The Incidence of Autosomal Dominant Polycystic Kidney Disease (ADPKD) in Patients with Intracranial Aneurysms

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Background: *There has been no previous study about the incidence of autosomal dominant polycystic kidney disease (ADPKD) and factors predicting possibility of ADPKD in patients with intracranial aneurysms.*
Objective: *To investigate the incidence of ADPKD in patients with intracranial aneurysms and predictive factor of ADPKD to screen and treat patients and family members who may have hidden abnormal genes of this disease.*
Material and Method: *This is a retrospective study which recruited patients with intracranial aneurysms who underwent abdominal imaging study, including ultrasonography (USG) or computerized tomography (CT). The incidence of ADPKD and factor predicting this disease were investigated.*
Results: *Of 94 patients with intracranial aneurysms, the incidence of ADPKD was 8.5%. Factors predicting ADPKD included high serum creatinine level and male gender. There was no significant difference in age, incidence of hypertension and diabetes mellitus between intracranial aneurysm patients with and without ADPKD.*
Conclusion: *The present authors recommend performing abdominal USG in patients with intracranial aneurysms for screening ADPKD because USG is non-invasive, inexpensive and useful in treatment and prevention of consequence of this disease in patients and family members who may have the abnormal genes.*

Keywords: *Autosomal dominant polycystic kidney disease, ADPKD, Incidence, Predictive factor, Serum creatinine*

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Intracranial aneurysm is a vascular disease causes by vessel wall pathology combined with hemodynamic stress on the vessel wall. The incidence of intracranial aneurysm in general population is about 2 to 6%[1-3]. In addition to hypertension, smoking, Ehler-Danlos syndrome type IV and neurofibromatosis, autosomal dominant polycystic kidney disease (ADPKD) is found to be a major risk factor for developing intracranial aneurysms.

ADPKD is a type of genetic disorder transmitted by autosomal dominant. The incidence in general population is about 1: 400 to 1,000[4]. Clinical manifestations of the disease include multiple cystic lesions within the internal organs, such as the kidney, liver, spleen and ovary, mitral valve prolapse and intracranial aneurysm. An autopsies series reported that intracranial aneurysms were found in 25% of patients with ADPKD[5]. Other reports showed that intracranial aneurysms were encountered by using cranial magnetic resonance angiograph (MRA) or computerized tomography angiography (CTA) in 5 to 10% of ADPKD patients[6-8]. On the other hand, 2 to 7% of ADPKD patients have intracerebral aneurysms[5,9]; however, there has been no report about the incidence of ADPKD in patients harboring intracerebral aneurysms in Thailand.

Nowadays screening test for detecting intracranial aneurysm is not standard recommendation in ADPKD patients except in cases with familial history of intracerebral aneurysm because the aneurysm can be found in 10 to 25% of this patient group[7,10,11]. The diagnosis of ADPKD bases on abdominal ultrasonography (USG) or computerized tomography (CT) showing multiple cystic lesions of the internal organs, particularly the kidneys (Fig. 1). Most of ADPKD patients have 2 to 4 cystic lesions in the

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kidneys depending on their age and sometimes enlarged kidneys can be seen as well.

In Thailand, there has been no previous report of the incidence of ADPKD in patients with intracranial aneurysms. This study was conducted to answer this question and it may have additional benefits as the follows: 1) giving the diagnosis and treatment of ADPKD patients because if the abdominal imaging study is not performed, the diagnosis of ADPKD cannot be made, 2) counseling patients and their family about natural history of the disease and screening procedure for their family, and 3) evaluation of cost-effectiveness of neuroimaging study for detecting intracranial aneurysm in ADPKD patients. Additionally, we also investigate factor for predicting a possibility of ADPKD in patients with intracranial aneurysms.

Material and Method

The present retrospective study recruited patients with intracranial aneurysms treated at Siriraj Hospital from January 2009 to February 2014. The patients who underwent abdominal USG or CT were included. Age, gender, hypertension, diabetes mellitus and renal function assessed by serum creatinine level were collected for analyzing predictive factor of ADPKD. This research was ethically approved by Siriraj Institutional Board Review (SIRB) for human research.

The SPSS version 19.0 was used for statistical analysis. The predictive factor was identified by using Fisher's exact test and independent t-test or Mann-Whitney U test. Strength of association was studied by using odds ratio (OR) and 95% confidence interval (95% CI). The significant level was signified as $p<0.05$.

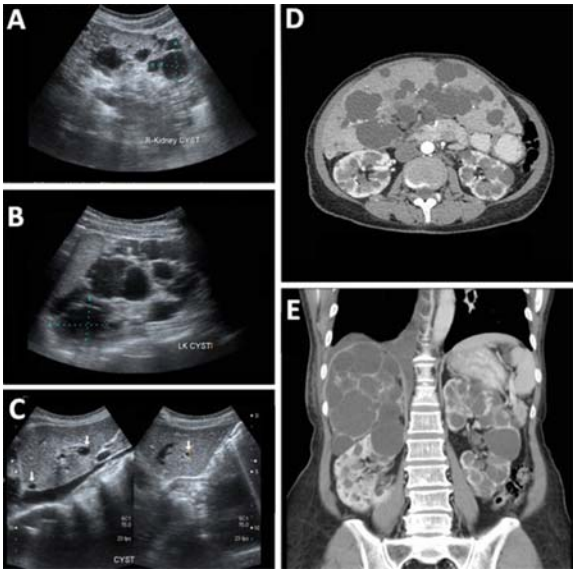

Fig. 1 Abdominal imaging study for diagnosis of ADPKD. Ultrasonography of the right (A) and left (B) kidneys showing multiple cystic lesions of both kidneys; (C) Ultrasonography showing multiple cysts (arrows) in the liver; Abdominal CT in axial (D) and coronal (E) views showing multiple large cystic lesions of the liver and both kidneys as well as enlargement of the kidneys in an ADPKD patient.

Results

Ninety-four patients with intracranial aneurysms were enrolled in this study. Mean age was 56.6 (15 to 83) years. Twenty-five patients were male with mean age of 49.7 (24 to 79) years and 69 were female with mean age of 59.1 (15 to 83) years. Of all patients, ADPKD was identified in 8 (8.5%) subjects; 5 were male and 3 were female. Mean age of the ADPKS group was 59.6 (33 to 79) years. In 86 (91.5%) without ADPKD, 20 were male and 66 were female, mean age was 57.1 (15 to 83) years. Regarding location of intracranial aneurysm, the most common aneurysm was anterior and posterior communicating arteries aneurysm (Table 1).

In analysis of predictive factor of ADPKD, there was significant difference in gender (p = 0.029,

Table 1. Location of intracerebral aneurysms in this study

Location of intracranial aneurysm	Number of patient, n (%)
Total	94 (100)
Anterior circulation	69 (73.4)
Anterior communicating artery	21 (22.3)
Posterior communicating artery	21 (22.3)
Middle cerebral artery	9 (9.6)
Internal carotid artery	6 (6.4)
Anterior cerebral artery	5 (5.3)
Superior hypophyseal artery	3 (3.2)
Ophthalmic artery	2 (2.1)
Anterior choroidal artery	2 (2.1)
Posterior circulation	11 (11.7)
Basilar artery	6 (6.4)
Vertebral artery	2 (2.1)
Posterior inferior cerebellar artery	1 (1.1)
Posterior cerebral artery	1 (1.1)
Multiple aneurysms	14 (14.9)
Anterior circulation	8 (8.5)
Posterior circulation	2 (2.1)
Anterior and posterior circulation	4 (4.3)

Table 2. Comparison of clinical variables between ADPKD and non-ADPKD patients

	ADPKD	Non-ADPKD	*p*-value	OR (95% CI)
Total, n (%)	8 (8.5)	86 (91.5)	-	-
Gender, n (%)				
Male	5 (62.5)	66 (76.7)	0.029*	5.50 (1.21 to 25.05)
Female	3 (37.5)	20 (23.3)		
Age (years), mean (range)	59.6 (33 to 79)	57.1 (15-83)	0.659	-
Hypertension, n (%)	5 (62.5)	53 (61.6)	1.000	0.96 (0.22 to 4.30)
Diabetic mellitus, n (%)	1 (12.5)	13 (15.1)	1.000	1.25 (0.14 to 10.99)
Serum creatinine (mg/dl), mean (range)	1.9 (0.7 to 7.3)	0.81 (0.3 to 3.3)	0.003*	-

* Indicates statistically significant

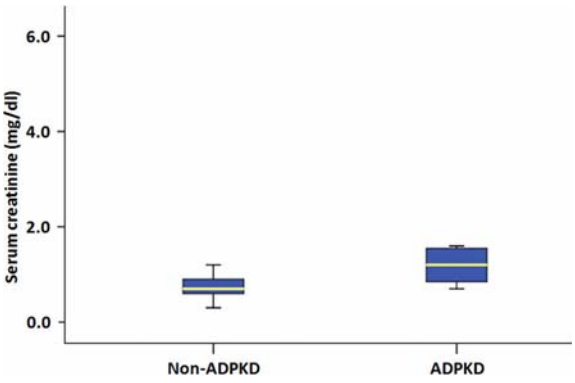

Fig. 2 Difference of serum creatinine level between the non-ADPKD and ADPKD groups.

OR 5.50, 95% CI 1.21 to 25.05) and serum creatinine level ($p = 0.003$) between both groups (Table 2) (Fig. 2). These results indicated that ADPKD was associated with male with intracranial aneurysms who had high serum creatinine level. There was no other variable associated with the occurrence of ADPKD.

Discussion

According to previous studies conducted by Schievink et al[5] and Suter et al[9], the incidence of ADPKD in patients with intracranial aneurysms was ranged from 2 to 7%. In this study, the authors found the incidence is 8.5% close to that of the previous studies.

In the analysis of predictive factor of ADPKD in patients with intracranial aneurysms, we focused on age, gender, hypertension, diabetes mellitus and renal function. A high proportion of male gender was found in the ADPKD group. Importantly, poorer renal function revealed by high serum creatinine level was significantly encountered in the ADPKD patients. This association is most likely caused by the renal function of ADPKD patients will be gradually impaired with time. Cystic lesions in the kidneys and other visceral organs can progress and sometimes end up with chronic renal failure.

Owing to a relatively high incidence of ADPKD in our series and a high opportunity of recurrent ruptured aneurysm in ADPKD patients with previous ruptured brain aneurysms, we recommended performing abdominal USG for screening cystic lesions of the internal organs in all patients with ruptured intracranial aneurysms because this investigation is not expensive (about 300 to 500 baht per case in Thailand) and useful in diagnosis of the disease. Once the multiple cystic lesions are detected, patients and family members should be counseled for treatment or screening investigation to prevent progressive renal impairment, intracranial aneurysm or other consequences of the disease.

In terms of screening test for cerebral aneurysms in ADPKD patients, there is currently no official standardized recommendation[12]; however, several recommendations for aneurysm screening by using MRA or CTA were proposed. The screening study should be considered in ADPKD patients with a family history of intracranial aneurysm or subarachnoid hemorrhage, previous aneurysm rupture, high-risk vocations, undergoing major elective operation and developing significant headache[13-16].

Two major limitations of this study existed.

1) This study used only an abdominal imaging study to make a diagnosis of ADPKD, but in the patients younger than 30 years old, most of them had not yet developed cystic lesions in the internal organs. Because of this reason the exact incidence of ADPKD may be higher.

2) The present research is a retrospective study; a prospective study, which includes all patients harboring intracranial aneurysms with long-term interval screening test for ADPKD, would be better to investigate the true incidence of ADPKD.

Conclusion

In patients with intracerebral aneurysms, the incidence of ADPKD in this study is 8.5%. Predictive factors associated with ADPKD include renal impairment revealed by high serum creatinine level (mean 1.9 mg/dl) and male. When considering the cost of abdominal USG in Thailand, it seems reasonable to perform this investigation in patients with intracranial aneurysms.

What is already known on this topic?

Intracranial aneurysms are increasingly found in patients with ADPKD. The diagnosis of ADPKD bases on imaging study, such as abdominal USG or CT to identify multiple cystic lesions of the internal organs, especially the kidneys.

What this study adds?

The incidence of ADPKD in patients with intracranial aneurysms is 8.5%. ADPKD should be suspected in aneurysm patients with increased serum creatinine level. Abdominal USG is recommended for detecting multiple cystic lesions of the visceral organs and giving diagnosis of ADPKD in patients with intracranial aneurysms.

Potential conflicts of interest

None.

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อุบัติการณ์ของโรคถุงน้ำที่ไตที่มีการถ่ายทอดทางพันธุกรรมแบบลักษณะเด่นในผู้ป่วยโรคหลอดเลือดโป่งพองในกะโหลกศีรษะ

หลักชัย พลวิจิตร, ภาสกร ประทีปะวณิช, ปฤณัต อิทธิเมธินทร์, บรรพต สิทธินามสุวรรณ, ทวีศักดิ์ เอื้อบุญญาวัฒน์, ประจักษ์ ศรีรพีพัฒน์

ภูมิหลัง: ยังไม่เคยมีการศึกษาเกี่ยวกับอุบัติการณ์ของโรคถุงน้ำที่ไตที่มีการถ่ายทอดทางพันธุกรรมแบบลักษณะเด่นและปัจจัยที่ช่วยบ่งชี้ว่าเป็นโรคนี้ในผู้ป่วยโรคหลอดเลือดโป่งพองในกะโหลกศีรษะ

วัตถุประสงค์: เพื่อศึกษาอุบัติการณ์ของโรคถุงน้ำที่ไตที่มีการถ่ายทอดทางพันธุกรรมแบบลักษณะเด่นในผู้ป่วยโรคหลอดเลือดโป่งพองในกะโหลกศีรษะ รวมทั้งปัจจัยที่ช่วยบ่งชี้ว่าเป็นโรคนี้ เพื่อนำไปสู่การคัดกรองและรักษาโรคแก่ผู้ป่วยและคนในครอบครัวที่อาจมียีนผิดปกติของโรคนี้

วัสดุและวิธีการ: ศึกษาแบบย้อนหลังโดยรวบรวมผู้ป่วยที่ได้รับการวินิจฉัยเป็นโรคหลอดเลือดโป่งพองในกะโหลกศีรษะ และได้รับการตรวจทางรังสีวินิจฉัยของช่องท้อง ได้แก่ การตรวจคลื่นเสียงความถี่สูงและการตรวจเอกซเรย์คอมพิวเตอร์ทำการศึกษาเพื่อหาอุบัติการณ์และปัจจัยที่ช่วยบ่งชี้ว่า เป็นโรคถุงน้ำที่ไตที่มีการถ่ายทอดทางพันธุกรรมแบบลักษณะเด่น

ผลการศึกษา: ในผู้ป่วยโรคหลอดเลือดโป่งพองในกะโหลกศีรษะทั้งหมด 94 ราย พบอุบัติการณ์ของโรคถุงน้ำที่ไตที่มีการถ่ายทอดทางพันธุกรรมแบบลักษณะเด่นร้อยละ 8.5 ปัจจัยที่ช่วยบ่งชี้ว่าเป็นโรคนี้ ได้แก่ ระดับครีอะตินีนในซีรัมสูงกว่าปกติและเป็นเพศชาย ไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติของอายุ อุบัติการณ์ของโรคความดันโลหิตสูงและโรคเบาหวานระหว่างกลุ่มผู้ป่วยโรคหลอดเลือดโป่งพองในกะโหลกศีรษะที่เป็น และไม่เป็นโรคถุงน้ำที่ไตที่มีการถ่ายทอดทางพันธุกรรมแบบลักษณะเด่น

สรุป: ผู้นิพนธ์แนะนำให้ทำการตรวจคลื่นเสียงความถี่สูงของช่องท้องในผู้ป่วยโรคหลอดเลือดโป่งพองในกะโหลกศีรษะ เพื่อคัดกรองโรคถุงน้ำที่ไตที่มีการถ่ายทอดทางพันธุกรรมแบบลักษณะเด่น เพราะสามารถทำได้ง่าย ราคาไม่แพง และมีประโยชน์ในการรักษาและป้องกันภาวะแทรกซ้อนจากโรคนี้แก่ผู้ป่วยและคนในครอบครัวที่อาจมียีนผิดปกติของโรคนี้