CASE REPORT

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Intracranial aneurysm as extra-renal manifestation of polycystic kidney disease – A case report

Intrakranijalna aneurizma kao ekstrarenalna manifestacija policistične bolesti bubrega

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Abstract

Introduction. Polycystic kidney disease is a hereditary kidney disease characterized by the occurrence of cysts (fluid-filled enlargements) in cortex or medula of the kidney, and is inherited in an autosomal dominant or autosomal recessive manner. In addition to multiple cysts in kidneys, there may be many extra-renal manifestations (cysts of the liver, pancreas, lungs, heart, etc.), among which the most serious one is intracranial aneurysms. **Case report.** A 57-year-old female patient with polycystic kidney disease and stage IV renal failure was hospitalized at our clinic due to decreased renal function, the development of urinary tract infections, headaches and unregulated blood pressure despite the usual treatment. This patient also had a number of associated diseases: obesity, diabetes mellitus (the insulin-dependent type), hypothyroidism, and depression syndrome. After better regulation of blood pressure, resolved urinary tract infections and improved renal function, there were still persistent headaches (resulting in the excessive use of analgesics). With adequate preparation, multislice computed tomography (MSCT) angiography of blood vessels of the head was performed. As a result, we diagnosed the saccular intracranial aneurysm (IA) with anterior localization. Regarding the symptoms, age and comorbidity, digital subtraction angiography (DSA) was performed, and showed saccular IA (5.2 mm × 4 mm), with wide neck affecting both middle cerebral artery branches (MCA). During the procedure the stent was placed, which filled the aneurysm with spirals, cutting it off from circulation. After the successful procedure and without further complications, the patient no longer had headaches and blood pressure was maintained within the required limits with stable parameters of chronic renal failure. **Conclusion.** The case of the patient with polycystic kidney disease, stage IV chronic renal failure, with a number of comorbidities (headache, obesity, hypertension, diabetes mellitus, hypothyroidism) and diagnosed with symptomatic intracranial aneurysm was successfully solved with a multidisciplinary approach, emphasizing the importance of teamwork in daily practice.

Key words:
polycystic kidney disease; kidney failure, chronic; intracranial aneurysm; diagnosis; angiography, digital subtraction; stents; treatment outcome.

Apstrakt

Uvod. Policistična bolest bubrega je oboljenje koje karakteriše pojava cista (proširenja ispunjenih tečnošću) u kori ili srži bubrega, a nasleđuje se autozomno dominantno ili autozomno recesivno. Osim multiplih cista u bubrezima, mogu se javiti i mnoge ekstra-renalne manifestacije (ciste jetre, pankreasa, pluća, srca, itd) među kojima je najozbiljnija pojava intrakranijalnih aneurizmi. **Prikaz bolesnice.** Bolesnica u dobi od 57 godina sa policističnom bolešću bubrega i hroničnom bubrežnom slabošću – IV stadijum, primljena je u našu ustanovu zbog pogoršanja bubrežne funkcije, razvoja urinarne infekcije, pojave glavobolja i neregulisanog arterijskog pritiska i pored redovne terapije. Inače, kod bolesnice su bile prisutne i pridružene bolesti: gojaznost, dijabetes melitus (insulin-zavisan tip), hipotireoza, depresivni sindrom. Nakon bolje regulacije arterijskog pritiska, sani-

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ranja urinarne infekcije, poboljšanja parametara bubrežne funkcije, zbog upornih glavobolja (zbog kojih je prekomerno koristila analgetike), uz odgovarajuću pripremu učinjena je *Multislice Computed Tomography* (MSCT) angiografija krvnih sudova glave, kojom je dijagnostikovana sakularna intrakranijalna aneurizma anteriorne lokalizacije. Obzirom na simptomatologiju, godine i komorbiditete, a u cilju dalje dijagnostike i lečenja učinjena je digitalna subtrakciona angiografija (DSA) u toku koje je zapažena sakularna aneurizma širokog vrata dimenzija 5,2 × 4 mm iz koje izlaze obe grane ACM. U toku procedure plasiran je stent, kojim je aneurizma ispunjena spiralama i isključena iz cirkulacije. Procedura je protekla bez komplikacija, a nakon toga bolesnica nije imala glavobolje, arterijski pritisak se održavao u zadovoljavajućim granicama, uz parametre hronične bubrežne slabosti koji su bili stabilni. **Zaključak.** Prikaz bolesnice sa policističnom bolešću bubrega, hroničnom bubreznom slabošću – stadijum IV, sa brojnim komorbiditetima (gojaznost, arterijska hipertenzija, dijabetes melitus, hipotireoza) kod koje je dijagnostikovana simptomatska intrakranijalna aneurizma, uspešno je rešena multidisciplinarnim pristupom, što naglašava značaj timskog rada u svakodnevnoj praksi.

Ključne reči:
bubreg, policistična bolest; bubreg, hronična insuficijencija; mozak, aneurizma; dijagnoza; angiografija, digitalna suptrakciona; stentovi; lečenje, ishod.

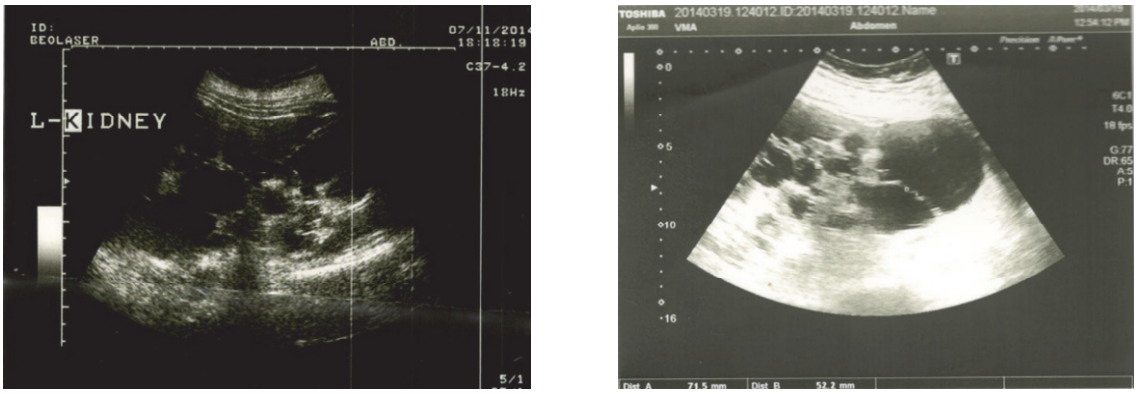
Introduction

Polycystic kidney disease is an inherited kidney disease that is characterized by the occurrence of cysts localized in the cortex or medulla of the kidney [1, 2]. This disease is inherited as an autosomal dominant (incidence 1: 500 to 1,000) or autosomal recessive one (incidence 1: 6,000 to 40,000), which determines the clinical manifestation and prognosis [3, 4]. The progression of autosomal dominant polycystic kidney disease (ADPKD) leads to a decrease in renal function and development of chronic renal failure, with further progress towards the terminal stage [1, 2]. In addition to multiple cysts in the kidneys, there are extra-renal manifestations of ADPKD in the form of cysts of other organs (liver, pancreas, lungs, spleen, brain, etc.) [1, 2]. In 4%–41.2% of patients, one of the most severe complications of the disease is the occurrence of intracranial aneurysms (IA) [2, 5, 6]. IA are usually localized in the anterior circulation, and opinions about their size and the manner of monitoring and methods of treatment are divided [5–7]. Also, there is no standardized protocol for screening of intracranial aneurysms in patients with ADPKD [6]. Some authors believe that there is a minimal risk of rupture of asymptomatic aneurysms of 5–7 mm in size, while other authors believe that there is a risk of rupture even with small aneurysms [7–11].

Case report

A 57-year-old female patient was admitted to the hospital due to worsening of chronic renal failure as a result of polycystic kidney disease, the development of urinary tract infections, intense headaches and high blood pressure. Since the age of 35 she had been treated for polycystic kidney disease, chronic kidney failure (serum creatinine 130 μmol/L) and hypertension and she had occasionally been treated by a nephrologist. Three months before hospitalization, she started experiencing frequent headaches, and she was taking analgesics every day. Her blood pressure was not regulated satisfactorily, despite antihypertensive therapy (max. value was 190/105 mmHg). During the outpatient visit, the physician observed serum creatinine 294 μmol/L, urea 21.7 mmol/L, glomerular filtration rate (GFR) [Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)] 15.2 mL/min/1.73 m^2, and recommended hospitalization. Other observed conditions were hypothyroidism (on substitution therapy with levothyroxine sodium), diabetes mellitus – insulin dependent type, obesity, and depressive syndrome. Also, there was family history of polycystic kidney disease. In addition to obesity of general type [body mass index (BMI) 40.51 kg/m^2] objective examination revealed light abdominal tenderness on deeper palpation (palpated enlarged kidneys) while other findings were regular. Laboratory analysis showed: erithrocyte sedimentation rate (ESR) 83 mm/h, serum urea 20.0 mmol/L, serum creatinine 208 μmol/L, and in the urine sediment: leukocyturia with a positive urine culture at *Escherichia colli* > 100,000 CFU/mL, GFR (CKD-EPI) 22.2 mL/min/1.73 m^2. The kidney ultrasound showed both kidneys enlarged (> 18 × 7.3 cm, with echogenic parenchyma to 1.2 cm), cystic changes with the largest cyst in the right kidney 7.1 × 5.3 cm, and 5.1 cm in the left kidney, nephrolithiasis and without hydronephrosis (Figure 1). After the antibiotic treatment, according to the findings of urine culture and bacterial sensitivity, the infection was resolved, the parameters of inflammation were normalized along with the stabilization of parameters of azotemia (serum creatinine 193 μmol/L). The blood pressure was regulated by adjusting antihypertensive medication. In order to examine persistent and intense headaches and through the further exploration of polycystic disease (after patient preparation for a contrast examination), multislice computed tomography (MSCT) angiography of the head with the blood vessels of the brain was performed. The image revealed a saccular aneurysm in the area of the right branch of middle cerebral artery (MCA). Other images of the arterial blood vessels of the head did not reveal changes. In the interest of further diagnosis and treatment, digital-subtraction angiography (SA) was performed, revealing saccular aneurysm (5.2 × 4 mm) in the area of MCA branch, with wide neck, encompassing both MCA branches (Figures 2 and 3). During the procedure, a stent was placed in the neck of the MCA aneurysm, which was filled with spirals and the aneurysm was cut off from circulation (Figure 4). The procedure was performed without

complications, thus eliminating headaches and the need for excessive analgesic use. Arterial pressure was maintained within the required limits and parameters of chronic renal failure were stable. During the follow-up examination after 18 months, the headaches had not reoccurred, arterial pressure was maintained within the required limits, and laboratory analysis showed: serum creatinine 264 umol/L, serum urea 19.2 mmol/L, and GFR (CKD-EPI) of 17.1 mL/ min/1.73 m^2.



a) b)

Fig. 1 – Renal ultrasound of polycystic changed kidneys: a) left and b) right. Several cysts in both kidneys, which are changed and enlarged.

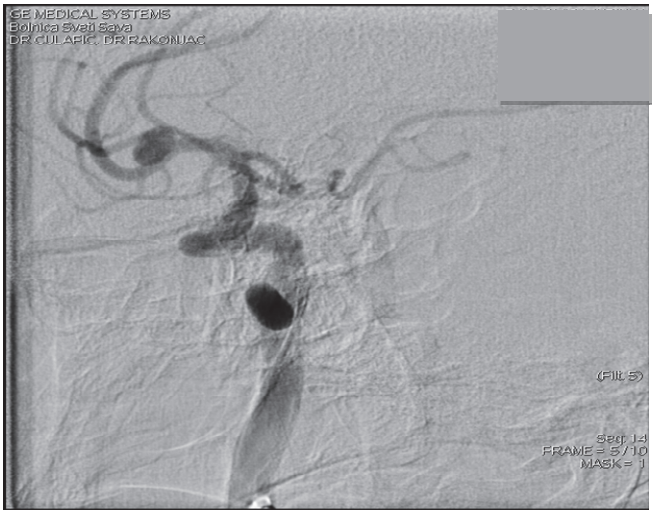


Fig. 2 – Digital subraction angiography (DSA) of right carotid arthery, showing saccular aneurysm in the region of midle cerebral artery (MCA) branch, with wide neck, affecting both MCA branches.

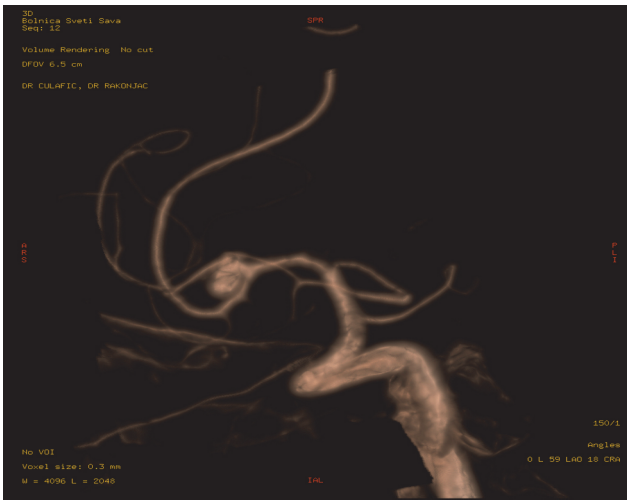


Fig. 3 – 3D angiography of right carotid arthery confirming aneurysm of right branch of middle cerebral artery (MCA) with both branches exiting.

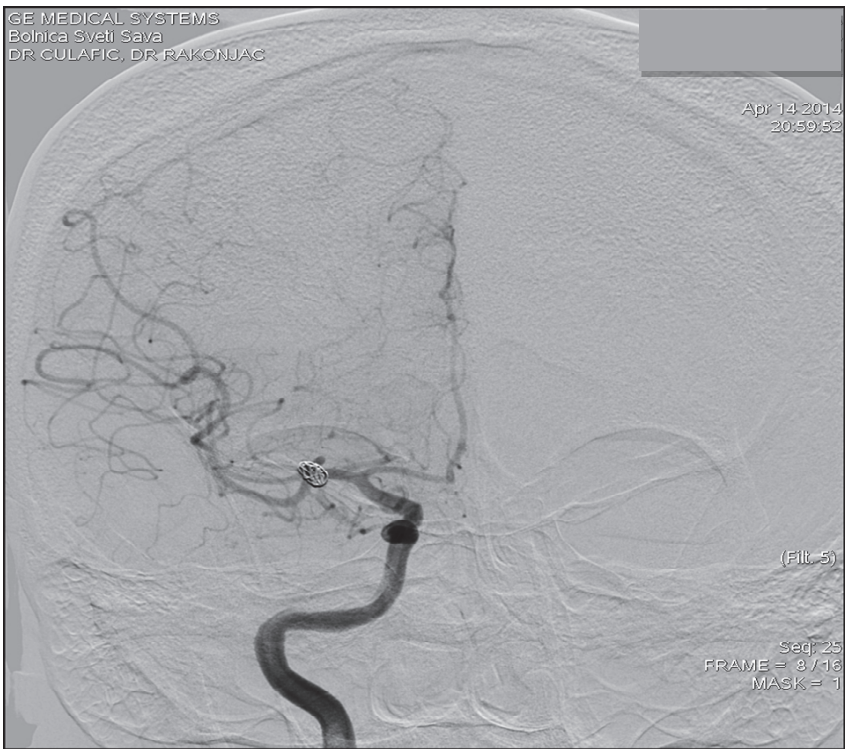


Fig. 4 – Digital subfraction agiography (DSA) of right internal carotid artery (ACI) showing stent placed in the neck of aneurysm of middle cerebral artery (MCA), filled with spirals and cut-off from circulation.

Discussion

ADPKD is the fourth most frequent renal disease with progression leading to terminal renal failure [12]. However, this disease is characterized by severe extrarenal manifestations, one of which is the appearance of IA. Their formation in ADPKD is linked to mutation of polycystin-1 (PKD1) and polycystin-2 (PKD2) [13, 14]. It is believed that the expression of these two proteins in the endothelium and smooth muscle of blood vessels and their reduced level, observed under experimental conditions, are responsible for the development of IA [14]. The incidence of IA in ADPKD is 4–7 times higher than in the general population, more frequent (22%) in patients who have a family history of IA or cerebral bleeding [5, 15]. Asymptomatic IA in an ADPKD occur with a prevalence of 9.3%, while unruptured aneurysms in patients with a family history of IA is observed in 21.2% [8]. The most serious complication is rupture of IA representing life-threatening complication. In some studies, it is stated that the average age of patients with ADPKD and ruptured aneurysm is 41, while in the general population, the average age of ruptured IA is 51 years [15, 16]. Also, many authors note that the risk of ruptured IA increases with age, and describe the prevalence of 23.3% in those older than 60 [15, 16]. For this reason, Niemczyk et al. [17] recommend that the screening examination of the head and the blood vessels of the brain should be performed in patients with ADPKD older than 45 years.

Our patient, who had a family history of polycystic kidney disease, developed symptoms of renal failure and hypertension at the age of 35. IA was discovered 22 years later, after the onset of headaches and arterial hypertension, which had not been sufficiently regulated with therapy.

Many authors suggest that uncontrolled hypertension with ADPKD is an additional risk of complications. The impact of hypertension on the occurrence IA or aneurysm rupture was the subject matter of many studies, and opinions are divided. Some authors believe that hypertension is a risk factor for rupture and massive subarachnoid hemorrhage, and others have found that arterial hypertension in ADPKD represents only indication for screening tests in the vicinity of IA, especially in patients older than 45 years [18–20]. According to Kulesza et al. [20], risk is most associated with the duration of hypertension.

Headaches may represent neurological symptoms, which is associated with the occurrence of IA, and also may precede subarachnoid hemorrhage. Niemczyk et al. [21] report previous occurrence of headache as the most common neurological manifestations in 63% of patients with ADPKD who had IA and cerebral hemorrhage. They also noted that in this group of patients, hypertension was present in 63%, and that 38% had data related to the occurrence of family history of subarachnoid hemorrhage [21].

The occurrence of headaches in our patient and the excessive use of analgesics, along with several years of arterial represented a risk for the long-term progression of chronic renal failure. Tests revealed intracranial aneurysm, which was symptomatic and associated with arterial hypertension. Special precautions were used in preparation for recording contrast, bearing in mind that this was a patient with stage IV chronic kidney disease.

Many authors have an opinion that in patients with ADPKD, the size of the aneurysm is the leading risk factor [22]. Thus, Morita et al. [23] described 6.697 intracranial aneurysms that were discovered by accident in 91% of patients. They observed that the aneurysm > 3 mm had an annual rupture rate of 0.95%, and the risk is increased with increasing size of the aneurysms, especially for those with diameter IA > 7 mm. Results of some studies indicate that in IA larger than 5 mm there is a risk of increase, and in IA larger than 7–10 mm there is a high risk for rupture [7]. A group of Chinese authors described that in IA smaller than 5 mm rupture was observed in 50.9% of patients, but also that rupture of of 2–5 mm was observed in 47.2 % of patients [24].

Our patient had an aneurysm of 5.2 mm, a medium-sized IA according to Liu et al. [24], which was symptomatic and required the appropriate treatment.

Intracranial aneurysms in ADPKD are most often (more than 90% of cases) anterior localized (internal *a. carotis*, a. *cerebri media*, *a. comunicans anterior*, *a. cerebri anterior*), and can sometimes be multiple (18%–31%), while other localizations (such as the posterior) are rare [6, 15, 17, 25]. In addition, the shape of the aneurysm is most frequently saccular intracranial, while fusiform ones are less frequent [15].

Our patient had a saccular aneurysm that was anterior localized, and bearing in mind the accompanying headaches, increased blood pressure and other co-morbidities (obesity, diabetes mellitus, hypothyroidism, depressive syndrome) it was decided to carry out the treatment of endovascular stent implantation. Today IA is treated by endovascular or standard neurosurgical methods, and the primary goal is to prevent subarachnoid hemorrhage [26, 27]. When comparing these methods, Quresh et al. [26] concluded that surgical treatment of ruptured IA has advantages compared to endovascular methods, because the obliteration rate of the aneurysm is higher and the need for additional treatment decreases. However, the one-year survival rate was better in the group treated with endovascular methods. They pointed out that the clinical outcome was not impacted by the need for retreatment or incomplete obliteration during the endovascular treatment. According to many authors, in the treatment of unruptured aneurysms, endovascular treatment should be the method of choice, because of a good outcome and shorter hospitalization [26, 27]. It is particularly recommended in patients with unruptured aneurysms who have associated comorbidities, weaker clinical status, or in case when they are older than 65 years [27–29].

Conclusion

A case of a female patient with polycystic kidney disease, stage IV chronic kidney failure, a number of co-morbidities (obesity, hypertension, diabetes mellitus, hypothyreoidism) and diagnosed with symptomatic intracranial aneurysm which was successfully resolved, demonstrates the importance of a multidisciplinary approach and stresses the importance of teamwork in daily practice.

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