Case Report
Refractory hypertension due to renal artery stenosis in a solitary kidney: case report and literature review

Xiquan Yan1,2, Mingxia Ding1, Jin Li2, Hui Zhan1, Yigang Zuo1, Haifeng Wang1, Yinglong Huang1, Jiansong Wang1

1Department of Urology, The Second Affiliated Hospital of Kunming Medical University, Kunming 650101, Yunnan, P.R. China; 2Department of Urology, Xiangtan Central Hospital, Xiangtan 411100, Hunan, P. R. China

Received June 4, 2017; Accepted December 15, 2017; Epub March 15, 2018; Published March 30, 2018

Abstract: In this article we reported a patient with the refractory hypertension which attribute to the severe atherosclerotic renal artery stenosis (ARAS) in a solitary kidney. The percutaneous transluminal renal angioplasty with stent (PTRAS) was proved to be an effective method in refractory hypertension. Then we systematically reviewed related articles to evaluate the benefit of PTRAS on patients with ARAS, especially those who combined with other certain clinical conditions. Although several clinical trials failed to show that stenting has any significant benefit over medical therapy in ARAS, we propose that the procedure should be considered as a viable option for acute critical cases.

Keywords: Atherosclerotic renal artery stenosis, renovascular hypertension, solitary kidney, percutaneous transluminal renal angioplasty with stent

Introduction
Renal artery stenosis (RAS), which presents in 1% to 5% of patients with hypertension [1], is mostly caused by atherosclerosis [2]. Treatments for atherosclerotic renal artery stenosis (ARAS) include surgical revascularization, percutaneous transluminal renal angioplasty with stent (PTRAS), as well as the management of high blood pressure (BP) and the control of other atherosclerotic risk factors with medical therapy [3]. However the optimal treatment of ARAS remains controversial. Here, a patient with a solitary kidney presented with refractory hypertension. After the angiographic which showed a severe (85%) right RAS, she was treated with PTRAS. During 2 years follow-up, she presented normal blood pressure and renal function. This case is a demonstration that PTRAS is safe and effective in patients with high risk ARAS. We then systematically reviewed related articles about whether PTRAS is superior to medical therapy in the ordinary patients and high risk patients. In this study, we concluded that though the lack of randomized data to support PTRAS for ARAS, certain subgroups of patients with high risk ARAS may benefit from this treatment.

Case report
A 55-year-old female presented with headache associated with dizziness was transferred to our institution. The physical examination revealed hypertension of 186/110 mmHg. Her medical history was significant for left radical nephrectomy because of kidney cancer at age of 42, and type 2 diabetes mellitus (T2DM) at age of 40. Her medication has been only insulin to control glucose in the recent 5 years.

Laboratory examination revealed that serum aldosterone, catecholamine, potassium, sodium, creatinine and urea levels were within normal limits. While the blood-lipid parameters, indicated the patient with a hyperlipemia. The level of plasma renin activity and plasma angiotensin II were both above the reference range. Despite administration with antihypertensive (nifedipine, metoprolol, valsartan and hydrochlorothiazide), the mean 24 h-ambulatory BP was in the high range of 168/93 mmHg (day-
time mean BP was 189/118 mmHg, nighttime mean BP was 161/80 mmHg). Enhanced CT scan pointed out a severe right RAS at the beginning segment and absence of the left renal (Figure 1).

Angioplasty of the left main RAS was performed using a 5 mm balloon. A 6 mm Genesis stent (Cordis, South Ascot Berks) was inserted. After confirmed with right RAS during the angiographic, the patients underwent percutaneous transluminal renal angioplasty with stent (PTRAS). And then the completion angiogram showed patency of vessels. The next day, the patient’s BP was 128/78 mmHg without any antihypertensive medications. According to the observation of normal BP in the next 48 h, she was successfully discharged back home and prescribed aspirin 100 mg per day and clopidogrel hydrogensulfate tablets 75 mg per day.

One week after operation, the patient had normal serum plasma renin activity, angiotensin II and aldosterone. The BP was 125/76 mmHg without any antihypertension medication. And CT scan showed the renal artery recover normal size (Figure 2). In view of 15 year history of T2DM and the higher level of LDL, she was
advised to use insulin (16 units twice a day) to control blood sugar and simvastatin (5 mg/day) to alleviate hyperlipidemia. During the 24 months’ follow-up, her BP maintained normal and the data from serum biochemical indexes and Doppler ultrasound of the renal arteries indicated the good clinical outcomes.

Discussion and literature review

Here we report a patient with ARAS in a solitary kidney. Because of the refractory hypertension, she was treated with PTRAS and present good clinical outcomes. As the population aging process accelerating the prevalence of ARAS continues to increase, which is an important public issue [4, 5]. However it is still in the debate about the benefit of PTRAS verse medical therapy alone in the adults with ARAS [6].

The medical administration on ARAS include antiplatelet medication (such as aspirin or clopidogrel) and other drugs to control blood pressure, glucose and lipid level [7, 8]. The PTRAS procedures were usually performed by femoral approach under local anesthesia. Two large studies, Angioplasty and Stenting for Renal Artery Lesions (ASTRAL) [4] and Cardiovascular Outcomes in Renal Atherosclerotic lesions (CORAL) [5] compared the outcomes of PTRAS and medical therapy alone. The ASTRAL trail was conducted as a randomized and unblinded trial during a 5-year period. It compared renal function trail blood pressure, the time to renal

Table 1. Characteristics and improvements of RAS patients with PTRAS

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Reference</th>
<th>Specific clinical conditions coexist</th>
<th>Clinical improvements</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>George et al., 2005</td>
<td>19</td>
<td>RAS in a single functioning kidney</td>
<td>Improvement in renal function</td>
<td>1 month</td>
</tr>
<tr>
<td>Kumar et al., 2006</td>
<td>20</td>
<td>Bilateral RAS, flash pulmonary edema</td>
<td>Asymptomatic</td>
<td>-</td>
</tr>
<tr>
<td>Kuznetsov et al., 2007</td>
<td>21</td>
<td>Bilateral RAS, hypertensive emergency, acute renal failure</td>
<td>Immediate recovery of renal function, improvement in BP</td>
<td>-</td>
</tr>
<tr>
<td>Campbell et al., 2008</td>
<td>22</td>
<td>Anuric renal failure, bilateral RAS</td>
<td>Renal function</td>
<td>-</td>
</tr>
<tr>
<td>Wykrzykowska et al., 2008</td>
<td>23</td>
<td>Refractory hypertension, congestive heart failure, pulmonary edema</td>
<td>Improvement in BP, alleviate symptoms of congestive heart failure and pulmonary edema</td>
<td>-</td>
</tr>
<tr>
<td>Chrysochou et al., 2009</td>
<td>24</td>
<td>Anuric acute renal failure, pulmonary oedema, bilateral renal artery, poorly controlled hypertension</td>
<td>Improvement in BP, renal function</td>
<td>8 months</td>
</tr>
<tr>
<td>Dziemianko et al., 2009</td>
<td>25</td>
<td>Refractory hypertension, bilateral RAS</td>
<td>Improvement in renal function and blood pressure</td>
<td>6 months</td>
</tr>
<tr>
<td>Islam et al., 2009</td>
<td>26</td>
<td>Acute renal failure, bilateral RAS, acute pulmonary edema</td>
<td>Improvement in renal function, no recurrence of chest pain or dyspnea</td>
<td>4 months</td>
</tr>
<tr>
<td>Kanamori et al., 2009</td>
<td>27</td>
<td>Acute renal failure, acute pulmonary edema, bilateral RAS, poor controlled BP</td>
<td>Improvement in BP, asymptomatic</td>
<td>-</td>
</tr>
<tr>
<td>Zanki et al., 2009</td>
<td>28</td>
<td>A solitary kidney, anuric renal failure</td>
<td>Improvement in renal function</td>
<td>6 months</td>
</tr>
<tr>
<td>George et al., 2011</td>
<td>29</td>
<td>Recurrent flash pulmonary edema, bilateral renal artery, uncontrolled hypertension</td>
<td>Prevents recurrent flash pulmonary edema, improvement in renal function</td>
<td>2 months</td>
</tr>
<tr>
<td>Kindo et al., 2011</td>
<td>30</td>
<td>Flash pulmonary edema, bilateral RAS</td>
<td>Asymptomatic, improvement of renal function</td>
<td>36 months</td>
</tr>
<tr>
<td>Navaravong et al., 2011</td>
<td>31</td>
<td>Heart failure, anuric renal failure</td>
<td>Improvement in renal function and BP</td>
<td>-</td>
</tr>
<tr>
<td>Li et al., 2012</td>
<td>32</td>
<td>Bilateral RAS, pulmonary oedema</td>
<td>No further episodes of pulmonary oedema</td>
<td>48 months</td>
</tr>
<tr>
<td>Noce et al., 2012</td>
<td>33</td>
<td>Refractory hypertension, acute renal failure, bilateral RAS</td>
<td>Improvement in renal function and BP</td>
<td>-</td>
</tr>
<tr>
<td>Alonso et al., 2013</td>
<td>34</td>
<td>Acute pulmonary edema, bilateral RAS</td>
<td>No further episodes of pulmonary oedema</td>
<td>3 months</td>
</tr>
<tr>
<td>Chrysochou et al., 2013</td>
<td>35</td>
<td>Acute flash pulmonary oedema, bilateral RAS</td>
<td>Improvements in the cardiac morphology and function, renal function</td>
<td>12 months</td>
</tr>
<tr>
<td>Demming et al., 2013</td>
<td>36</td>
<td>Recurrent flash pulmonary oedema, renal failure, poor controlled BP, bilateral RAS</td>
<td>Improvement in renal failure and BP, alleviate symptoms of pulmonary oedema</td>
<td>18 months</td>
</tr>
<tr>
<td>Ishida et al., 2013</td>
<td>37</td>
<td>Progressive renal failure</td>
<td>Improvement in renal function</td>
<td>12 months</td>
</tr>
<tr>
<td>Luiken et al., 2013</td>
<td>38</td>
<td>RAS in a solitary kidney, progressive renal failure, poor controlled BP</td>
<td>Improvement in renal failure and BP</td>
<td>-</td>
</tr>
<tr>
<td>Nagashima et al., 2014</td>
<td>39</td>
<td>Acute worsening of chronic renal failure, pulmonary oedema</td>
<td>Renal function, improvement in pulmonary oedema</td>
<td>-</td>
</tr>
<tr>
<td>Mizuma et al., 2016</td>
<td>40</td>
<td>Malignant hypertension, posterior reversible encephalopathy syndrome</td>
<td>Improvement in renal failure and BP, brain MRI were improved</td>
<td>-</td>
</tr>
</tbody>
</table>
and major cardiovascular events, and mortality in the participants receiving PTRAS or medical therapy alone. The trail failed to find a clinical superiority of the patients undergoing PTRAS over medical therapy alone. The CORAL trail performed a randomized clinical trial to analyze the occurrence of adverse cardiovascular and renal events during the follow-up in a large sample of patients receiving PTRAS or medical therapy alone. They found that the rate of composite primary end point or any of its individual components, including death from cardiovascular or renal causes, stroke, myocardial infarction, congestive heart failure, progressive renal insufficiency, and the need for renal-replacement therapy did not differ significantly between the two groups. Other trails, including randomized controlled trials [9-11] and non-randomized studies [12, 13] assessed whether renal artery stenting bringing benefit to the RAS and showed no significance in the rate of mortality and renal replacement therapy. Moreover, a meta-analysis with 2,139 patients compared the efficacy of revascularization verse medical therapy in ARAS patients. They concluded that angioplasty with or without stenting was not superior to medical therapy [14]. All these studies seemed to be proved that revascularization and medical therapy alone might be similar in ARAS [15]. However these conclusions had some limitations, such as the relatively small sample size and stable kidney function, the moderate hypertension and degree of stenosis (50%-70%), the exclusion of patients with serious complications [6]. That is to say, these trails failed to find potential benefits from the subset of patients who with a sever stenosis or decompensated ARAS.

As we know, severe renal stenosis results in poor controlling of hypertension, progressive renal insufficiency, left ventricle hypertrophy and heart failure. Nevertheless few studies evaluated the benefits of stenting on the patients with significant renal stenosis when compared to the patients with medical therapy [6]. Milewski et al. [16], analyzed the clinical improvement of 265 consecutive patients with ARAS treated with stenting. All participants had more than 50% de novo RAS and accorded to at least one of the following inclusion: poorly controlled hypertension (mean systolic blood pressure of more than 160 mmHg) under at least three anti-hypertensive medications, deterioration of renal function (estimated Glomerular Filtration Rate (eGFR) of less than 60 mL/min/1.73 m²), and unexplained congestive heart failure or recurrent acute pulmonary oedema. They did not find any significant benefits of eGFP and systolic blood pressure with the administration of anti-hypertensive medications before the procedure and follow up. However, after the treatment with stenting and a median about 2 years’ follow up, they concluded that PTRAS treatment in RARS may confer preservation of renal function and improvement of blood pressure control. Moreover, a retrospective analysis evaluates outcomes of endovascular therapy of ARAS in patients with a solitary functioning kidney [17]. They assessed preoperative GFR, renal size, the occurrence of acute functional injury after the procedure and proved that patients with a solitary functioning kidney got clinical benefit from the intervention. Considering the few applicable data to guide the therapy for high risk patients with ARAS, James et al. explored the effect of revascularization compared to medical therapy on presentation with flash pulmonary edema, refractory hypertension or rapidly declining kidney function [18]. Interestingly, their data supported that patients presenting with high risk presentation may benefit from the treatment of revascularization in reducing risk for death and cardiovascular event. However, some caveats exist in the study, such as the non-randomized design, the lack of other parameters which influenced the clinical outcomes. Many recently published case reports presented the patients with ARAS as well as other certain clinical conditions (Table 1) and suggested that all of them benefited from stenting [19-40]. In these reports, rapid clinical improvements were seen after treated with stenting. However the inclination of reporting the success after stenting and the over-emphasis of benefit of some certain patients limited their ability to reveal the difference between PTRAS and medical therapy alone in most RARS patients.

Since the patient with a sever stenosis in the solitary kidney presented a poor controlled blood pressure in our report, she was treated with PTRAS. As reported previously [17], the treatment has proved to be a safe procedure and improved the clinical conditions. Although clinical benefits of PTRAS on ARAS remain controversial, revascularization with stenting has been commonly accepted by the patients with...
high risk. Future studies should focus on determining appropriate candidates who are putatively most likely to benefit from PTRAS [41, 42]. Those who are proved to be resistant to drug therapy, hemodynamically significant ARAS or have signs of decompensation should consider to be treated with PTRAS.

Acknowledgements

We are grateful to the patient for the participation in our study. This study was supported by the National Natural Science Foundation of China (Nos. 81260374 and 81460384), the Yunnan Provincial Department of Education Fund (No. 2014Z072).

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Jiansong Wang, Department of Urology, The Second Affiliated Hospital of Kunming Medical University, Yunnan Institute of Urology, 374 Dianmian Road, Kunming 650101, Yunnan, P.R. China. E-mail: jiansongwang@126.com

References


RAS in a solitary kidney: case report and literature review
