

11-2015

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Citation of this paper:

Speer, Stacey; Wiseman, Daniele; Moussa, Madeleine; and Bütter, Andreana, "Renal Oncocytosis in a Pediatric Patient: Case Report and Review of the Literature" (2015). *Surgery Publications*. 115.
<https://ir.lib.uwo.ca/surgerypub/115>



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



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ARTICLE INFO

Article history:

Received 5 August 2015

Received in revised form

11 September 2015

Accepted 14 September 2015

Key words:

Renal oncocytoma

Oncocytosis

Pediatric

ABSTRACT

Renal oncocytosis is a rare condition in which the kidney develops numerous oncocytomas. We present a case of a 12-year-old female who presented with right-sided flank pain of one-year duration. Imaging revealed several masses in the right kidney. Tissue biopsy confirmed multiple benign oncocytomas. Due to the presence of multiple oncocytomas throughout the kidney, a radical nephrectomy was performed. Given the rarity of this condition, as well as its known association with von Hippel-Lindau disease and Birt-Hogg-Dube syndrome, genetic investigations were pursued but failed to identify any abnormalities. This patient remains well and disease free six years after surgery. A review of the literature of this rare condition was performed.

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Renal oncocytosis is a rare pathological condition in which a wide spectrum of oncocytic changes occur in the kidney [1]. Warfel and Eble initially described oncocytomatosis in an adult patient in whom both kidneys had more than 200 oncocytomas [2]. Tickoo et al. described 14 cases of renal oncocytosis in which each diseased kidney contained numerous oncocytic nodules as well as a dominant mass. This mass is usually a renal oncocytoma although rarely, it can be a chromophobe renal cell carcinoma. Therefore, radical nephrectomy is often warranted due to concern about possible malignancy [3].

Renal oncocytomas are epithelial tumors composed of oncocytes that are well differentiated, contain eosinophilic cells and are arranged in a tubular pattern [1]. Specific genetic conditions, such as Birt-Hogg-Dube (BHD) and Von Hippel-Lindau syndrome, can also be associated with renal oncocytosis [1]. However, very few pediatric cases of renal oncocytoma have been described [4–8].

We report a case of a 12-year-old girl who was found to have multiple renal oncocytomas, bilateral macular degeneration and bilateral sensorineural hearing loss, prompting a thorough genetic investigation. To our knowledge, this is only the 5th reported pediatric patient with renal oncocytosis.

1. Case report

A 12-year-old female presented to her primary care physician with right-sided flank pain of one-year duration. Medical history was significant for bilateral macular degeneration as well as bilateral sensorineural hearing loss. Physical examination was unremarkable. Laboratory investigations revealed a normal complete blood count, liver and kidney function tests. Urinalysis was normal. A nuclear medicine bone scan was unremarkable. Abdominal ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI) were performed. Ultrasound and CT confirmed multiple well-defined complex cystic and solid masses scattered throughout the right kidney (Figs. 1 and 2). The left kidney was normal. The largest mass was located anteriorly within the lower pole measuring 3.7 cm × 4.6 cm (Fig. 1c). This along with several other renal masses showed complex cysts with solid irregular septations. The solid components confirmed flow within them on Doppler suggesting a neoplasm as opposed to a hemorrhagic cyst. Ultrasound imaging confirmed the presence of echogenic shadowing punctate components consistent with calcifications in one lesion. Fat suppressed image sequences on MRI and ultrasound imaging confirmed the lack of macroscopic fat within the lesions thus excluding the diagnosis of angiomyolipomas. No lesion exhibited a classic stellate central scar. In this clinical context and in conjunction with multiple indeterminate unilateral kidney masses in a child, a variety of differential diagnoses were considered

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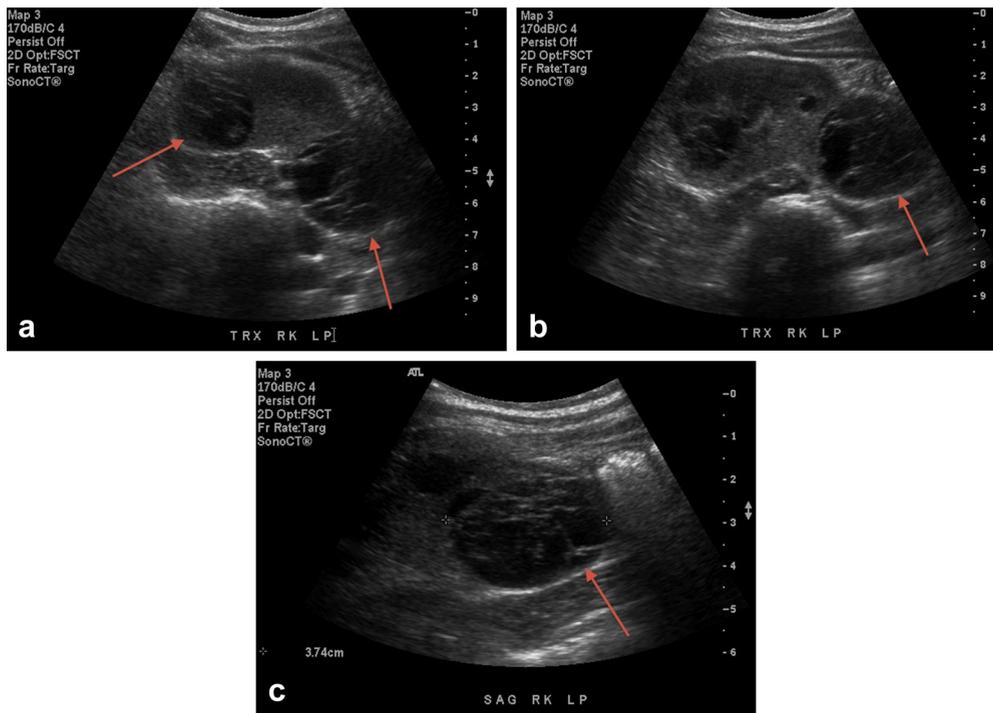


Fig. 1. (a–c) Transverse image of the lower pole of the right kidney demonstrates multiple complex masses. These appear as complex cysts with multiple irregular solid septations in which flow could be seen on color Doppler (not included). The largest was located within the lower pole measuring 3.7×4.6 cm.

including: (a) Birt-Hogge-Dube syndrome with renal tumors composed of chromophobe renal cell carcinoma and/or renal oncocytomas, (b) Von Hippel-Lindau disease in the context of multiple renal lesions, (c) tuberous sclerosis with renal

angiomyolipomas despite a lack of family history for this diagnosis and lack of macroscopic fat, (d) benign renal oncocytomas and finally (e) renal cell carcinoma.

Given the diagnostic uncertainty and concern about potential malignancy, the patient underwent laparotomy and open biopsies of her right kidney. Intraoperatively, multiple cystic nodules were noted throughout the kidney. Two biopsies were taken of the largest mass. Frozen section suggested that the lesion was benign (Fig. 3). Definitive treatment was deferred, pending permanent sections. Final pathology revealed neoplastic lesions composed of oncocytic cells arranged in small nests and a tubular architecture with areas of cystic change. The cells appeared monomorphic with minimal nuclear atypia. Mitotic activity was not identified. Clear cytoplasmic change was not identified and there was no necrosis or lymphovascular invasion. The tumor cells were negative for colloidal iron. Immunohistochemistry revealed that the tumor cells stained diffusely for vimentin and epithelial membrane antigen. Entrapped non-neoplastic tubules were positive for cytokeratin 7, while the tumor cells were negative. Rare cells showed cytoplasmic positivity for CD57. Chromogaphin, synaptophysin, WT-1 stains were negative. Final pathologic diagnosis was multiple right renal oncocytomas and oncocytosis. As a result of these pathologic findings, the diffuse involvement of her entire right renal parenchyma, multiple case reports describing renal oncocytosis as a possible precursor lesion to renal cell carcinoma and extensive discussion with the patient and her mother, a right radical nephrectomy was performed.

Due to the rarity of renal oncocytomas in the pediatric population and its known association with certain genetic conditions (i.e. Birt-Hogge-Dubé and Von Hippel-Lindau syndromes), our genetics team was consulted. In addition, her co-existing bilateral macular degeneration and bilateral sensorineural hearing impairment suggested an underlying genetic abnormality. Chromosomal analysis revealed a 46XX karyotype without any chromosomal abnormalities. Point mutations were not identified on the FLCN gene



Fig. 2. CT confirms multiple well-defined, low attenuating cystic and solid masses within the right kidney. There is an impression of fine septations configuring into a stellate pattern centrally within the largest lesion but not a classic central scar. There is no fat within these lesions.

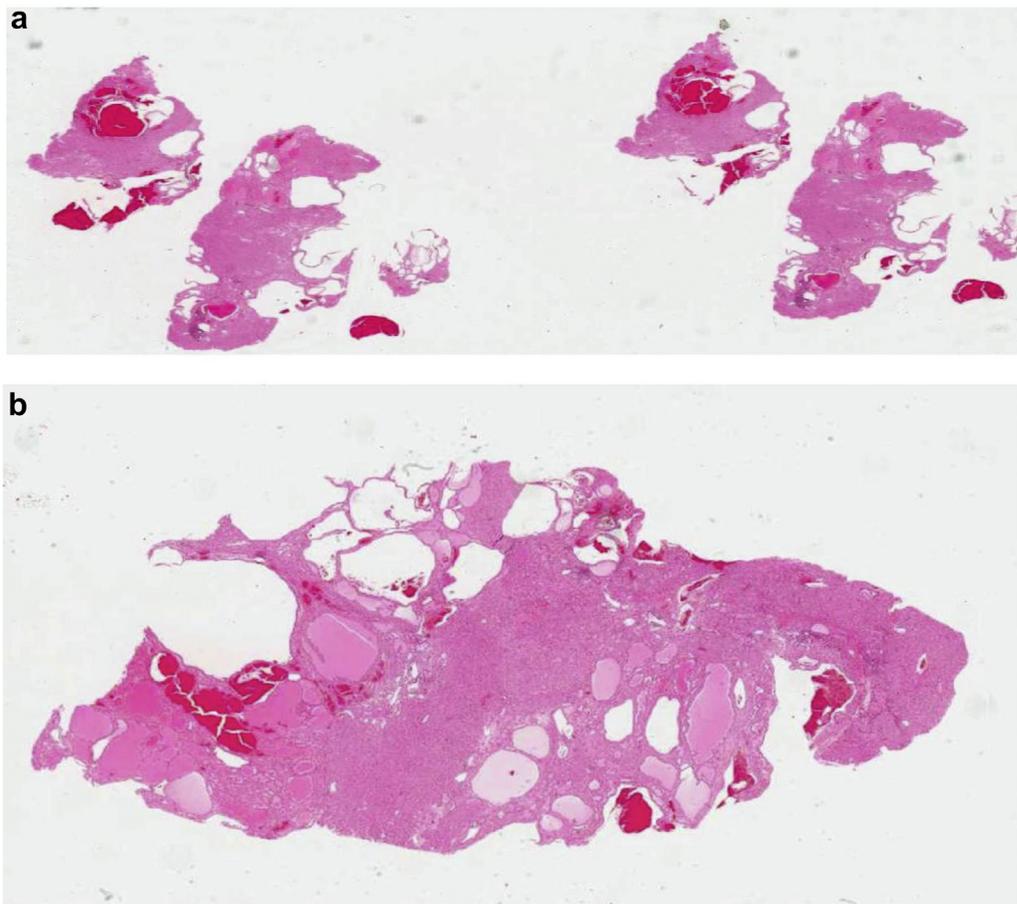


Fig. 3. (a and b): H&E stained slides showing features of renal oncocytoma. The tumor consists of sheets of cells arranged in small nests and having tubular architecture with focal cystic changes. The tumor cells have large eosinophilic cytoplasm with no significant nuclear atypia.

which encodes the protein folliculin on chromosome 17p11.2, which is the gene associated with Birt-Hogg-Dubé syndrome [1]. As well, there was no evidence of a Von Hippel-Lindau gene deletion and full sequencing of the coding regions of the Von Hippel-Lindau gene revealed no sequence variation from normal. An underlying mitochondrial disorder was considered but mitochondrial analysis was also normal. It remains possible that our patient possesses an unknown genetic condition.

2. Discussion

Renal oncocytosis results in diffuse oncocytic changes throughout the kidney as well as possible tumor development, such as oncocytomas and/or chromophobe renal cell carcinoma [1]. Renal oncocytomas are benign, epithelial tumors that are composed of uniform and well differentiated oncocytes [9,10]. The incidence

of renal oncocytomas varies between 3 and 7% of all primary renal tumors [11]. Most patients present with unilateral oncocytoma [12]. However, 4–6% will have multifocal disease while 4% will have bilateral disease [4]. Patients range in age from 10 to 94 years of age [1–12], with most occurring in the seventh decade of life. Our 12-year-old patient is one of the younger ones described to date. There is a male to female preponderance of up to 2.2:1 [4]. Most patients are asymptomatic, with the oncocytomas detected incidentally during imaging for non-urological complaints [4,12]. If symptomatic, microscopic hematuria, abdominal pain and flank mass have been reported [4,8,11].

Renal oncocytoma has traditionally been regarded as a benign neoplastic tumor; however, chromophobe renal cell carcinoma has been described within the same kidney [1,8,11]. If possible, nephron sparing surgery should be undertaken. Specifically, if the oncocytoma is a solitary, well encapsulated

Table 1
Pediatric renal oncocytomas found in the literature.

Ref.	Sex	Age	Presentation	Treatment	Genetic association	Tumor characteristics
[4]	Male	13 yrs	Left flank pain	Partial nephrectomy	None	Heterogenous, hypoechoic, solid, hypervascular mass.
[5]	Male	17 yrs	Viral illness, left abdominal mass palpated	Nephrectomy	None	Complex multicystic mass
[7]	Male	10 yrs	Recurrent abdominal pain, malaise, anorexia, macroscopic hematuria and dysuria.	Nephrectomy	None (maternal uncle had nephrectomy for hypernephroma)	Multiple kidney cysts
[8]	Female	12 yrs	Left sided abdominal fullness.	Nephrectomy	None (father had horseshoe kidney)	Complex multicystic mass
Current case	Female	12 yrs	Right flank pain	Nephrectomy	None	Multiple cystic and solid/cystic masses.

tumor which is 5 cm or less in diameter, then a partial nephrectomy should be performed [8,13]. However, if there are multifocal lesions, as seen in our patient, then a radical nephrectomy is required.

Clinical consideration was given to a variety of genetic possibilities for the development of renal oncocytoma in this young girl. Birt-Hogg-Dube syndrome is a rare autosomal dominant condition characterized by the development of fibrofolliculomas of the skin, pulmonary cysts and spontaneous pneumothorax [14]. The most serious complication of Birt-Hogg-Dube syndrome is the potential development of renal cancer that can present histologically with hybrid chromophobe and oncocytic features, which are characteristic and hallmark traits of this syndrome. Alternatively, Von Hippel-Lindau syndrome is a rare autosomal dominant genetic condition in which hemangioblastomas are found in the cerebellum, spinal cord, retina and kidney [15]. It can be associated with the development of cystic tumors of the kidneys, liver and pancreas and with the development of renal clear cell carcinomas occurring in up to 70% of patients [15]. Renal oncocytomas and renal clear cell carcinomas can both present with oncocytic features, which necessitates immunohistochemical analysis for diagnostic distinction. Although visual loss is a common manifestation in Von Hippel-Lindau syndrome, specific testing failed to detect any genetic abnormalities. Although most patients with renal oncocytosis possess an underlying genetic disorder, many case reports exist of patients without any identifiable genetic abnormality [4,7,8] (Table 1).

Although renal oncocytosis is more prevalent in the adult population, it rarely occurs in the pediatric population, with only four previously documented cases. The pediatric case reports range in age from 10 to 13 years. Surgical treatment was performed in all cases. There was a 1:1 male to female predominance with abdominal pain and/or flank pain as the most common presenting symptom. While renal oncocytosis can be linked with specific genetic syndromes, none of the documented pediatric cases were associated with any genetic conditions.

3. Conclusion

We presented a 12-year-old girl with renal oncocytosis characterized by multiple unilateral oncocytomas, requiring a radical

nephrectomy. No associated genetic syndrome could be identified. Although rare, renal oncocytomas should be considered in the differential diagnosis of renal masses in children.

Conflict of interest

None of the authors have a financial or personal conflict of interest to disclose.

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