CASE REPORT

Nephron-Sparing Surgery For Bilateral Sporadic Giant Angiomyolipomas

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A 40-year-old female complains of right flank plain associated with progressive abdominal enlargement. She had stable vital signs and normal renal function. CT urogram revealed bilateral flank masses suggestive of bilateral giant angiomyolipomas. She was counseled on the various treatment options and opted to undergo open surgical excision. She underwent an open clamp-less partial nephrectomy with no intraoperative events. Operative time was 120 minutes and estimated blood loss was 250cc. She was discharged in good clinical condition on postoperative day 4. Final histopathological analysis revealed angiomyolipoma. Genetic testing was positive for mosaic variant of tuberous sclerosis. After a year of follow up, she remains stable and is maintained on everolimus. Open ischemia-free partial nephrectomy may be done safely for giant renal angiomyolipomas. Radical nephrectomy should be reserved for the last option because the presence of contralateral disease may also require surgical excision in the future.

Key words: Giant angiomyolipomas, hamartomas, nephron-sparing surgery

Introduction

Giant angiomyolipomas, defined as tumors larger than 10 cm in its greatest diameter, may cause significant discomfort and pain. In addition, spontaneous retroperitoneal hemorrhage (Wunderlich syndrome) may occur and can be fatal which often happens in patients with masses more than 4cm.[1] Therefore, these patients need to counseled properly on the need for close monitoring and timely intervention.

There are several options for the treatment of angiomyolipomas. A recent updated review described the evolution of therapy for angiomyolipomas, spanning several decades of experience.[2] These include active surveillance, minimally invasive or open nephron-sparing approaches, radical nephrectomy, selective renal artery angioembolization, or novel chemotherapeutics. The choice of therapy depends on the extent and severity of the lesion, laterality, over-all renal function and patient's hemodynamic condition.

Herein is case of an adult female with bilateral giant AML who was treated successfully with open partial nephrectomy. The objective was to emphasize the need for a nephron-sparing approach when dealing with bilateral tumors of massive sizes. The operative technique is described followed by a review of literature on the other alternative therapies.

The Case

A 40-year-old female consulted because of right-sided abdominal pain of one year duration.

She denies gross hematuria or any other associated symptoms. Her family history is negative for any renal disease. Abdominal ultrasound revealed large, bilateral, hyperechoic renal masses consistent with large hamartomas (angiomyolipomas). Physical examination showed multiple hypopigmented macules over the face, chest, and in both upper and lower extremities suggestive of adenoma sebaceum (Figure 1). The abdomen was noted to be globular but soft and slightly distended, with bilateral palpable large flank masses. Other physical exam findings were unremarkable.

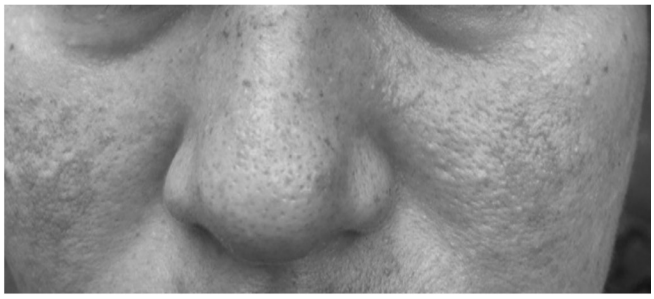

Figure 1. Photo of the patient's face.
Note the presence of adenoma sebaceum which is typically seen in patients with tuberous sclerosis complex.

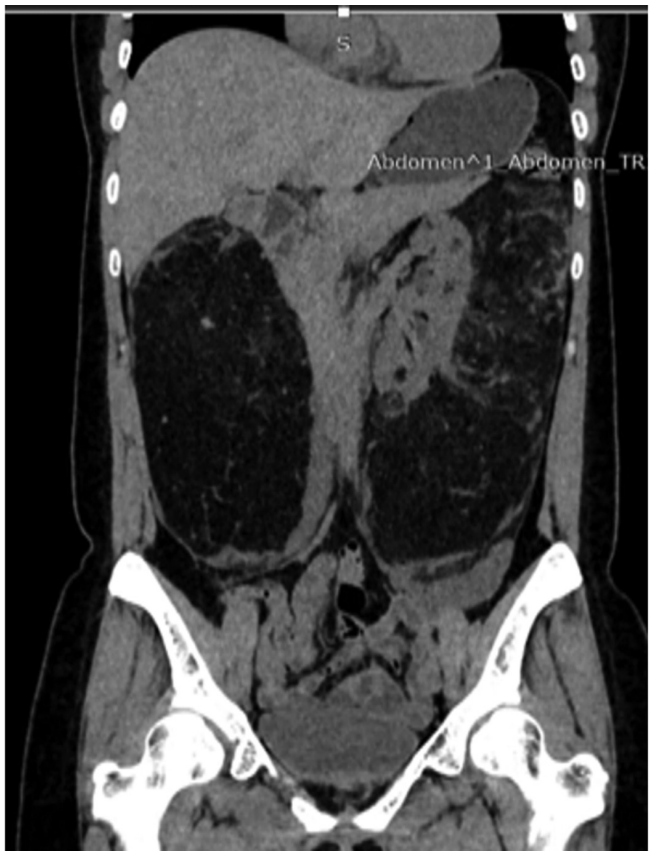

Figure 2. Contrast enhanced CT scan of the whole abdomen.
Note the presence of large fat attenuating exophytic masses bilaterally occupying the retroperitoneal region.

She had normal blood count, a serum creatinine of 0.8mg/dL and unremarkable urinalysis. A CT urogram confirmed the presence of bilateral enhancing renal masses measuring 19.3cm (-93 HU) on the right and 14 cm (-135 HU) on the left, respectively, engulfing both kidneys (Figure 2). These were all consistent with the diagnosis of bilateral giant renal angiomyolipomas.

Intervention

After a comprehensive preoperative evaluation, the patient was counselled on the different therapeutic options, as well as the risks and benefits of surgery. She preferred an open surgical excision and signed an informed consent.

Under general endotracheal anesthesia, the patient underwent transabdominal clamp-less open partial nephrectomy through a right anterior subcostal incision. Upon entering the abdomen, the ascending colon was identified and dissected along the white line of Toldt, and freed of its lateral attachments until it was reflected medially off the renal mass. Intraoperatively, two lesions were found on the right kidney, One of which is a large 24cm x 18cm anterior mass and the other was a smaller mass measuring 3cm x 3cm on the inferior pole (Figure 3). Through a combination of blunt dissection and the use of electrocautery, the mass was gently freed off the surface of the right kidney. The feeding vessels were isolated and divided using a vessel-sealing device, LigaSure™ Technology (Medtronic, Minneapolis, MN). Larger vessels were controlled by ligation with silk sutures. Extreme caution was observed in order to avoid injury to the renal hilum, renal parenchyma, and the ureter. After a meticulous dissection, two lesions (Figure 3) were excised. The total operative time was 120 minutes, with zero ischemia time and an estimated blood loss of 250 cc. There were no adverse intraoperative events.

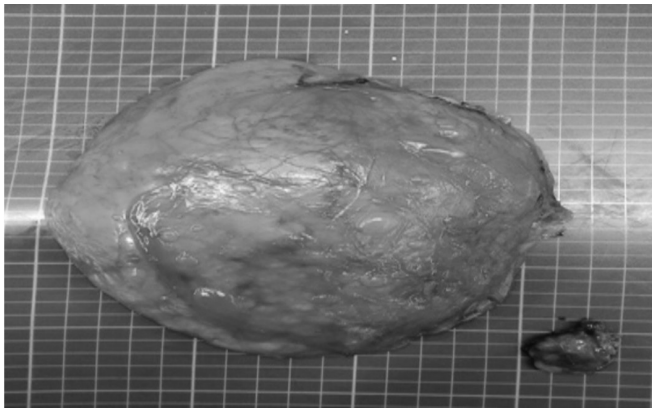

Figure 3. Excised specimens from the right kidney.
Note the yellowish ovoid tan to yellow fibrofatty tumors measuring 20 cm in largest diameter and weighing 1.1kilograms. A small 3 cm tumor was likewise excised from the lower pole of the right kidney.

Outcome

Histopathological analysis showed a predominant population of polygonal cells with clear eosinophilic cytoplasm and hyperchromatic nuclei. Mature adipose tissue and dysmorphic thick-walled blood vessels without elastic lamina were also seen. There was no evidence of cellular atypia nor pleomorphism. These findings were consistent with those of renal angiomyolipoma (Figure 4).

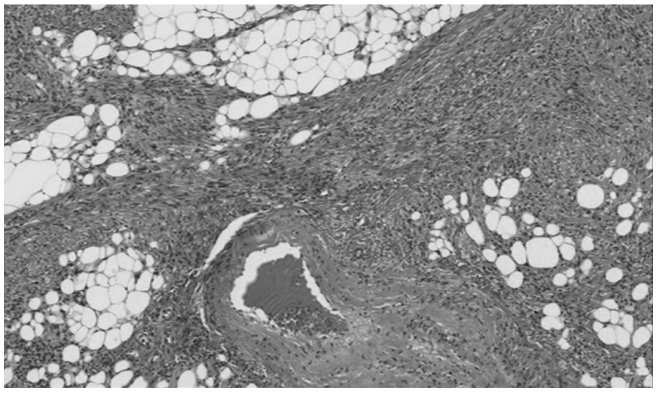

Figure 4. Microscopic view of the specimen.
Note the polygonal cells with clear eosinophilic cytoplasm and hyperchromatic nuclei specimen.

The patient had an unremarkable postoperative recovery and was discharged in a good clinical condition on postoperative day 4. Genetic testing was positive for one possibly mosaic pathogenic variant associated with autosomal dominant tuberous sclerosis complex (i.e. TSC2: c.3305_3306dup (p.Arg1103*.)

After one year of follow-up, the patient had stable renal function (eGFR: 115ml/min). She is currently doing well, back to work and performs her usual activities of daily living. She was started on everolimus starting at 2.5mg/day.

Discussion

Renal angiomyolipoma was first described by Grawitz in 1900 and accounts for more than 10% of renal tumors. It occurs in less than 1% of the population and with a female predisposition occurring in the 4th to 5th decade of life. It is a benign tumor composed of dysmorphic blood vessels, smooth muscles, and adipose tissue and occurrence may be sporadic in nature or as a clinical manifestation of a syndrome (i.e. tuberous sclerosis complex, lymphangioleiomyomatosis). Most cases are unilateral in nature while 20% are bilateral, the latter of which are common in patients with tuberous sclerosis. The most common genetic cause of angiomyolipoma arises from the mutation in either TSC1 (Hamartin) or TSC 2 (Tuberin) caused by unregulated mTOR activation leading to variable manifestation of epilepsy, neurocognitive impairment, autism, cortical tubers, astrocytoma, cardiac rhabdomyomas and shagreen patches. The patient tested positive for TSC2 and this confirms her genetic predisposition to this renal anomaly.

Giant angiomyolipomas, defined as tumors >10cm. are at risk for spontaneous rupture and hemorrhage, (Wünderlich syndrome), a urological emergency which may manifest as hemodynamic instability and hypovolemic shock.[1,2] Treatment of giant angiomyolipomas can be very challenging particularly when the disease involves bilateral kidneys. A radical nephrectomy leads to chronic kidney disease and when bilateral excision is performed, the patient ends up with minimal residual functioning nephrons or even an anephric state.

Active surveillance consisting of biannual or annual CT scan imaging is a viable option for some patients who are clinically stable. Grassano, et al. recommended this approach for large AMLs >4cm.[3] Of the 35 patients who were managed with expectant treatment, more than 50% were still on active surveillance at 5 years without any serious consequences. A conservative approach was not considered in the patient because she had bothersome and disabling symptoms for a year necessitating a more aggressive and definitive therapy.

Percutaneous selective renal arterial embolization is also a considerable option. In conjunction with nephron-sparing or radical surgery, it facilitates excision by restricting renal blood flow, and reducing the risk of intraoperative hemorrhage. However, it is often complicated by fever, flank pain, nausea and vomiting in about 42.8%. Von, et al. described its utilization in patients with uncontrollable symptoms and in the presence of vascular malformations.[4] When angioembolization is performed exclusively without adjunctive surgery, regrowth of the lesion and bleeding may still occur in 17-37% of patients. In this situation, a repeat embolization may be warranted. These two options were discussed lengthily with our patient, who opted for a more definitive approach while conserving as much renal parenchyma as possible.

Nephron-sparing surgery was therefore adjudged to be the best option in her case. A meticulous review of the CT scan imaging was needed to assess the kidneys for a possible partial nephrectomy. Intraoperative efforts were exhausted to avoid a radical nephrectomy. A clamp-less partial nephrectomy was performed to minimize ischemic renal injury. Careful identification, ligation and division of all neovascularization was achieved with a vessel sealing device Ligasure™ (Medtronic, Minneapolis, MN) was. Severe cases of sporadic giant angiomyolipomas may require radical nephrectomy when hemorrhage occurs. Patients with AML disease on a solitary kidney need counselling on possible progression to end-stage kidney disease, requiring renal replacement therapy. The patient was informed of the possibility of future excision for the contralateral disease. This is the compelling reason for a nephron-sparing approach for her right kidney.

An emerging option for giant AMLs is the use of targeted chemotherapeutic agents known as the mTOR inhibitors such as everolimus.[5] Everolimus induces cell cycle arrest, reduces cell proliferation, and prompts angiogenesis regression, contributing to the suppression of tumor enlargement and promoting their regression. The EXIST-2 phase III trial investigated the use of everolimus for renal AML associated with TSC showing that over half of patients experienced at least a 50% reduction in AML volume after 6 months of treatment. However, treatment-related adverse events such as stomatitis (48%), nasopharyngitis (24%), acne-like skin lesions (22%), headache (22%), cough (20%) and hypercholesterolemia (20%) may affect compliance. After nephron-sparing surgery, the patient was given adjunctive therapy with oral everolimus (2.5mg/day for a month, gradually increased to 5mg/day.) This dose reduction had been shown to benefit some patients, while reducing the drug's adverse effects.[6,7]

Conclusion

Excision of large giant sporadic renal angiomyolipoma via an open partial nephrectomy is challenging but feasible. A careful review of imaging is necessary for preoperative planning. Utilization of energy-based vessel sealing devices such as Ligasure™ can help reduce potential intraoperative hemorrhage. Nephron-sparing surgery should be considered in patients with bilateral disease. Radical nephrectomy should be avoided because contralateral disease may require another surgical intervention in the future.

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