Microsurgical Treatment of ADPKD Patients with Intracranial Aneurysms: clinical experience of a tertiary vascular neurosurgery center

Tratamento Microcirúrgico de Pacientes com Rins Policísticos e Aneurisma Intracraniano: experiência clínica de um centro terciário

Lucas Crociati Meguins¹
André Salotto Rocha²
Eberval Gadelha Figueiredo³
Dionei Freitas de Morais⁴

ABSTRACT

Introduction: Autosomal dominant polycystic kidney disease (ADPKD) is one of the most common genetic disorders with a prevalence rate of approximately 1 in 400 to 1 in 1000 individuals. Intracranial aneurysms are one of the most frequent vascular anomalies in ADPKD and still an important cause of morbidity and mortality in these patients. Methods: A retrospective observational investigation was carried out in two Brazilian tertiary referral vascular neurosurgery center, from January 2015 to March 2018. Results: Sixteen patients, 13 of them electively and 3 as emergency, and underwent treatment for twenty brain aneurysms were operated on. Twelve of them were female (75%) and the mean age was 58.3 years (47-73 years). The majority of aneurysms location was the anterior circulation, with 40% in the middle cerebral artery (MCA) and 35% in anterior communicating artery (ACoA). Fifteen patients (93.7%) underwent surgical clipping alone and one patient undergone surgical clipping plus endovascular treatment. In the elective group, 30% of the patients had postoperative hemorrhagic complications and 2 patients died, while in the other group, 2 patients had a good outcome and one died. Conclusion: Intracranial aneurysms are very common in patients with ADPKD and an important cause of morbidity and mortality for them, especially in cases with subarachnoid hemorrhage. If well-planned these patients treatment is safe and essential to maintain their quality of life and avoid the dreaded rupture of the aneurysm and the complications of subarachnoid hemorrhage.

Keywords: Autosomal dominant polycystic kidney disease; ADPKD; Intracranial aneurysm; Subarachnoid hemorrhage; Screening
INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is one of the most common genetic disorders with a prevalence rate of approximately 1 in 400 to 1 in 1000 individuals. This group of people have mutations, in the majority of cases, either in chromosome 16 (PKD1 – about 78-85%) or in chromosome 4 (PKD2 – about 14-15%), resulting in dysfunction of the corresponding proteins (polycystin 1 and polycystin 2, respectively). ADPKD is characterized by progressive development of bilateral kidney cysts and early-onset chronic renal failure and is associated with major extrarenal complications, including hepatic and pancreatic cysts, cardiac valve disease and intracranial aneurysms.

Intracranial aneurysms are one of the most frequent vascular anomalies in ADPKD and still an important cause of morbidity and mortality in these patients. The prevalence of aneurysms associated with ADPKD ranges from 3 to 12% (about four or five times higher than in the general population), with an increase up to 21.6% in patients with a family history of intracranial aneurysms or hemorrhagic stroke. However, the overall risk of rupture is similar to that of the general population.

The aim of this study was to present 16 consecutively ADPKD patients with 20 intracranial aneurysms (ruptured or unruptured) treated by open surgery and compare our outcomes and complications with the current literature.

METHODS

Study delineation

A retrospective observational investigation was conducted with data collection from all inpatients and outpatients diagnosed with ADPKD with IA from January 2015 to March 2018, treated at the Faculdade de Medicina de São José do Rio Preto and Austa Hospital, both Brazilian tertiary referral vascular neurosurgery centers. Clinical data were obtained retrospectively from the patient records and files. For all patients with the diagnosis of IA on magnetic resonance angiography, computed tomography angiography and/or digital subtraction arteriography, the following data were collected: Gender, age at the date of surgery, location of aneurysms, elective or emergency surgery, type of surgery, complications after surgery and patient outcomes.

All elective patients underwent at least one preoperative imaging exam, among which we can mention the computed tomography angiography with 128 channels, magnetic resonance angiography with 1.5 Tesla or 3D digital subtraction angiography. Patients with sudden headache were evaluated on admission by the clinic team...
in the emergency room and, upon confirmation of subarachnoid hemorrhage by tomography further underwent angiotomography and were transferred to the care of the neurosurgery team. No patient was submitted to a neuropsychological assessment before or after surgery. Pterional craniotomy was used for aneurysms of the anterior circulation, except for pericallosal aneurysm, which used interhemispheric craniotomy. For aneurysms of the posterior circulation was used frontotemporal-orbitozygomatic craniotomy. Surgery was performed using classical neurosurgery techniques and all patients were referred to the intensive care unit after surgery.

Follow-up was carried out for 6 months. All patients received a neurological examination including an observation of behavior disorder, signs / symptoms of hydrocephalus and postoperative seizure.

The project of the present study was analyzed by the Ethical Committee of our institution which approved the performance of our investigations. All patients and/or parents signed the consent form. The study complies with the Declaration of Helsinki.

The data collected from all the patients were organized in tables. Averages are expressed as the mean for parametric data.

RESULTS

During the study period, sixteen patients underwent surgical clipping of twenty brain aneurysms. Twelve were female (75%) and mean age was 58.3 years (47-73 years). The majority of aneurysms location was the anterior circulation, with 40% in the middle cerebral artery (MCA) and 35% in anterior communicating artery (ACoA). Three of these patients (18.7%) arrived at the emergency department with sudden headache and were taken to a computed tomography which confirmed subarachnoid hemorrhage, and two of them also presented hydrocephalus in preoperative exams. Fifteen patients (93.7%) underwent surgical clipping alone and one patient undergone surgical clipping plus endovascular treatment. Table 1 summarizes the demographic and clinical data of all patients.

Nine patients (56.2%) had no complications and presented a great outcome. However, seven patients (43.7%) showed severe postoperative complication. Two of these patients had a subarachnoid hemorrhage, one of them evolved to hydrocephalus (underwent a VP shunt) and had a good outcome. The other patient had vasospasm, evolving to death. The case 11 kept epilepsy after surgery, but had a good outcome. The case 5 presented epidural hemorrhage and the case 14 presented cerebellar hemorrhage after surgery, both evolved with good outcome without need for further surgery. The case 15 (Figure 1) presented a right mydriasis after surgery, and an image exam detected a right subdural hemorrhage in the immediate postoperative period, which required the patient to return to the operating room to perform a decompressive craniectomy. The case 16 (Figure 2) was extubated after postoperative image exam showing no evidence of bleeding. However, on the first postoperative day, the patient evolved to a decrease in the consciousness level preceded by a period of agitation and hypertension, demanding a decompressive craniectomy.

![Figure 1. Case 15. 3D MR Angiography showing right middle cerebral artery aneurysm (arrow).](image1)

![Figure 2. Case 16. CT Angiography showing the 5 aneurysms (arrows) of this patient. A. 3D reconstruction. B. A reconstruction of the maximum intensity projection (MIP) focusing on the left superior cerebellar artery aneurysm.](image2)
Table 1. Clinical data of ADPKD patients with intracranial aneurysm.

<table>
<thead>
<tr>
<th>Case</th>
<th>Gender</th>
<th>Age (years)</th>
<th>Aneurysm location</th>
<th>Type of surgery</th>
<th>Preoperative treatment findings</th>
<th>Treatment</th>
<th>Postoperative treatment findings</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>49</td>
<td>PComA L</td>
<td>Elective</td>
<td>-</td>
<td>Clipping</td>
<td>-</td>
<td>Good</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>61</td>
<td>ACoA</td>
<td>Urgent</td>
<td>SAH + Hydrocephalus</td>
<td>Clipping</td>
<td>Hydrocephalus</td>
<td>Good</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>67</td>
<td>MCA M1M2 R</td>
<td>Elective</td>
<td>-</td>
<td>Clipping</td>
<td>-</td>
<td>Good</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>51</td>
<td>ACoA</td>
<td>Urgent</td>
<td>SAH</td>
<td>Clipping</td>
<td>-</td>
<td>Good</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>73</td>
<td>PComA R</td>
<td>Elective</td>
<td>-</td>
<td>Clipping</td>
<td>Epidural hemorrhage</td>
<td>Good</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>59</td>
<td>MCA M1M2 L</td>
<td>Elective</td>
<td>-</td>
<td>Clipping</td>
<td>-</td>
<td>Good</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>65</td>
<td>ACoA</td>
<td>Elective</td>
<td>-</td>
<td>Clipping</td>
<td>-</td>
<td>Good</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>67</td>
<td>MCA M1M2 R</td>
<td>Urgent</td>
<td>SAH + Hydrocephalus</td>
<td>Clipping</td>
<td>Vasospasm</td>
<td>Death</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>63</td>
<td>ACoA</td>
<td>Elective</td>
<td>-</td>
<td>Clipping</td>
<td>-</td>
<td>Good</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>54</td>
<td>MCA M1M2 L</td>
<td>Elective</td>
<td>-</td>
<td>Clipping</td>
<td>-</td>
<td>Good</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>61</td>
<td>ACoA</td>
<td>Elective</td>
<td>Epilepsy + Brain edema</td>
<td>Clipping</td>
<td>Epilepsy</td>
<td>Good</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>47</td>
<td>ACoA</td>
<td>Elective</td>
<td>-</td>
<td>Clipping</td>
<td>-</td>
<td>Good</td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>58</td>
<td>Pericallosal</td>
<td>Elective</td>
<td>-</td>
<td>Clipping</td>
<td>-</td>
<td>Good</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>54</td>
<td>SCA</td>
<td>Elective</td>
<td>-</td>
<td>Clipping</td>
<td>Cerebellar hemorrhage</td>
<td>Good</td>
</tr>
<tr>
<td>15</td>
<td>F</td>
<td>54</td>
<td>MCA M1M2 R</td>
<td>Elective</td>
<td>-</td>
<td>Clipping</td>
<td>Subdural hemorrhage</td>
<td>Death</td>
</tr>
<tr>
<td>16</td>
<td>M</td>
<td>51</td>
<td>2 MCA L + 1 MCA R</td>
<td>Elective</td>
<td>-</td>
<td>Clipping</td>
<td>Intracerebral hemorrhage</td>
<td>Death</td>
</tr>
</tbody>
</table>

F: Female; M: Male; L: Left; R: Right; SAH: subarachnoid hemorrhage; ACoA: Anterior communicating artery; MCA: Middle cerebral artery; PComA: Posterior communicating artery; SCA: Superior cerebellar artery; M1M2: MCA transition segment M1 and segment M2.
since a new image exam indicated intracerebral hemorrhage (Figure 3). Both patient that underwent to decompressive craniectomy evolved to death.

DISCUSSION

ADPKD is a great prevalent genetic disorder in general population and a relevant cause of morbidity and mortality. This disease has a wide variety of presentation and can remain clinically silent until adulthood, with patients presenting PKD2 mutations having milder phenotype than patients with PKD1 mutations\(^1\).

Intracranial aneurysms are more prevalent in these patients than in general population. Intracerebral and subarachnoid hemorrhage by IA rupture is the most serious complication of ADPKD, resulting in severe neurological morbidity and mortality with a range from 35% to more than 50% of cases\(^3,5\). In this study, for example, 3 patients had an aneurysm rupture with 1 patient presenting with hydrocephalus and subsequent shunt surgery and another patient developing hydrocephalus in the postoperative period, in addition to a third patient (case 8 – ruptured IA) who developed vasospasm and evolved to death.

In the present study, we showed our surgical series of 20 intracranial aneurysms in 16 patients with ADPKD. Higher prevalence in female patients like in previous studies was found\(^1,2,8,\) and the age of patients ranged from 47 to 73 years. An unpredictable finding in this study was the average age of 59 years of those who presented with ruptured aneurysm, showing different results from previous publications which indicated an average of 41 years (approximately 10 years earlier than in the general population)\(^4,5\). The most frequent location of unruptured aneurysm in our series was MCA (41%), followed by ACoA (29%), whereas the most common location of ruptured aneurysm was ACoA (2 aneurysms). Cagnazzo et al.\(^1\) showed that the majority of unruptured aneurysms are in the internal carotid artery (ICA, 40%) and the ruptured aneurysms in the MCA (45%), while Nurmonen et al.\(^2\) revealed MCA (48%) and ACoA (44%), respectively, in accordance with our data.

ADPKD patients have a higher risk of complications related to invasive investigative exams\(^8,17\) and treatment\(^1,7,9,18,19\) of brain aneurysms than general population. Rozenfeld et al.\(^19\) showed that these patients presented more frequently iatrogenic hemorrhage or infarction after surgical clipping for unruptured IA than patients without ADPKD (11.8% vs 6.4%). Moreover, Yoo et al.\(^20\) exhibited that ADPKD patients in hemodialysis had increased risk of intracranial hemorrhage and ADPKD patients with intracranial hemorrhage had a cumulative mortality risk higher than patients without intracranial hemorrhage (64% vs 44%). In the present study, 30.7% of the patients with unruptured IA evolved with hemorrhage after surgical treatment and two of them evolved to death (both dialysis patients). It’s also important to state that one patient (case 11 – unruptured IA) maintained epilepsy and another patient (case 2 – ruptured IA) maintained hydrocephalus in the postoperative period, in addition to a third patient (case 8 – ruptured IA) who developed vasospasm and evolved to death.

In view of all the findings previously expressed, including elevated morbidity and mortality especially in ruptured aneurysms, it is necessary to perform a better screening of these patients. Since they may be asymptomatic, most have normal renal function at moment of aneurysm rupture and subarachnoid hemorrhage may be the first sign/symptom in many patients\(^5,13\). However, until now this topic remains controversial in the literature\(^4,21,22\). Malhotra et al.\(^23\) demonstrated that screening in patients with ADPKD with MR angiography is cost-effective, suggesting repeat screening every 5 years after a negative initial study and annual surveillance imaging in patients with incidentally detected IA, with growth and high-risk aneurysms. In addition, based on the non-negligible incidence of de novo aneurysms in these patients, many other studies advised to keep the follow-up for a prolonged period with MR angiography (mainly time-of-flight technique without gadolinium-based contrast agent injection)\(^1,2,6,15,16,18,23\).
CONCLUSION

IA is very common in patients with ADPKD and an important cause of morbidity and mortality for them, especially in cases with subarachnoid hemorrhage. Early diagnosis is essential and screening can be an important resource, at least in ADPKD patients with higher risk of IA (family history of hemorrhagic stroke or IA), patients with prior subarachnoid hemorrhage, individuals on high-risk professions (such as pilots) or those undergoing major elective surgery. The treatment of these patients when well-planned is safe and essential to maintain their quality of life and avoid the dreaded rupture of the aneurysm and the complications of subarachnoid hemorrhage.

REFERENCES


16. Xu HW, Yu SQ, Mei CL, Li MH. Screening for intracranial aneurysm in 355 patients with autosomal-dominant polycystic


CORRESPONDING AUTHOR

Lucas Crociati Meguins, MD
Assistant Neurosurgeon
Department of Neurological Sciences
Division of Neurosurgery at the Base Hospital
Faculty of Medicine of São José do Rio Preto – FAMERP
São José do Rio Preto, São Paulo, Brazil
E-mail: lucascmeguins@gmail.com

Funding: nothing to disclose.
Conflicts of interest: nothing to disclose.