Radiologic imaging of the inflammatory renal diseases: literature review

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ABSTRACT

Background and aim: Inflammatory diseases of the kidney are a broad group of various renal pathologies. They are usually recognized by clinical symptoms and laboratory tests. However, radiology also has a role. The aim of this article is to assess radiologic imaging possibilities in diagnosis and follow-up of the most common inflammatory renal diseases.

Materials and methods: A selective search was carried out for relevant studies regarding radiologic imaging of acute pyelonephritis, renal and perinephric abscesses, emphysematous pyelonephritis, emphysematous pyelitis, chronic pyelonephritis and glomerulonephritis. ClinicalKey, Cochrane Library, Medline (PubMed), ScienceDirect and SpringerLink databases were used.

Results: Ultrasound is usually used as the initial imaging tool to evaluate patients with symptoms of acute pyelonephritis. However, computed tomography is the most appropriate imaging modality. If an abscess or gas-forming infection are suspected, CT is the modality of choice. The findings characteristic, yet not pathognomic to chronic pyelonephritis can be assessed using all of the previously mentioned imaging tools. In cases of glomerulonephritis, US and MRI are the most suitable.

Conclusion: Radiology plays an important role in diagnosis of inflammatory renal diseases. Imaging allows to identify renal abnormalities and differentiate between a few feasible pathologies. It may also evaluate the activity of the disease. Moreover, it can assess sequelae, such as renal scarring and decreased renal function.

Keywords: pyelonephritis, renal abscess, glomerulonephritis, ultrasound, computed tomography, magnetic resonance imaging.

1. INTRODUCTION

Inflammatory diseases of the kidney are a broad group of various renal pathologies. These diseases can be intrinsic or manifest as systemic illnesses. The etiology of inflammation may be diverse, e.g. infectious or autoimmune. Inflammatory diseases are usually recognized by clinical symptoms and laboratory tests, such as blood count, C-reactive protein, autoantibodies and urinalysis [1, 2]. In some cases, percutaneous renal biopsy is the sole method that can confirm the diagnosis. However, it is an invasive procedure with potential complications [3]. Therefore, radiology also plays a role in the diagnosis. Radiologic imaging is constantly evolving and new techniques emerge. With a wide variety of renal imaging tools, it is important to choose the modality which would provide the most information about the nature and extent of inflammatory lesions.

2. AIM

To assess radiologic imaging possibilities in diagnosis and follow-up of the most common inflammatory renal diseases.

3. MATERIALS AND METHODS

A selective search was carried out for relevant studies regarding radiologic imaging of acute pyelonephritis (APN), renal and perinephric abscesses, emphysematous pyelonephritis (EPN), emphysematous pyelitis (EP), chronic pyelonephritis (CPN) and glomerulonephritis (GN). We selected databases from the subscription list of Lithuanian University of Health Sciences. ClinicalKey, Cochrane Library, Medline (PubMed), ScienceDirect and SpringerLink databases were used.

4. RESULTS

Intravenous urography (IVU) has been replaced
almost completely by other modalities in diagnosis of APN, although this imaging technique was commonly performed in the past.

Ultrasound (US) is used as the initial imaging tool to evaluate patients with symptoms of APN. However, examination is usually normal due to relatively low sensitivity and specificity of this modality [4].

Computed tomography (CT) is the most appropriate imaging modality for diagnosing APN and its complications [5–8]. CT can also be useful in predicting the clinical course of the disease [9–11].

Magnetic resonance imaging (MRI) is not commonly used in diagnosing acute renal infections. Nonetheless, it is a radiation-free alternative for those patients who should not be exposed to radiation or are allergic to iodinated contrast agents.

Renal cortical scintigraphy (RCS) has high sensitivity in diagnosing renal infection [5, 12, 13]. RCS is considerably superior to IVU and US [14], as reliable as CT [5] and inferior to enhanced MRI [15] and DWI-MRI [16] in the acute phase of APN. Planar RCS is also slightly inferior or equivalent to single photon emission computed tomography (SPECT) in detecting pyelonephritic lesions [13, 17, 18].

If renal or perinephric abscess is suspected, CT is the modality of choice [19, 20]. MRI is not a frequently used imaging technique. US is inferior to CT and MRI in diagnosing renal abscesses [21].

US underestimates the depth of parenchymal involvement and perinephric extension of emphysematous pyelonephritis [22]. Therefore, CT is the most reliable imaging modality [23, 24].

Findings characteristic, yet not pathognomic to chronic pyelonephritis can be assessed using all of the above mentioned modalities. However, CT and MRI depict these findings in more detail. In cases of glomerulonephritis, US and MRI are the most appropriate imaging tools.

Figure 1. Bilateral focal acute pyelonephritis. Axial contrast-enhanced CT depicts a few hypodense wedged-shaped pyonephritic lesions in both kidneys. (Wang JH. Acute focal pyelonephritis. Urol Sci 2013; 24: 56-57)
Figure 2. Renal abscess. A well-defined hypodense lesion with peripheral enhancement is observed on coronal contrast-enhanced CT scan. (Linder BJ, Granberg CF. Pediatric renal abscesses: a contemporary series. J Pediatr Urol 2016; 12: 99.e1-99.e6)

Figure 4. Emphysematous pyelitis. Gas in the bilateral pelvises and ureters (arrows) is observed on coronal native CT scan. Also, gas is seen in the left ureterovesicular junction (arrowhead). Asterisks show fat stranding. (Wiesel S, Hutman A, Abraham JE, Kiroycheva M. Foley follies: emphysematous pyelitis from instrumentation in obstructive uropathy. Cureus 2017; 9: e1612)

Figure 5. Chronic pyelonephritis. On US, the right kidney is apparently smaller than the left one (7.6 cm vs. 11.5 cm). The renal parenchyma is echogenic and thin. Hypertrophy of the left kidney is observed. (Paltiel HJ, Babcock DS. The pediatric urinary tract and adrenal glands. In: Rumack C, Levine D. Diagnostic ultrasound. 5th ed. Philadelphia, PA, USA: Elsevier; 2018. pp. 1775-1832)
Figure 6. Chronic pyelonephritis. Axial (a) and coronal (b) contrast-enhanced CT demonstrates scarring with cortical retraction (arrows) and calyceal deformation characteristic to CPN. (Ifergan J, Pommier R, Brion MC, Glas L, Rocher L, Bellin MF. Imaging in upper urinary tract infections. Diagn Interv Imaging 2012; 93: 509–519)

Figure 7. Chronic glomerulonephritis. ADC maps (a-e) and FA maps (f-j) are shown in different disease stages (1-5) using MRI-DTI. Low signal region of the renal medulla on ADC maps and high signal region on FA maps decreases with each stage. Loss of corticomedullary differentiation is also apparent with increased stages. (Feng Q, Ma Z, Wu J, Fang W. DTI for the assessment of disease stage in patients with glomerulonephritis - correlation with renal histology. Eur Radiol 2015; 25: 92–98)
5. DISCUSSION

APN is an inflammation of the renal parenchyma and collecting system. Incidence rates of APN are highest in young females, infants and the elderly population [25, 26]. The most frequent causative uropathogen is Escherichia coli (70-80%) [25]. In most cases, APN is unilateral [27]. Diagnosis of APN is based on clinical and laboratory findings, therefore, radiologic imaging is not routinely used. However, diagnostic imaging allows to exclude urgent urinary pathologies. In approximately 75% cases of uncomplicated APN, IVU is normal [14].

Abnormal findings characteristic to acute renal infection are diffuse renal enlargement, striated or delayed renal nephrogram and effacement or dilatation of the collecting cavities with delayed contrast medium filling [14]. Papillary necrosis, one of the possible complications of APN, can also be diagnosed on IVU [28].

Excretory urography is useful for assessment of the pelvocalyceal anatomy, however, it visualizes the renal parenchyma poorly [29].

On conventional US (CUS), generalised edema of the affected kidney, loss of corticomedullary differentiation, pelvicalyceal thickening and dilatation without any evident obstruction are typical features of diffuse APN [4, 14, 30]. Hyperechoic perirenal fat, implying inflammatory response of the adjacent tissue, is also suggestive of diffuse APN.

In cases of focal APN, wedge-shaped or round hyper-, iso- or hypoechoic areas with regional loss of corticomedullary differentiation can be seen in the renal parenchyma [4, 14, 31, 32]. These abnormal mass-like areas can be of low attenuation and have indistinct margins [33, 34]. Therefore, differentiation from renal abscess and tumours is important.

As a result of APN, renal scarring can develop, especially in patients with vesicoureteral reflux or recurrent infection [35]. On CUS, irregular contour, focal parenchymal thinning and underlying calyceal deformation are indicative of scars caused by previous infection [36–38]. The additional use of color or power Doppler increases sensitivity of CUS in diagnosis of focal APN [39, 40]. These imaging techniques present pyelonephritic lesions as hypovascular or even avascular foci [41–43].

However, several studies established that contrast-enhanced ultrasonography (CEUS) displays parenchymal abnormalities, associated with APN, better [44, 45]. Characteristic to focal APN, wedge-shaped or round hyperechoic lesions are hypoechoic during the cortical and early parenchymal phase, isoechoic and then hypoechoic in the late parenchymal phase [43, 46]. These CEUS findings allow to exclude the growth of an abscess if a patient is unresponsive to antibiotic therapy. Nonetheless, using contrast enhancement in evaluating the affected kidney has not yet become the general practice because it does not significantly improve the accuracy of US [47].

Lastly, more recent techniques, such as tissue harmonic imaging (THI) and pulse inversion harmonic imaging (PIHI), has become valuable in abdominal imaging. These techniques provide higher spatial resolution. According to Kim et al., THI and PIHI, whether or not contrast material is used, are superior to CUS in the detection of focal pyelonephritic lesions [34].

Multiphasic helical CT protocol allows to evaluate kidneys accurately for APN [48]. Non-contrast CT may appear without any abnormal findings in patients with diffuse APN. It can also demonstrate only secondary signs of renal infection, such as low-attenuation renal parenchyma [49], general renal enlargement, pelvicalyceal thickening and enhancement, soft tissue perinephric stranding and thickening of the anterior pararenal (Gerota’s) fascia [28, 50]. If radiologic imaging is performed early, wall thickening of the pelvis and calyces can be the only feature of the disease [48].

On native CT scans, focal APN presents in a different manner. Involved areas usually appear oval or wedge-shaped, ill-defined and hypodense owing to edema or necrosis [7, 21, 49, 50]. In rare cases of haemorrhagic focal APN, non-contrast CT shows hyperdense lesions due to parenchymal bleeding [32]. Therefore, abnormal density of renal lesions on CT correspond to echogenicity on CUS [7, 32]. Focal pyelonephritic lesions have a lobular distribution, contrary to renal abscesses. If a CT scan presents with round, not
wedge-shaped low attenuation peripheral renal lesions in a patient displaying symptoms of APN, hematogenous seeding should be considered. A recent study demonstrated association of focal APN to atypical radiological findings. Pleural effusion, presence of fluid around the gallbladder, thickened gallblader wall, perinephric fluid and ascites are more frequent in patients with focal form of APN [51].

Postcontrast CT examination commonly shows solitary or multiple wedge-shaped zones of low attenuation extending from the papilla to the cortical surface with poor corticomedullary differentiation (Figure 1). Enhancement of abnormal areas is inhomogeneous, delayed and only moderate, always less than of unaffected parenchyma [7, 42, 50, 52]. Moreover, sharply defined alternating bands of increased and decreased attenuation (“striations”) within the wedge-shaped lesions can be observed during nephrographic phase [47]. These uni- or multifocal lobular striations are the result of tubular stasis of contrast material due to inflammatory tubular obstruction [53]. However, “striated nephrogram” is characteristic, but not pathognomonic of APN. It may also be observed in cases of contusion, renal vein thrombosis, ureteric obstruction and dehydration [54].

CT can promptly lead to the diagnosis of APN. However, it should be preserved for patients with history of diabetes mellitus, renal calculi or renal surgery and those who are unresponsive to antibiotic therapy after 72 hours.

MRI findings of APN are similar to those of CT. The affected kidney is focally or diffusely enlarged with poor corticomedullary differentiation and typical heterogeneous edematous lesions, i.e., low signal intensity (SI) on T1-weighted (T1W) images and high SI on T2-weighted (T2W) images [55, 56]. These edematous areas are better represented using T2W images with fat suppression technique [48]. Perirenal effusion, stranding and pelvocalyceal wall thickening can be found, but these signs are not pathognomonic to APN [48, 55].

Renal scarring, a sequela of APN, appears as a contour deformity without signal change [15]. MRI with gadolinium depicts renal lesions as wedge-shaped or round, sometimes striated regions of decreased or absent enhancement [56]. Inversion recovery MRI with gadolinium uses the negative enhancement effect of the contrast material. Unaffected renal parenchyma becomes hypointense, contrary to the inflammatory areas that remain hyperintense due to edema and poor delivery of the contrast medium [15].

However, T1W and T2W images are not sensitive enough to detect pyelonephritic lesions [56]. Various studies reveal the utility of diffusion weighted imaging (DWI) in cases with suspected APN. According to De Pascale et al., sensitivity and specificity of DWI-MRI is 95.2% and 94.9%, respectively [55]. On DWI, APN presents as areas of restricted diffusion, corresponding to the T1W and T2W parenchymal signal changes. Pyelonephritic lesions are hyperintense. Reduced SI is seen on apparent diffusion coefficient (ADC) maps [55, 57, 58]. DWI displays high diagnostic agreement with gadolinium-enhanced images [55, 57]. Moreover, DWI does not require contrast medium, hence, it can be used in patients with renal insufficiency or pregnant women. Therefore, unenhanced MRI with DWI should be a comprehensive examination in diagnosing APN [55, 57].

MR urography (MRU) allows to assess the urinary tract for obstruction which may predispose APN [59, 60]. Thus, the combination of conventional MRI and MRU is appropriate to evaluate renal infection, its complications and the urinary tract for dilatation. Furthermore, conventional MRI together with MRU allows to obtain morphologic and functional data and eliminates the need for renal scintigraphy, especially in children [61, 62].

There is no general agreement for the use of RCS in diagnosis of pyelonephritis. In pediatric population, clinical and laboratory findings frequently do not correlate to RCS, thus, RCS is important in diagnosis of APN [63]. Nevertheless, it is not recommended in routine practice [64, 65].

Several tracers are available, although 99mTc-dimercaptosuccinic acid (99mTc-DMSA) is the most appropriate. The uptake of 99mTc-DMSA correlates to the volume of functioning renal parenchyma. In patients with APN, scintigraphy usually displays reduced focal or diffuse buildup of the radiopharmaceutical without cortical
or volume loss [12, 15, 17]. Relative left and right 99mTc-DMSA uptake can be measured, normal lowest value being 45%. In cases of APN, relative uptake can be decreased [12]. These findings are not specific to the disease, hence, combination of RCS and other imaging modalities should be used.

RCS is also used for detecting the consequences of APN [16, 66, 67]. In adult patients, renal scarring is rare, therefore, RCS examination is more frequent in children. In 42% of pediatric population, persistent cortical abnormalities are found [68]. Normal RCS scans during the acute phase of APN show a low risk of scarring later [69]. Scars present as defects in uptake with cortical thinning and loss of volume in the same area as pyelonephritis [16]. Inflammatory parenchymal changes tend to disappear only after a few months after the episode of APN [70]. In order to assess possible sequelae, it is recommended to undergo scintigraphy for pediatric patients at least 6 months after APN [65].

Renal abscess is a collection of pus limited to the kidney. In most cases of APN, patients do not experience this complication. However, if inflammation is severe, liquefactive necrosis and, consequently, abscess can form. Several studies show that renal abscesses are more common in patients with diabetes mellitus and urolithiasis [19, 71]. Clinical and laboratory findings cannot identify patients with or without abscesses, therefore, radiologic imaging is important [21, 72].

In most cases of acute renal abscess, the kidney is enlarged with distorted outer contour. The abscess itself presents as a hypoechoic mass with through transmission and hazy borders [43, 52, 73, 74]. A fluid-filled mass with a thickened definite margins suggests a mature abscess [48]. Mobile debris can be observed inside the collection of pus [74]. On power Doppler, absent internal flow is seen [43]. Depiction of abscesses is better using THI and PIHI than CUS [34]. CEUS may demonstrate round unenhanced abscess cavities with possible rim or septa enhancement which allows to differentiate it from focal APN [43]. Nevertheless, US is inferior to CT and MRI in diagnosing renal abscesses [21].

Liquefaction of affected region is seen as a hypoattenuating area in the peripheral cortex on unenhanced CT [52]. Contrast-enhanced CT shows early renal abscess as a round hypodense well-defined fluid-filled area with an irregular wide halo of decreased enhancement, as shown in Figure 2 [74–77]. The outer contour of capsule can be irregular owing to surrounding inflammatory infiltration. Septations and areas of gas may also be observed within a suppuration [74], the latter being pathognomonic of an abscess. Secondary features of infection, such as thickening of Gerota's fascia, can also be found [52].

Collections of pus may be also observed in perinephric spaces [52]. Perinephric suppuration usually originates from ruptured renal cortical abscesses into the pararenal space. Furthermore, it can involve the muscles of the posterior abdominal wall, most frequently the psoas muscle. Hypodense mass with indistinct borders, gas bubbles or air-fluid levels in the enlarged psoas muscle leads to diagnosis of abscess [75, 78]. MRI is used as a substitute when CT scans cannot be performed. In cases of suppuration, MRI shows round inhomogenous hypointense lesions with thick walls on T1W images and hyperintense lesions with hypointense periphery on T2W images [56, 57]. Gadolinium-enhanced MRI scans display unenhanced areas, surrounded by high SI peripheral rim [56, 76]. Cellular debris and irregular septations can also be seen within the abscess. Edema or fine streaks of fluid can be found in the perirenal space [56].

On DWI-MRI, inflammatory changes are hyperintense with restricted ADC [57, 79]. EPN is a rare life-threatening, usually fulminant urologic infection with gas accumulation within or around the kidneys. Emphysematous pyelitis (EP) is a less severe gas-forming renal infection with gas limited only to the renal collecting system. However, mortality between patients with EPN and EP does not significantly differ [80]. Uropathogens, such as E. coli, Klebsiella, Proteus, use the necrotic tissue as a substrate to produce carbon dioxide, thus, gas formation is seen. EPN and EP are more common in female patients [22, 23, 80–83]. These diseases are usually
unilateral [22, 23, 80, 81]. Uncontrolled diabetes mellitus and urolithiasis are associated with EPN [23, 81, 84].

Abdominal radiograph can display mottled gas shadows over the renal fossa, which should not be mistaken for bowel gas [85, 86]. If EPN progresses, speckled or crescent-shaped gas collection can be seen. Calculi may be observed as well [23].

CUS shows an enlarged kidney with parenchymal or pelvocalyceal hyperechoic foci with posterior dirty acoustic shadowing that are characteristic of gas [85].

In cases of EPN, native CT detects the presence and extent of gas in the renal parenchyma and around the kidney, possible accumulation of perinephric fluid, abscesses, along with the origin of obstruction if present [86]. Intraparenchymal gas appear as small bubbles or fine streaks of air radiating from papillae on native CT (Figure 3). Contrast-enhanced CT may show irregular enhancement or delayed excretion [48].

Wan et al. characterized two types of EPN based on CT findings. Type 1 exhibits focal tissue necrosis with mottled or loculated gas collections in the renal parenchyma or collecting system. Gas can extend to the subcapsular, perinephric and pararenal spaces. In type 2, these features are accompanied by renal or perirenal fluid collections. Type 1 is more aggressive and, consequently, has a higher mortality rate than type 2 (69% vs. 18%) [87].

Huang et al. classified EPN into several classes according to CT. Class 1 presents only pelvocalyceal gas, class 2 is distinguished by parenchymal gas, in class 3A abscess or gas are extended to perinephric space, in class 3B extension is seen in pararenal space. Class 4 represents bilateral EPN [88].

These classifications allow to predict the course of EPN and apply the most appropriate treatment [22].

The lack of intraparenchymal gas differentiates EP from EPN [89]. In cases of EP, non-contrast CT demonstrates bubbles of gas or gas-fluid levels in the collecting system and pelvic or calyceal dilatation, as seen in Figure 4.

CPN is a chronic tubulointerstitial fibrosing nephritis that involves renal parenchyma and the collecting system. The purpose of radiologic imaging is to detect not only chronic renal damage, but also the underlying cause of the recurrent inflammation.

In cases of CPN, IVU usually shows focal contraction of the renal parenchyma with adjacent calyceal clubbing [90, 91]. However, this modality is not so commonly used. On US, may display focal or diffuse renal atrophy, hypertrophy of residual normal tissue (psuedotumor), irregular borders, cortical thinning, poor corticomedullary differentiation, parenchymal scars, calyceal distortion and clubbing (Figure 5). Moreover, contralateral renal hypertrophy, as a compensatory mechanism, can be observed [48].

CTU and MRI depict the disease more in detail with renal atrophy, hypertrophy of residual normal tissue (psuedotumor), irregular borders, cortical thinning, poor corticomedullary differentiation, parenchymal scars, calyceal distortion and clubbing (Figure 6). Moreover, contralateral renal hypertrophy, as a compensatory mechanism, can be observed [48].

RCS displays defects of 99mTc-DMSA uptake characteristic to renal scarring.

Renal needle biopsy is a gold standard for diagnosing glomerulonephritis (GN). However, radiologic imaging is useful prior to biopsy. Enlarged kidneys with either reduced or increased visibility of pyramids can be seen on CUS. Ecchogenicity of the renal parenchyma is associated to tubulointerstitial, not glomerular changes [95], [96]. In proliferative glomerulonephritis and interstitial nephritis tubulointerstitial compartment is severely damaged, therefore, renal cortex is hyperechoic. Contrary, renal parenchyma is normal in membranous glomerulonephritis, IgA nephropathy, minimal-change glomerulonephritis and focal glomerulosclerosis at first. Nonetheless, progression of these diseases extend to the tubules and interstitium, hence, parenchyma gradually becomes hyperechoic [97]. In addition, CUS may demonstrate inhomogeneous renal sinus with poor renal sinus-parenchymal differentiation.

Doppler US allows to assess renal function precisely in patients with chronic GN. Several studies show that resistive index (RI) correlates to the extent of arteriolosclerosis, glomerulosclerosis and interstitial fibrosis [98, 99]. T.Yura et al. also established correlation between creatinine clearance and both peak systolic velocity and end-di-
astolic velocity. Moreover, inverse correlation between creatinine clearance, RI and pulsatility index (PI) was determined in their study [100]. RI usually increases only in acute crescentic and proliferative glomerulonephritis and diseases of the tubulointerstitial compartment. However, these findings are not specific to GN.

CEUS benefits in diagnosing early glomerular disease. According to M. Nestola et al., histological activity of GN correlates with persistence of contrasts material signal in the wash-out phase. Slower contrast agent wash-out purposes disturbed glomerular perfusion in early GN [101]. A recent study concluded that a quantitative elastography technique can also contribute to the early diagnosis of GN. Shear wave based elastography point quantification (ElastPQ) determines renal cortical stiffness, which is higher in pediatric patients with glomerular disease [102]. Nonetheless, further research is needed.

MRI is another imaging modality that is helpful in diagnosis and follow-up of patients with chronic GN. Diffusion tensor imaging (DTI) allows to evaluate renal function and the degree of histopathological abnormalities. Glomerulosclerosis and tubulointerstitial fibrosis reduces parenchymal perfusion, leading to decreased diffusivity. These histopathological changes may also influence diffusion direction along the tubules. As a result, ADC and fractional anisotropy (FA) values decreases with increased chronic GN stages. Furthermore, corticomedullary differentiation is poorer with each stage, as shown in Figure 7 [103]. Contrast-enhanced MRI may differentiate active and treatable glomerular disease between sclerotic ones. In cases of chronic GN, ultrasmall superparamagnetic iron oxide particles (USPIO) are used as a contrast agent. USPIO displays cortical macrophage infiltration, corresponding to inflammatory renal regions. Due to accumulation of iron particles in mononuclear cells, MRI demonstrates diffusely decreased enhancement of renal parenchyma on T2W images after USPIO administration [104].

In conclusion, radiology plays an important role in diagnosis of inflammatory renal diseases. Imaging allows to identify renal abnormalities and differentiate between a few feasible pathologies. It may also evaluate the activity of the disease. Moreover, it can assess sequelae, such as renal scarring and decreased renal function. Although US is the first-line imaging modality in most of the cases, CT is usually referred to be the most informative one. MRI is a radiation-free alternative and is not routinely used. Nonetheless, it is relevant in the early detection of glomerulonephritis. In order to identify the sequelae of these diseases, RCS can be beneficial, especially in the pediatric population.
REFERENCES


