Ruptured Berry Aneurysm as the initial presentation of Polycystic Kidney Disease: A case report and review of literature

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ABSTRACT

Intra-cranial saccular aneurysms, also known as Berry aneurysms, have a well-known association with autosomal dominant polycystic kidney disease (ADPKD). Aneurysmal rupture can be the initial presentation of the disease. ADPKD has two types of gene mutations: PKD1 and PKD2.The latter one is of a milder form presenting later in life. Imaging plays a crucial role in the diagnosis and assessment in order to provide adequate management of these patients however, there are no official standardized guidelines established for screening of these intracranial aneurysms.

CASE REPORT

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A 57 years old male brought to the emergency department following a road traffic accident where he developed a generalized tonic-clonic convulsion on site. On physical examination, the Glasgow coma scale was 3/15, the pupils were dilated bilaterally, and the documented BP was 176/131 mm Hg. The patient was intubated and sedated.

An urgent non-contrast computed tomography (CT) of the brain revealed a large right frontal intracerebral hematoma extending into the ventricular system with associated subarachnoid hemorrhage (Figure 1). Cerebral angiography showed a saccular contrast filled structure in the region of the anterior cerebral artery.

CT scan of the chest, abdomen and pelvis was done according to the trauma protocol of the institute. It showed bilateral minimal pleural effusion and basal atelectasis. An incidental finding of multiple renal cysts of varying sizes were seen (22 cysts in the right and 17 in the left kidney). Additionally, five small simple hepatic cysts were also detected (Figure 2). Nevertheless, no intraabdominal posttraumatic sequel was encountered.

Followed by a digital subtraction cerebral angiography, which showed a narrow neck saccular aneurysm arising from the left anterior cerebral artery (A2 segment) (Figure 3A). Through endovascular approach the aneurysm has been coiled successfully (Figure 3B).

The patient was admitted to the intensive care unit. His clinical condition showed progressive improvement throughout his hospital stay.

There is no known past medical history or family history of polycystic kidney disease as reported by the patient. Renal function tests were normal. Vital signs were stable with blood pressure readings within normal limits.

A diagnosis of a milder form of polycystic kidney disease was made as the patient met the criteria for CT diagnosis of 10 or more cysts in each kidney despite no positive family history [14], in addition to the detected liver cysts and ruptured Berry

aneurysm. However, genetic testing was not done for a definitive diagnosis.

Follow up CT scan of the brain showed partial resolution of subarachnoid and intraventricular hemorrhage however; a subsequent parenchymal infarction of bilateral anterior cerebral arteries territories has occurred. Left anterior cerebral artery aneurysm coil was noted giving metal artefacts (Figure 4).

DISCUSSION

Etiology & Demographics:

Autosomal dominant polycystic kidney disease (ADPKD) is by far the most common hereditary renal cystic disease resulting in bilateral renal enlargement with multiple cysts of various sizes [9]. It is counted as the third most common cause of renal insufficiency with almost 5-10% of patients undergoing hemodialysis by their late middle age years [9, 10].

ADPKD is due to a single gene mutation [3]. There are two well-known types of gene mutations: PKD1 and PKD2 [11]. PKD1 is more common accounting for approximately 85% of cases whereas PKD2 accounts for only 15% [10].

Clinical & Imaging findings:

Patients with PKD 1 mutation show a more severe clinical course with an earlier presentation and a median age of onset of renal failure 16 years earlier than PKD2 [10]. PKD 2 mutation patients have a clinically milder course of the disease with an older age at presentation and a later onset of hypertension and end stage renal disease at a median age of 74 years [3, 12, 13]. Nevertheless, 10% of cases are due to spontaneous mutations with no positive family history [11].

Imaging plays a crucial role in the diagnosis, evolvement and detection of extra-renal manifestations and complications of this disease [9].

Sonography is used for diagnosis and monitoring of renal cysts in ADPKD. It has a 90% sensitivity of cyst detection and is cheaper and widely available [11]. Less than two cysts in a patient over the age of forty years old rules out the disease [10].

MRI volumetric studies are used to assess renal cyst volume giving an indication whether the disease is progressing or stationary [9]. MRI also estimates the renal blood flow in which its decrease signifies an increase in renal volume reflecting negatively on the disease progression [9].

Differential diagnosis:

Renal cystic disease consists of a wide variety of hereditary, acquired, and developmental conditions, which can lead to end-stage renal disease in adults. Different defective genes that are involved in the formation and functioning of the primary cilia of the renal tubular epithelium are the cause of the inherited cystic renal diseases. On the other hand, non-inherited cystic renal diseases are usually secondary to obstructive, stromal-epithelial malinductive, and neoplastic mechanisms [9].

Some pediatric renal cystic diseases may overlap with adult renal cystic diseases. Even though affected children may survive into adulthood, many of them die of kidney disease and its associated complications. The pediatric renal cystic disease includes autosomal recessive polycystic kidney disease and multicystic dysplastic kidney. In addition, renal cysts may develop in some hereditary conditions such as von Hippel-Lindau disease and tuberous sclerosis [9].

Associations & Prognosis:

ADPKD is associated with cysts in the liver, spleen, pancreas and seminal vesicles. There is an increased risk for the formation of aneurysms, dolichoectasia, abdominal hernias, diverticulosis and valvular disease in these patients [9, 11]. However, no increase in risk of development of renal cell carcinoma was ever established [9].

Patients with ADPKD have a higher incidence of intracranial aneurysms (8 %) in comparison to the general population (2%) [3, 6, 8]. However, the overall risk of rupture is equal to that of the general population [4, 8]. Those with either ADPKD, positive family history or previous intracranial hemorrhage have an even higher risk of intracranial aneurysm formation by 21.6 % according to a recent study of Xu et al [1]. ADPKD is now counted as the number one risk factor for intra-cranial aneurysm formation higher than that of atherosclerosis and those with a positive family history [1, 6].

It is the most severe complication of ADPKD due to the catastrophic sequelae of subarachnoid hemorrhage, thrombosis and local mass effect [1]. The PKD1 and PKD2 genes play an important factor in the structural integrity of vasculature hence the increased incidence of vascular diseases in ADPKD such as aneurysmal formation and spontaneous dissection [5].

Intracranial aneurysms are seen more commonly in females in both the general population and in ADPKD patients with a greater risk of rupture also in females thus the higher incidence of females presenting to the emergency department with subarachnoid hemorrhage [1, 6]. 10% of undiagnosed ADPKD patients will have intracranial aneurysm rupture as the first presentation [1]. In 4-7% of patients with ADPKD, subarachnoid hemorrhage from a ruptured intracranial aneurysm is the main cause of mortality [7]. Approximately 25% of subarachnoid hemorrhages are complicated by cerebral ischemia 5 to 14 days after the bleed due to vasospasm [5]. Mortality after a re-bleed is increased to 50% [5].

The overall estimated risk of rupture of these aneurysms in ADPKD patients is still unknown [7]. However, the median age of rupture is 41 years [5]. In general, other risk factors may contribute to risk of aneurysmal rupture, which include uncontrolled high blood pressure, smoking and excessive alcohol consumption [4]. The risk of rupture also depends on the size, site and a positive past history of subarachnoid hemorrhage [8]. The risk of rupture in intracranial aneurysms less than 1 cm is 0.05 % annually with an increase to 0.5% if there is a positive history of previous subarachnoid

hemorrhage [8]. For aneurysms larger than 1cm, the risk of rupture is less than 1% which increases to 6% in lesions greater than 2.5 cm in diameter [8]. Those with positive family history of ruptured aneurysms in addition to ADPKD have a higher risk of rupture [4].

More than 90% of intracranial aneurysms are seen in the anterior circulation [5]. A lower risk of rupture is seen in aneurysms that are intra-cavernous and in the infra-clinoid ophthalmic regions [8]. The development of a new aneurysm or an increase in the size of an already present aneurysm is seen in 25% of patients with intracranial aneurysms and ADPKD [7].

The risk of developing intracranial aneurysms cannot be correlated with the renal function as almost 50% of these patients have normal renal function tests [1]. However, ADPKD patients with renal failure on hemodialysis have an increased risk of intracranial hemorrhage in general [3]. This risk seems to decrease after a renal transplant [3].

There is no standard protocol for screening for intracranial aneurysms in ADPKD patients [1]. 3D high-resolution time of flight magnetic resonance imaging can be used for screening, as the patient will not be exposed to ionizing radiation with no need of intravenous contrast administration [8].

The KDIGO panel stated that the majority of detected intracranial aneurysms by screening are small with a low risk of rupture and in which prophylactic repair is risky [4].

However, Buttler and Xu et al recommended screening if the patient has a positive family history of intracranial aneurysms and/or a history of subarachnoid hemorrhage along with ADPKD as the risk is increased [1]. Rozenfeld et al recommended screening all ADPKD patients at the time of initial diagnosis [1]. Screening should be considered in ADPKD patients who are physically able and willing to undergo intervention [7].

Treatment:

A multidisciplinary setting in a tertiary hospital is ideal for the management of detected aneurysms [1]. The consideration of conservative, endovascular or surgical management is decided upon the actual size of the aneurysm, site and morphology such as a wide or narrow neck, saccular or fusiform shape and if there is incorporation of a parent or branching vessel [1,4]. A special consideration of the patient's age and other comorbidities is also taken into account [4].

More than 90% of intracranial aneurysms are now efficiently managed by endo vascular techniques [1]. Coil embolization is recommended if the aneurysm is larger than 7 mm. It has a lower mortality rate of 0.6% than clipping 1.2% of un-ruptured aneurysms. Modification of other contributing risk factors is also recommended [1].

TEACHING POINT

Intra-cranial aneurysms have a higher incidence in autosomal dominant polycystic kidney disease. The milder form of ADPKD (type 2 gene mutation) may present at an older age with a ruptured intracranial aneurysm as the initial presentation of the disease.

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FIGURES

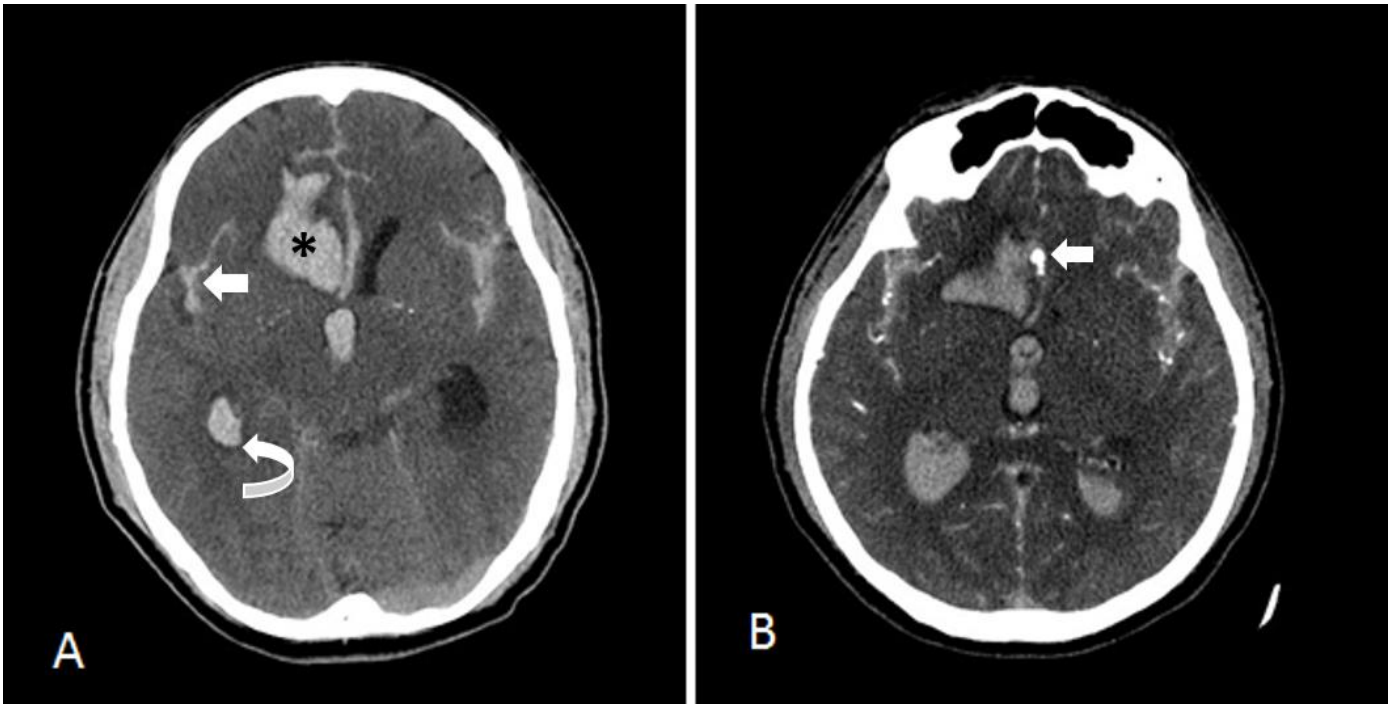

Figure 1: A 57 years old male with unknown polycystic kidney disease presented with subarachnoid hemorrhage due to ruptured left anterior cerebral artery saccular aneurysm.
Technique: GE healthcare 64 slice helical CT brain on axial plane of 2.5 mm slice thickness, 160 mA, and kV is 140. Followed by helical CT cerebral angiography with intravenous contrast administration (Omnipaque 350 - 100ml - bolus tracking)
Findings:
A. There is flame shaped right frontal intracerebral hematoma (asterisk) having intraventricular extension within the lateral and third ventricle. Intraventricular extension in right trigon (curved arrow). Mild associated mass effect and mild midline shift to the contralateral side. Diffuse edematous changes with effacement of the cortical sulci seen. Subarachnoid hemorrhage in both Sylvian fissures seen (straight arrow).
B. A saccular contrast filled structure arising from anterior cerebral artery (arrow).

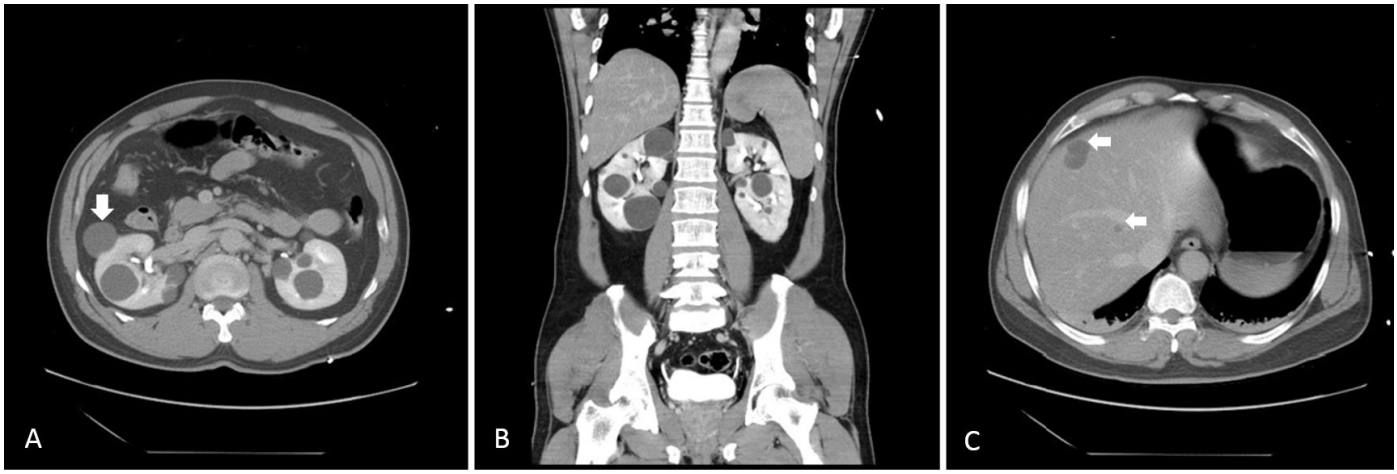

Figure 2: A 57 years old male with unknown polycystic kidney disease presented with subarachnoid hemorrhage due to ruptured left anterior cerebral artery saccular aneurysm.
Technique: GE healthcare 64 slice helical CT abdomen and pelvis with intravenous contrast administration (Omnipaque 350 - 100ml, 60 seconds delay) on axial and coronal planes (600 mA, kV: 120, slice thickness: 5 mm).
Findings:
A& B. There are bilateral multiple renal cysts of varying sizes (arrow).
C. Right hepatic lobe simple cysts (arrows).

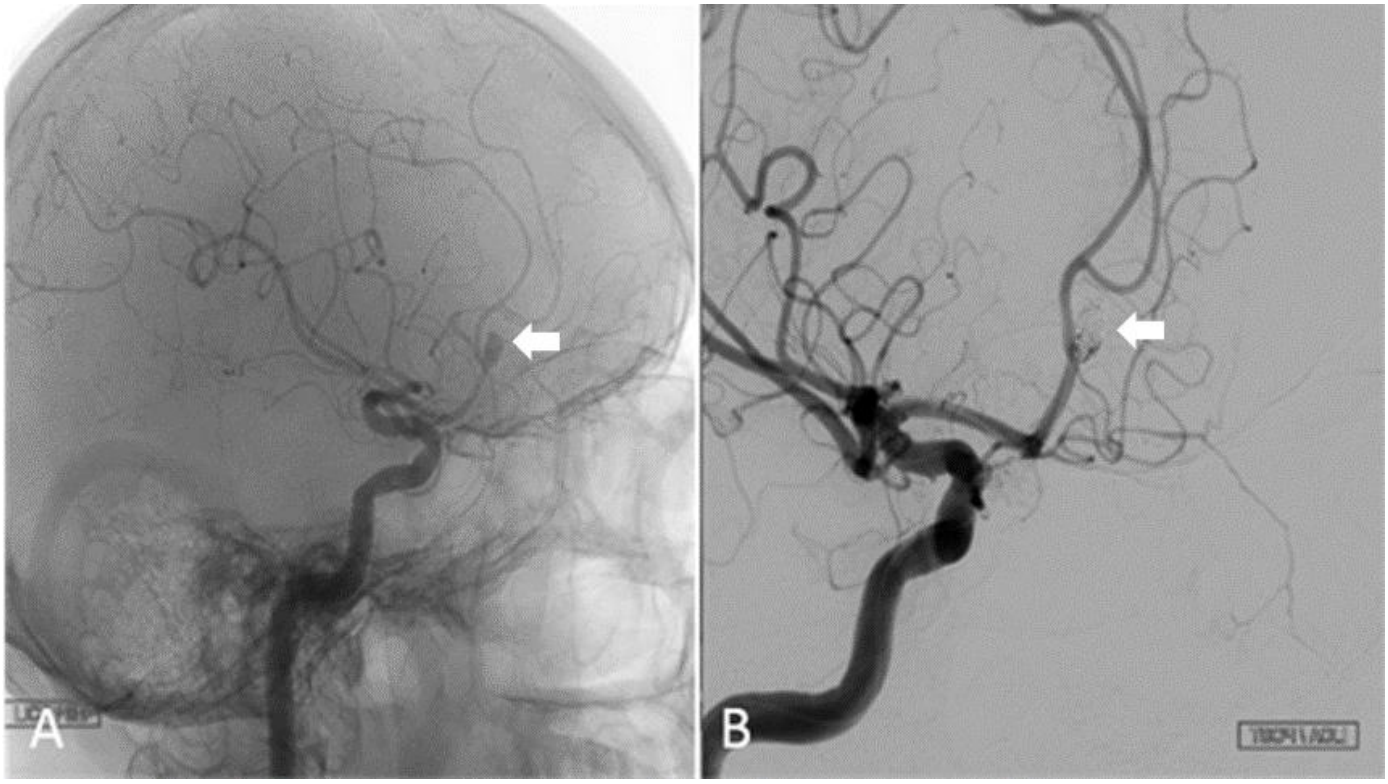

Figure 3: A 57 years old male with unknown polycystic kidney disease presented with subarachnoid hemorrhage due to ruptured left anterior cerebral artery saccular aneurysm.
Technique: Selective left internal carotid artery angiography on 3D RA (figure A) lateral view (figure B). Philips alurra centron (197 mA, kV: 80, contrast material: omnipaque 300 mg-50ml). Post coiling image (3D basket 4mm x 12cm, fills 2mm x 8 cm, fills 4mm x 8cm).
Findings:
A. A small saccular aneurysm arising from A2 segment of left anterior cerebral artery having narrow neck is seen (arrow). The aneurysm measures measuring 8 x 5 mm in diameter.
B. Post coiling image showing no contrast filling of the aneurysm (arrow).

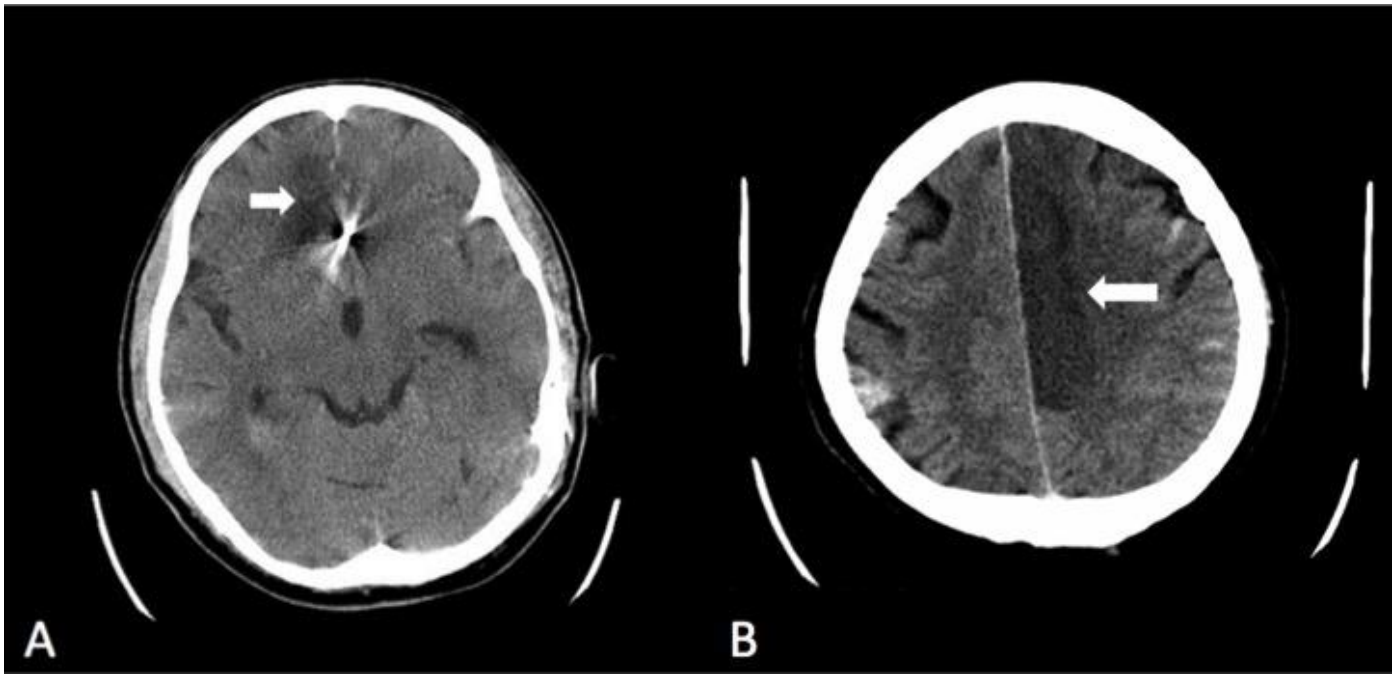

Figure 4: A 57 years old male with unknown polycystic kidney disease presented with subarachnoid hemorrhage due to ruptured left anterior cerebral artery saccular aneurysm.
Technique: GE healthcare 64 slice helical CT brain without contrast on axial plane (120 mA, kV: 120, slice thickness: 2.5 mm).
Findings:
A. Metallic artifacts related to anterior cerebral artery coil. Complete resolution of the right frontal hematoma noted with small area of ischemic changes (arrow) involving right anterior cerebral artery territory. Resolved intraventricular and subarachnoid hemorrhage. Resolved hydrocephalic changes.
B. Established infarction of left anterior cerebral artery territory.

Gene mutation	**PKD1**	**PKD2**
Incidence	85%	15%
Presentation	Earlier presentation 5th decade.	Late presentation 7th decade
Clinical course	Severe, lead to end stage renal disease.	Milder course

Table 1: Adult polycystic kidney disease types.

Adult renal cystic disease		**Intravenous pyelography (IVP)**	**Ultrasound US**	**Computed tomography CT**	**Magnetic resonance imaging MRI**
Hereditary	Autosomal dominant polycystic kidney disease	Stretching of calyces by the cysts giving the appearance of spider leg.	Multiple variable sized cysts. In PKD type 1 kidneys are enlarged and distorted. Simple cysts are anechoic well-defined cysts having thin walls with posterior acoustic enhancement. Complicating cysts may show calcification/ hemorrhage or infection demonstrated by internal echogenic material without internal blood flow.	Simple cysts appear as rounded structures with near water attenuation (~ 0 HU). The wall is very thin and regular. Complicating cysts may be hyperattenuating, with internal non-enhancing septations and/or calcifications.	Multiple cysts (range few mm to cm). Hypointense on T1 (hemorrhagic debris may have mildly increased signal). Strongly hyperintense on T2 (hemorrhagic debris may have mildly decreased signal). The presence of enhancement of a solid component or septa should raise the possibility of a renal cell carcinoma (RCC).
Non-hereditary	Simple renal cysts		Cysts are fewer in number. Kidneys are not enlarged. Simple cysts are anechoic having thin walls with posterior acoustic enhancement. Complicating cysts may show calcification/ hemorrhage or infection.	Simple cysts of near water attenuation (~ 0 HU). The wall is imperceptible. Complicating cysts may be hyperattenuating, with internal non-enhancing septations and/or calcifications.	Hypointense on T1 (haemorrhagic debris may have mildly increased signal). No post-contrast enhancement. Strongly hyperintense on T2 (hemorrhagic debris may have mildly decreased signal). Diffusion (DWI) show increased signal, but no restricted diffusion.
	Acquired cystic kidney disease (ACKD)		Multiple bilateral small renal cysts, occurring in both the cortex and medulla (>3-5 cysts in each kidney). Both kidneys are typically small.	Multiple bilateral small renal cysts. Both kidneys are typically small.	Multiple bilateral small renal cysts. Both kidneys are typically small.
Pediatric renal cystic disease					
Hereditary	Autosomal recessive polycystic kidney disease	Streaky appearance may be demonstrated representing the ectatic collecting ducts.	Oligohydramnios may be identified on antenatal ultrasound. Cysts initially too small to resolve but with time may become discernible. Kidneys are enlarged and echogenic. Liver may show coarsened echotexture along with biliary tract cystic change.		Oligohydramnios is demonstrated in better detail if performed on antenatal MRI. Kidneys are enlarged with diffusely increased T2 signal.
	Medullary cystic kidney disease		Normal to small kidneys with multiple small medullary cysts located at the corticomedullary junction. (sometimes cysts are too small to visualise)		
Non-hereditary	Multicystic dysplastic kidney		Lobulated renal contour with multiple internal cysts of varying sizes and shapes. The renal parenchyma is usually fibrous and echogenic with absent or small hilar vessels. The cysts typically cluster and are non-communicating.		Non-communicating cysts are clearly demonstrated on T2 sequences.

Table 2: Differential diagnosis of cystic renal disease based on radiological findings.

Etiology	Vascular weakness
Incidence	8% in ADPKD 2% in general population
Gender ratio	Female
Age predilection	Median age of rupture is 41 years
Risk factors	ADPKD Family history Atherosclerosis
Treatment	Endovascular (coil embolization) Surgical management (clipping)
Prognosis	High morbidity and mortality
Findings on imaging	Abnormal saccular dilatation of the intracranial vessels diagnosed on cerebral angiography and digital subtraction angiography.

Table 3: Summary table of Berry aneurysm.

ABBREVIATIONS

ADPKD: Autosomal dominant polycystic kidney disease
KDIGO: Kidney disease improving global outcomes®
PKD: Polycystic kidney disease

KEYWORDS

Intracranial berry aneurysm; intracranial hemorrhage; Polycystic kidney disease; conventional angiography; coil embolization