Renal Infections

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KEYWORDS

• Acute pyelonephritis • Chronic pyelonephritis • Xanthogranulomatous pyelonephritis
• Malacoplakia • Viral interstitial nephritis • Polyomavirus nephropathy • Fungal pyelonephritis

ABSTRACT

This review discusses the various gross and histologic findings seen in renal infections due to bacteria, viruses, fungi, and mycobacteria. It is crucially important to separate infectious processes in the kidney from other inflammatory or neoplastic processes, as this will have a major impact on therapy. We describe the diagnostic features of renal infections with a specific focus on the differential diagnosis and other processes that may mimic infection. The topics discussed include acute bacterial pyelonephritis, chronic bacterial pyelonephritis, xanthogranulomatous pyelonephritis, malacoplakia, viral infections in the kidney, fungal pyelonephritis and mycobacterial infection of the kidney.

OVERVIEW

Renal infections can be seen in a wide variety of settings, and identifying the cause of infection so that proper treatment can be pursued is critical. Also important is the recognition that inflammation in the kidney is not necessarily indicative of infection, and other processes, such as glomerulonephritis, transplant rejection, and vasculitis, can mimic infection. It is necessary for the pathologist to carefully examine renal specimens for histologic features of infection, and correlate with other pertinent clinical and laboratory data to arrive at an accurate diagnosis. This review addresses the main types and patterns of renal infections, their histologic appearances, the pitfalls of diagnosis and how to resolve them.

ACUTE BACTERIAL PYELONEPHRITIS

Direct infection of the renal parenchyma by bacterial organisms is the defining feature of acute bacterial pyelonephritis. In practice, acute bacterial pyelonephritis is most commonly encountered by the pathologist in specimens removed in the setting of urinary tract obstruction, which results in ascending infection from the lower urinary tract into the renal parenchyma. The most common organism in ascending forms of pyelonephritis is *Escherichia coli* but other common bacteria that cause lower urinary tract infections are also seen.[1] Less common than the obstructive form of pyelonephritis is direct infection of the renal parenchyma through the hematogenous spread of bacteria. The most common organisms in these cases tend to be staphylococci and streptococci. Some pathologists consider this to be such a sufficiently distinct entity from the ascending form of pyelonephritis described previously that they use diagnostic terms, such as "diffuse suppurative nephritis" or "multiple cortical abscesses" to describe these hematogenously spread cases.[2] Regardless of the route of infection, the key feature of acute bacterial pyelonephritis is the direct infection of the renal parenchyma by bacteria.

GROSS FEATURES

In acute bacterial pyelonephritis related to obstruction, the kidney is generally enlarged and displays whitish abscesses of varying size. Collecting ducts filled with pus may be visible as

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thin yellow streaks running through the medulla. In a minority of cases, severe infection can result in papillary necrosis. The renal pelvis and calices may be dilated as a result of the obstruction, and in severe cases the renal pelvis may be filled with pus (termed pyonephrosis). In cases of hematogenous spread, both kidneys are typically involved. They are enlarged with numerous whitish abscesses visible on the subcapsular surface. On sectioning, the parenchymal surface will be diffusely involved by microabscesses of varying size. Calyceal dilatation is generally not seen in hematogenous spread, as urinary obstruction is not typical of these cases.

MICROSCOPIC FEATURES

Regardless of the route of infection, acute bacterial pyelonephritis is characterized by prominent neutrophilic inflammation of the renal tubules, which causes destruction of tubular basement membranes, resulting in inflammation spilling into the renal interstitium (**Fig. 1**A). Within days, the inflammatory infiltrate will become mixed, containing significant numbers of lymphocytes, plasma cells, histiocytes, and occasional eosinophils. Parenchymal involvement is often patchy, with areas of intense inflammation juxtaposed with relatively normal-appearing areas. Glomeruli and vessels are typically relatively preserved and may appear to "float" in a sea of neutrophils. In cases of ascending infection, sections of the renal pelvis will show severe inflammation of the mucosa. In hematogenously spread infection, the renal pelvis may be relatively uninvolved and numerous microabscesses can be seen diffusely throughout the renal parenchyma, particularly in the cortex (see **Fig. 1**B).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of acute tubulointerstitial inflammation includes noninfectious processes that can have a similar appearance to acute pyelonephritis. In severe cases of glomerulonephritis, there is often a significant element of associated tubulointerstitial inflammation by a mixed inflammatory infiltrate. In acute bacterial pyelonephritis, occasional glomeruli may be overtaken by the surrounding inflammatory infiltrate, but in the setting of more diffuse glomerular involvement, a thorough evaluation to exclude a primary glomerulonephritis should be undertaken. Likewise, various vasculitic processes, including antineutrophilic cytoplasmic antibody–mediated forms of disease, can be associated with prominent tubulointerstitial inflammation. Any evidence of artery wall inflammation in the setting of tubulointerstitial inflammation should raise the possibility of vasculitis. Of note, fungal organisms can occasionally cause a necrotizing vasculitis when directly invading a vessel wall (addressed further in the section on fungal pyelonephritis), but arteritis is highly unusual in bacterial infection. Also in the differential diagnosis of acute tubulointerstitial nephritis is a drug-induced hypersensitivity reaction. Hypersensitivity reactions are classically eosinophil-rich but also can have prominent numbers of neutrophils. The presence of prominently dilated tubules filled with neutrophils (see **Fig. 1**A) or microabscesses (see **Fig. 1**B) strongly favors the diagnosis of pyelonephritis over noninfectious forms of disease. Clinical correlation with urine cultures, medication history, and appropriate serologic workup is often important in differentiating these entities.

Pitfalls IN THE DIAGNOSIS OF ACUTE BACTERIAL PYELONEPHRITIS

- ! Not all neutrophil-rich inflammation in the kidney is infectious in origin.
- ! Severe acute glomerulonephritis can be accompanied by prominent tubulointerstitial inflammation containing neutrophils.
- ! Acute vasculitis can be associated with acute tubulointerstitial inflammation. Any evidence of arteritis favors the diagnosis of vasculitis over bacterial pyelonephritis.
- ! Fungal infections may have neutrophil-rich inflammation and may be overlooked unless appropriate stains are performed.
- ! Drug-induced or other hypersensitivity reactions can have significant numbers of neutrophils in the tubulointerstitial infiltrate, although eosinophils classically predominate in these cases.

CHRONIC PYELONEPHRITIS

Chronic pyelonephritis was liberally diagnosed in the past when significant lymphocytic inflammation of the renal interstitium was noted. It was presumed that this inflammation reflected prior bacterial infection that had caused destruction of the parenchyma. It is important to realize that scarring in the kidney from noninfectious conditions is also often accompanied by prominent, nonspecific chronic inflammation, and the presence of