Autosomal Dominant Polycystic Kidney Disease: multimodality imaging findings of renal and extrarenal manifestations

Poster No.: C-1697
Congress: ECR 2011
Type: Educational Exhibit
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Keywords: Pathology, Education, Ultrasound, MR, CT, Kidney
DOI: 10.1594/ecr2011/C-1697

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Learning objectives

To illustrate the spectrum of renal and extrarenal manifestations in patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD).
Background

Autosomal dominant polycystic kidney disease (ADPKD) is one of the most common inherited diseases, affecting between 1:400 and 1:1000 members of the white population and accounts for about 4% of end-stage renal disease (ESRD). At least two distinct gene defects are implicated in the pathogenesis of ADPKD. One is on the short arm of chromosome 16 (PKD1) and a second ADPKD gene (PKD2) was discovered on chromosome 4; the existence of another additional disease gene has been recently suggested but its exact location is not already mapped.

ADPKD is a systemic disorder with cystic and noncystic manifestations in many organ systems and the course of the disease is determined by the extent and severity of both renal and extrarenal manifestations.

ADPKD is diagnosed primarily through imaging studies. Because of its high sensitivity, low cost, and lack of radiation exposure, ultrasound (US) is the preferred imaging method. The presence of two or more cysts in one kidney and at least one cyst in the contralateral kidney in subjects with a family history of ADPKD points to the disease. Four or more cysts in subjects older than 60 years are required because of the increased frequency of benign simple cysts development. Because simple renal cysts rarely occur in children, any cyst detected by renal US in an at-risk child strongly suggests ADPKD. Prenatal diagnosis and selection of living related kidney donors may require gene-linkage testing if cysts are not visible in imaging studies.
RENAL MANIFESTATION

The primary renal manifestation of ADPKD is the development of bilateral renal cysts, which leads to functional changes and various clinical complications. Cyst formation begins in utero from any point along the nephron although <5% of total nephrons are thought to be involved. As the cysts accumulate fluid, they enlarge, separate entirely from the nephron, compress the neighboring renal parenchyma, and progressively compromise renal function. Ultimately, patients will need renal replacement therapy, dialysis or renal transplantation (fig.1 on page ).

Cysts present a diffuse distribution, both medulla and cortex are involved, and range in diameter from less than 1 cm to at least 5 cm. In the early disease stages, renal size may be normal and the reniform shape of the kidneys is well maintained (fig.2 on page ). With advancing disease, the size and number of cysts increase and the renal outline may become scalloped, with the cyst projecting beyond the renal outline (fig.3 on page ). Calcifications of cyst walls may be present (fig.4 on page ).

On US simple cysts appear as multiple anechoic lesion (fig.5 on page ). After ultrasound contrast medium administration no enhancement is seen and surviving islands of renal parenchyma may be better identify (fig.6 on page ). CT scan shows multiple hypodense lesions without enhancement (fig.7a on page /7b on page ). On MRI simple cysts appear hypointense on T1 weighted images (fig.8 on page ) and hyperintense on T2 weighted images (fig.9 on page ). After contrast medium administration, no enhancement is seen (fig.10 on page ).

CYST RUPTURE

Progressive cyst enlargement may cause cyst rupture. Patients present acute abdominal pain and, if cysts is connected to the urinary collecting system, hematuria. Radiological evaluation is generally required to exclude other possible causes of hematuria. CT is a modality of choice thanks to its better panoramicity. During excretory phase intracystic contrast medium blush is seen (fig.11a on page /11b on page ).

CYST HEMORRHAGE

Cyst hemorrhage is a frequent finding in ADPKD and has been suspected in patients presenting with acute flank pain. US shows echogenic lesion with no vascular signal on color Doppler examination and no enhancement on CEUS (fig.12a on page /12b on page ). Intracystic hemorrhage is shown as a high-attenuation mass both on unenhanced and enhanced CT scans (fig.13a on page /13b on page ).
MRI hemorrhagic cysts appear hyperintense on all image sequences (fig.14a on page /14b on page ), but appearances may depend on the age of the hemorrhage. Layering may be present with a recent intracystic bleeding (fig.15 on page ).

CYST AND URINARY TRACT INFECTIONS

Urinary tract infections occur in 40-68% of ADPKD patients and can involve the lower urinary tract, the renal interstitium (pyelonephritis), or renal cysts. Flank pain and fever may be observed.

Distinction between pyelonephritis and renal cyst infection is often difficult but it is important because each infection responds differently to antibiotics. If the causative organism is sensitive, pyelonephritis responds to conventional antibiotic therapy with penicillins, cephalosporines, or aminoglycosides, whereas cyst infections must be treated with lipid-soluble antibiotics such as trimethoprim-sulfamethoxazole, chloramphenicol, or ciprofloxacin, all of which can penetrate cyst walls.

US may demonstrate thickened and irregular cystic wall and, in case of pus collection, hyperechoic content. CEUS is helpful in the differential diagnosis between pus collection and neoplasm, because in case of cyst infection no enhancement is seen. CT shows thickened and irregular cyst walls (fig.16a on page /16b on page ) and hyperdense cyst content. On MRI cysts complicated by infection appear with an intermediate signal intensity both on T1 weighted and T2 weighted images.

KIDNEY STONES

Nephrolithiasis occurs in 20-36% of ADPKD patients. Urinary stasis in the distorted collecting system and metabolic abnormalities play a role in the pathogenesis of stone formation. Nephrolithiasis must always be considered in patient with flank pain and hematuria.

US is generally the first modality of imaging for stones detection; unfortunately diagnosis is not always simple because the distortion of the normal renal anatomy and the presence of parenchymal and cyst wall calcifications, secondary to cystic hemorrhage. Stones typically appear as hyperechoic lesions with acoustic shadow. Unenhanced CT is the modality of choice (fig.17 on page ) because better identifies stone and evaluates its size and location. A contrast medium administration may be required for evaluation of the entire collecting system. MRI is not used because its insensitivity to calcifications.

RENALE CELL CARCINOMA

The incidence of renal cell carcinoma (RCC) in ADPKD does not appear to be increased as compared to the general population. However RCC in ADPKD patients is more
often bilateral, multicentric, and sarcomatoid in type. Diagnosis is not easy since clinical presentation, hematuria and flank pain, mimics intracystic hemorrhage or infection.

The main goal of radiological evaluation is lesion enhancement demonstration. US shows an echoic lesion, indistinguishable from hemorrhagic cyst (fig.18a on page ). CEUS improves diagnosis, demonstrating contrast enhancement of the lesion (fig.18b on page ). Both CT and MRI performed before and after contrast medium administration can identify RCC (fig.19a on page /19b on page ).

URINARY TRACT OBSTRUCTION

Urinary tract obstruction is a possible complication of ADPKD. Progressive cyst enlargement may cause distortion and compression of the collecting system and, occasionally, obstruction with development of hydronephrosis. Patients present abdominal pain. US, generally performed first, shows dilatation of the collecting system (fig.20 on page ). CT or MRI are required because more panoramic.

RENNAL TRAUMA

Pre-existing renal pathological disease is thought to increase the risk of renal injury secondary to abdominal trauma. In case of trauma ADPKD patients require laboratory and radiological follow up to exclude renal lesions. CT is the modality of choice because its better panoramicity (fig.21a on page /21b on page ). In the follow-up, to avoid radiation exposure and potential nephrotoxicity of contrast medium administration, US and CEUS may be performed.

EXTRARENAL MANIFESTATION

LIVER CYST

The most common extrarenal manifestation of ADPKD is hepatic cystic involvement. Cysts are generally incidental findings and are not clinically significant. Although hepatic failure is uncommon, symptoms related to a massively enlarged cystic liver include loss of appetite, weight loss, esophageal reflux, and abdominal discomfort. Hepatic cysts vary widely in number, from a few to innumerable, and size, from less than 1 mm to more than 10 cm in diameter. Liver function is generally preserved. If liver enzymes are elevated, another superimposed liver disease may be present. Hepatic cyst complications such as bleeding and infection can occur.

In ADPKD patients two kinds of liver involvement may be observed: polycystic liver disease and Caroli disease. They could be considered as expressions of ductal plate malformation.
At radiology, polycystic liver disease typically manifests as an enlarged and diffusely cystic liver, with the cysts varying from less than 1 mm to 12 cm or more in diameter. Cystic wall calcifications, as a result of prior hemorrhage and inflammation, are occasionally detected (fig.22 on page ). US shows multiple round anechoic lesions. Cysts appear as homogeneous and hypoattenuating lesions with a regular outline on nonenhanced CT scans, with no enhancement after contrast medium administration (fig.23a on page /23b on page ). On MRI, cysts have very low signal intensity on T1 weighted images (fig.24 on page ) and do not enhance after administration of gadolinium contrast material. Owing to their pure fluid content, homogeneous high signal intensity is demonstrated on T2 weighted images (fig.25 on page ).

Carolii disease is characterized by multifocal segmental dilatation of the large intrahepatic bile ducts, which retain their communication with the biliary tree. At radiology, Carolii disease typically manifests as saccular or fusiform cystic dilatations of the intrahepatic bile ducts up to 5 cm in diameter, often containing calculi or sludge.

CT typically shows hypoattenuating dilated cystic structures of varying size that communicate with the biliary tree. The presence of tiny dots with strong contrast enhancement within the dilated intrahepatic bile ducts, the central dot sign, is considered very suggestive of Carolii disease. This finding is due to a portal vein branch protruding into the lumen of a dilated bile duct. On MRI, the dilated and cystic biliary system appears hypointense on T1-weighted images and markedly hyperintense on T2 weighted images (fig.26 on page ). After intravenous administration of gadolinium contrast material, the central dot sign may be seen. MR cholangiography can be extremely valuable in diagnosis of Carolii disease by demonstrating the pathognomonic feature of saccular dilated and nonobstructed intrahepatic bile ducts that communicate with the biliary tree (fig.27 on page ).

OTHER EXTRARENAL CYST

About 5-10% of ADPKD patients have pancreatic cysts, but these are functionally insignificant. Other locations of cysts include spleen, arachnoid membranes (fig.28a on page /28b on page ), and seminal vesicles in men. They usually are not associated with complications.

On radiological evaluation extrarenal cyst shows a classical appearance of simple cyst.

INTRACRANIAL ANEURYSM

Intracranial aneurysms are the most severe extrarenal manifestation of ADPKD and are present in approximately 5% of patients. They are caused by alterations in the vascular wall directly linked to mutations in PKD1 or PKD2. Aneurysm rupture depends on the size attained, and most ruptures occur in aneurysms that are greater than 10 mm in size.
Smaller aneurysms can be managed expectantly, but frequent surveillance every 1-2 years is probably wise.

Unenhanced CT may show hyperdense lesion due to aneurism thrombosis. CT angiography may clearly identify aneurism and depict its size and location (fig.29a on page /29b on page ). Also MRI, performed without contrast medium administration with three-dimensional time of flight sequences, may be used to identify berry aneurisms (fig.30 on page ).

CARDIAC VALVE DISEASE

Cardiac valvular abnormalities are common in ADPKD patients and occur in about one-third of them. The most common is mitral valve prolapse, usually mild. Patients may have symptoms such as atypical chest pain or palpitations. Mitral insufficiency may develop. US is generally the first line imaging modality (fig.31 on page ); selected cases may require MRI evaluation for a better therapy planning (fig.32 on page ).

Other abnormalities can also occur in the aortic valve and the left ventricular outflow tract.

Left ventricular hypertrophy is another common finding. It is due to hypertension secondary to activation of the renin-angiotensin system. US is generally the imaging modality of choice (fig.33 on page ). Some selected cases may require CT or MRI (fig.34 on page ) evaluation.

ABDOMINAL WALL AND INGUINAL HERNIA

Other extrarenal manifestations include a propensity to hernias, either abdominal or inguinal. Diagnosis is generally made on the basis of clinical examination. US or CT are indicated in dubious or complicated cases.

AORTIC ANEURYSM AND DISSECTION

Aneurysmal involvement of extracranial arteries, such as the coronary arteries, abdominal aorta, renal artery and splenic artery, dolichoectasias and dissections have also been reported in patients with ADPKD. As known PK1 and PK2 are both expressed in vascular smooth muscle cells and interactions of these proteins with a single pathway might have a role in the pathogenesis of vascular manifestation of ADPKD.

Imaging play a critical role in the diagnosis and follow-up of these abnormality, especially in case of aortic aneurysm and aortic dissection. US may be used but a more panoramic studies, such as CT angiography or MR angiography, are indicated. They clearly show aneurism dilatation (fig.35a on page /35b on page ) and exactly identify flap dissection (fig.36a on page /36b on page ).
DIVERTICULOSIS OF THE COLON

Colonic diverticulosis and related complications can occur in APKD patients. Diverticulosis is generally an incidental findings on radiological evaluation (fig.37 on page ); diverticulitis require CT scan.
Conclusion

ADPKD is the most common of the inherited renal cystic diseases. Imaging evaluation is essential for diagnosis and follow-up of patients with ADPKD. So it is important to become confident with possible imaging findings.
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References