Diagnosis of acute pyelonephritis with recent trends in management

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Renal infection can be regarded as a spectrum of clinical entities progressing from mild acute pyelonephritis (APN) to renal abscesses or emphysematous pyelonephritis. APN is traditionally characterized by bacterial or fungal invasion of the kidney, causing acute interstitial inflammation and tubular cell necrosis (Figure 1). The term chronic pyelonephritis applies to the findings of pelvicaliceal inflammation, fibrosis and deformity of the kidney on histopathologic examination. Previous estimates suggest an incidence of 250,000 episodes per year of APN in the USA with nearly 200,000 requiring admission [1, 2]. In this issue of the journal, Rollino et al. describe a series of 223 patients who presented with clinical evidence of APN to an emergency department during the course of 103 months. Their study sheds light on the inferiority of urine culture and blood culture over imaging modalities in the diagnosis of APN. The group was comprised predominantly of women who had a 9-fold increased risk of developing APN compared with men. This is in contrast to previous studies that reported only a 4-5-fold greater risk in women from a large US database [3].

Rollino’s study focused on imaging modalities as a tool for diagnosis of APN along with treatment and follow-up of patients with APN. All of the patients were treated as inpatients and were considered to have APN clinically diagnosed on the basis of fever, flank pain, leukocytosis and elevated C-reactive protein (CRP). Only 26.9% of the patients were considered to be at high risk at presentation. The diagnosis of pyelonephritis was not based on culture alone as there were positive urine cultures in only 23.5%, blood culture in 15.8% and both blood and urine culture in only 7.6% of patients. Computed tomography (CT) and magnetic resonance imaging (MRI), however, confirmed APN in 92% of the patients. This low culture positivity rate is surprising and may be related to prior antibiotic therapy in the outpatient setting, culture techniques, low virulence bacteria or atypical pathogens. This study also suggests that although imaging can detect a majority of cases, it cannot be used as a gold standard as twelve patients had negative CT results but typical symptoms and positive urine cultures. This highlights the previous recommendation that all patients with symptoms suggestive of APN should have a properly collected mid-stream urine sample and culture for identification of the organism and tailoring of the treatment [4]. Hospitalization as a result of APN is five times more common in women than in men, with 11.7 versus 2.4 hospitalizations per 10,000 cases [3]. Women, however, show a lower mortality rate than men with 7.3 versus 16.5 deaths per 1000 cases [3]. A seasonal variance in incidence with most infections occurring in summer is also seen [5]. Acute uncomplicated infections primarily occur in younger women as shown in the current study by Rollino where 54.4% of patients were <40 years of age.

Among the 23.5% of patients who had a positive urine culture, Escherichia coli was the most common organism (87.5%) followed by Klebsiella (6.3%), Proteus mirabilis (3.2%) Enterococcus faecalis (1.5%), and co-infection of Klebsiella with E. faecalis (1.5%) and blood cultures grew E. coli (90%), Acinetobacter iwoffii (2.5%), P. mirabilis (2.5%), Streptococcus saprophyticus (2.5%) and Staphylococcus hominis (2.5%) in 15.8% of patients. The study by Rollino et al. showed almost a similar microbiological pattern when compared with previous reports with E. coli being the most common organism [6]. Two special situations in which APN needs prompt intervention need to be mentioned. APN in pregnant women occurs in 1–2% of women increasing the risk of pre-term labor and low-birth weight infants [7]. Prompt diagnosis, hospitalization and intensive treatment are required in pregnant women with
pyelonephritis [8]. As 25% of the patients with mild APN who are pregnant have a chance of recurrence, these patients should have monthly urine cultures or antimicrobial suppression with oral nitrofurantoin, 100 mg daily, until 4 to 6 weeks postpartum [8]. In Rollino’s cohort of patients, there were very few patients who presented with APN during pregnancy and they have not highlighted the mode of diagnosis of APN. Urinary tract infection is common in renal transplant recipients with an incidence of 30–50% as a result of immunosuppression and postsurgical vesicoureteral reflux which may lead to graft pyelonephritis [9]. In a study by Kamath et al. from a tertiary care center in a developing country over a 10-year period, the incidence of APN in graft recipients was reported to be 16.5% [10]. Acute graft pyelonephritis (AGPN) (Figure 2) in the renal transplant setting is an ominous
event, as these patients are also more prone to develop bacteremia, acute rejection and cytomegalovirus disease, which could then lead to poor graft and patient survival \[10\]. Rollino’s study has not highlighted the importance of managing AGPN in their renal transplant patients. Often, one encounters difficulty assessing the severity of APN with clinical and laboratory parameters as demonstrated in the study by Rollino et al. The role of diagnostic imaging in the evaluation of patients with suspected urinary tract infection has been greatly debated. Previously, radiological imaging was not routinely considered to be requirement for the diagnosis and treatment of uncomplicated cases in adult patients. However, radiological images including CT and MRI, when applied, improve the diagnostic accuracy by delineating the nature and extent of involvement and the severity of disease and reveal complications such as abscess or obstruction \[11–13\]. Diagnostic imaging plays a role (a) to assist in the diagnosis of APN when the patient fails to respond to appropriate therapy within the first 72 h, (b) to look for previous occult structural or functional abnormalities that may require intervention, (c) to assess those patients at significant risk for more life-threatening complications as in diabetic, elderly or immunosuppressed patients, (d) to characterize the severity of the infection to direct future therapy or interventions and (e) to evaluate the extent of organ damage subsequent to a resolved acute infection. The imaging details have been discussed extensively by Rollino et al. Imaging using contrast CT scans manifests as hypoenhancing regions with or without renal swelling which may be focal or diffuse. Talner et al. have suggested that all radiological parenchymal abnormalities without abscess attributable to an acute infection should be termed APN \[14\].

Another recent study using CTs classified renal involvement according to severity into (i) simple APN with lesions appearing focal and wedge-shaped and radiating from the papilla in the medulla to the cortical space; (ii) severe APN with multi-focal or diffuse and heterogeneous lesions with pronounced perinephric stranding and (iii) renal abscesses with lesions appearing as target-shaped without central enhancement on contrast CT with peripheral enhancement in the late phase. There was good correlation between clinical and radiological severity in CT findings \[11\]. However, Rollino et al. did not apply these criteria for the diagnosis in their cohort of patients. More severe APN was seen in patients with diabetes, hypertension and non-obstructing renal stones using CT. Inflammatory markers including increased leukocytosis with left neutrophil shift and raised CRP were associated with more severe disease \[11\]. However, in the current study, inflammatory markers did not show any statistically significant association with abnormal CT and MRI findings. The current study by Rollino et al. shows that CT, and lately MRI, have overtaken routine radiography as a superior diagnostic imaging modality. It is important to note that a diagnosis of intrarenal abscess in 23.5% of the patients was confirmed by CT/MRI which was not evident by ultrasound examination. Even in those without abscess, renal ultrasound was reported to be normal in 52.1% of patients which grossly underestimated the diagnosis of APN. Concordance between CT and ultrasound in this study was 49%. In a previous study, Majd et al. reported a sensitivity and specificity of 74.3 and 56.7% for ultrasound diagnosis of APN \[15\]. Stojadinovic et al. reported that CT reduces the risk of missing renal abscesses 37 fold compared with ultrasound examination \[15, 16\]. The study also showed that patients with renal abscesses required on average, a hospitalization which was twice as long as that of patients with uncomplicated pyelonephritis (P < 0.001). The early detection of renal abscesses enabled appropriate hospitalization of patients and prolonged treatment, thereby ensuring a 100% cure rate. The contrast medium used for CT induced transient deterioration of renal function and hence, appropriate prophylactic measures should be undertaken to prevent such adverse effects. The study by Rollino et al. also highlighted the application of a second CT which was done after a 30-day treatment course in patients with renal abscess. The second CT showed complete resolution in all patients with renal abscess which may be attributable to the prolonged therapy (30 days) they received. Recurrent APN was investigated for the presence of vesicoureteral reflux which was seen in 20.9% of patients via a retrograde urethrocystography of which nine patients had evidence of vesicoureteral reflux (VUR). This was treated with an endoscopic procedure and there was a relapse in only one patient following endoscopic intervention. The authors did not mention the degree of vesicoureteral reflux and the mode of treatment in detail. In children, the approaches used include surgical and non-surgical repair of VUR using endoscopy to guide the injection of dextranomer/hyaluronic acid at the vesicoureteral junction \[17\]. In the study by Rollino et al., treatment consisted of intravenous ceftriaxone 2 g daily for 5 days followed by ciprofloxacin 500 mg twice daily orally for 14 days. If no response was observed after 72 h, treatment was modulated. Patients with abscesses were treated with ceftriaxone 2 g daily for 30 days. This led to 100% cure with relapse in 16.1% and multiple relapses in 1.7% of patients in the study. APN is a topic that has remained relatively neglected in terms of research and as
such, no conclusively evidence-based regimen has been
developed for treatment. Regardless, a few principles of
treatment have been documented and can be used as guide-
lines with appropriate consideration for local settings [4].
According to the Infectious Diseases Society of America
2010, the choice of agent should be individualized on the
basis of patient allergy, compliance history, local practice
patterns, local community resistance prevalence, availability,
cost and patient and provider threshold for failure [4, 18].
Optimal therapy for acute uncomplicated pyelonephritis
depends on the severity of illness at presentation and local
resistance patterns as well as specific host factors. In
addition, urine culture and susceptibility testing should be
performed and initial empirical therapy should be tailored
appropriately on the basis of the infecting organism. Strate-
gies for optimizing empirical therapy when local resistance
patterns are not known include using an initial intravenous
dose of a long-acting parenteral anti-microbial and starting
with a broader-spectrum agent until susceptibility results are
available [19]. To conclude, the diagnosis and management
of APN are still evolving. There are limitations of labora-
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of APN are still evolving. There are limitations of labora-
tory techniques which should be supplemented with appro-
priate contrast CT and MRI scans for early diagnosis and
appropriate antibiotic therapy to ensure a cure. Rollino et al.
have demonstrated the relevance and superiority of imaging by CT and MRI in the diagnosis of APN in complicated and uncomplicated cases [20]. Their study also
highlights the importance of CT/MRI in diagnosing renal
abscesses, appropriate treatment and follow-up of patients.
This may form a benchmark for the early diagnosis and
management strategies in the future.

Conflict of interest statement. None declared.

(See related article by Rollino et al. Acute pyelonephritis in adults:
a case series of 223 patients. Nephrol Dial Transplant 2012; 27:
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