–5]. Due to possible microscopic foci of malignant neuroblastoma cells within an otherwise benign tumor, complete surgical excision is usually required [8]. No MYCN gene alteration have been reported, nor any other diagnostic signals [2]. Most are diagnosed by chance, such as our case, or through secondary symptoms such as a cough, abdominal pain or weight loss [2,5,9].

Metastatic extensions of ganglioneuromas can also occur, but are rare and it is debated whether they develop naturally or are previous metastases of neuroblastomas that spontaneously matured [4,5,7]. These metastases most often occur in lymph nodes adjacent or in close proximity to the central ganglioneuroma, but have been reported to extend into bone [4,10]. Our patient was found to have nodules of tissue adjacent to her kidney. Multiple different pathologists were unable to determine whether these nodules represented nodules of ganglioneuroma versus lymph nodes occupied with tumor. However, because the tumor was removed from more than one location (regardless of whether there was disease in separate lymph nodes) and there was a positive margin, she was classified as stage 3.

Most often, ganglioneuromas are found arising from retroperitoneal and posterior mediastinal tissue (37.5% and 41.5% respectively), but can also occur in any sympathetic tissue [2–5].

Table 1
Pediatric renal ganglioneuromas found in the literature.

Ref.	Sex	Age	Presentation	Location of tumor	Treatment
[9]	Male	5 yrs	Hypertension	Perirenal ganglioneuroma	Complete tumor resection
[10]	Female	12 yrs	Incidentally detected abdominal mass	Renal ganglioneuroma	Complete resection (sacrificing a portion of inferior vena cava)
Current case	Female	4 yrs	Recurrent urinary tract infections	Renal ganglioneuroma	Radical nephrectomy

Retroperitoneal ganglioneuromas are rare and only make up 0.72–1.6% of primary retroperitoneal tumors [9]. Renal ganglioneuromas in pediatric patients are even more uncommon with only two other reported cases (Table 1). The first case was a 12-year-old female patient who was similar to our patient in that she was asymptomatic with normal VMA levels but had a palpable right renal mass. A CT scan revealed a right renal mass with nodular projections [10]. In contrast, the second case involved a 5-year-old boy who was symptomatic with abdominal pain and a physical examination revealed hypertension [8]. However, he also had normal catecholamine levels. An MRI identified a right renal mass encasing the renal artery. His hypertension resolved after resection. In all cases, including ours, complete resection was done to remove the tumors.

Surgical excision is the best treatment for ganglioneuroma, due to their resistance to chemotherapy or any other adjuvant option. With complete excision, almost no patients show signs of recurrence or metastasis in follow-up [2–6]. While post-surgical prognosis is usually very good, long-term follow-up is recommended as local recurrences have been reported in a small number of cases [5,7].

3. Conclusions

We presented a 4-year-old female who had a large renal ganglioneuroma with two possible metastatic lymph node extensions that required a radical nephrectomy. Few cases have been described in the literature. There are no diagnostic methods to identify ganglioneuromas. Surgical excision is the most effective treatment with few cases of recurrence. Routine physical and radiological follow-up is recommended.

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