Assessment of kidneys in adult autopsies

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Abstract

Medical kidney diseases, such as acute tubular injury, arterionephrosclerosis, and infections, are common in hospitalized patients and frequently seen at autopsy. In addition, we have encountered a wide spectrum of renal pathology in adult autopsies including diabetic nephropathy, thrombotic microangiopathy, glomerulonephritis (often infection-related), vasculitis, amyloidosis, light chain cast nephropathy, membranous nephropathy, focal segmental glomerulosclerosis, atheroembolic disease, polyomavirus nephropathy, bile cast nephropathy, oxalosis, nephrocalcinosis, and urate nephropathy. Since kidney biopsy is usually avoided in critically ill patients, histologic evaluation of autopsy kidneys may be the first and only opportunity to identify these diseases, allowing us to better understand their role in morbidity and mortality. The practicing pathologist should be aware of the frequency and spectrum of renal pathology that may be present in autopsy kidneys, and implement a systemic approach to their evaluation. We will discuss our approach and review the pathologic features of the most commonly encountered entities.

Keywords acute tubular injury; amyloidosis; arterionephrosclerosis; autopsy; diabetic nephropathy; glomerulonephritis; interstitial nephritis; thrombotic microangiopathy; vasculitis

Introduction

In the United States, more than 90,000 Americans die from kidney diseases annually. Chronic kidney disease (CKD) and end stage renal disease (ESRD) substantially increase the risks of cardiovascular disease and death. Additionally, acute kidney injury (AKI) occurs in approximately 25% of hospitalizations and greatly increases the risk of mortality. Therefore, histologic evidence of medical renal disease is common at autopsy.[1,2] We recently performed a retrospective histologic review of autopsy renal pathology at our institution in order to establish a baseline of diseases which the autopsy pathologist can expect to encounter (manuscript submitted). In addition to frequent findings of acute tubular injury and arterionephrosclerosis, we detected a wide variety of significant renal pathology in 35% of adult autopsies in a 2-year span, summarized in Table 1. These diseases may be overlooked due to a combination of factors including inadequate training in renal pathology and emphasis on determining the immediate cause of death at autopsy. Only one autopsy study has documented renal disease as a major cause of death,[1] accounting for 2.2% in their large series. We speculate that kidney disease contributes to mortality in a much larger percentage of patients than is currently appreciated. In this review, we discuss a systematic approach to autopsy renal pathology including tissue allocation, histologic evaluation, and ancillary studies. We will also review the pathologic features of commonly encountered kidney diseases in adult autopsy specimens, most of which can be identified or strongly suspected based on hematoxylin and eosin (H&E) staining alone, as they relate to clinical scenarios including AKI, cardiovascular disease, infection, malignancy, and toxic and/or metabolic insults.

Spectrum of medical renal diseases identified in adult autopsy specimens

Glomerular diseases	Tubulointerstitial diseases	Vascular diseases
Diabetic nephropathy	Acute tubular injury	Arterionephrosclerosis
Membranoproliferative glomerulonephritis	Pigment nephropathy (myoglobin, hemoglobin, and bile/bilirubin cast nephropathies)	Thrombotic microangiopathy
Endocarditis-associated glomerulonephritis	Acute interstitial nephritis	Atheroembolic disease
Pauci-immune crescentic glomerulonephritis	Parenchymal infection (pyelonephritis, polyomavirus)	Small vessel vasculitis
Membranous nephropathy	Metabolic diseases (oxalosis, nephrocalcinosis, urate nephropathy)	Amyloidosis
Focal segmental glomerulosclerosis	Light chain cast nephropathy	
Amyloidosis		

Table 1

A practical approach to evaluation

Prior to prosection, chart review should note any clinical suspicion for medical renal disease or history of systemic diseases with known renal manifestations. Evaluation of pre-mortem laboratory values should focus on renal functional abnormalities (i.e. elevated serum creatinine and blood urea nitrogen), the presence of hematuria and/or proteinuria, and any growth on urine culture. Significant gross findings include irregularities of the cortical surface following capsular stripping, cortical thickness, and the presence of calculi and/or hydronephrosis. Evaluation of cystic diseases and congenital abnormalities is detailed elsewhere.[3] At least one section from each kidney should be submitted for histologic processing, including cortex and medulla. If there is a known history or clinical suspicion of medical renal disease,

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cortical tissue may be saved in Michel transport media and glutaraldehyde for immunofluorescence microscopy (IF) and electron microscopy (EM), respectively. This step may be too time-consuming and costly to perform routinely, especially given the desire to minimize autopsy costs. Notably, both IF and EM can be performed on formalin-fixed, paraffin-embedded tissue, although there is some decreased sensitivity in the former and processing artifact in the latter.[4,5] When direct IF microscopy is performed on the paraffin tissue sections, we routinely stain for immunoglobulin (Ig) G, IgA, IgM, κ and λ light chains, and albumin. Given the strong association between renal vein thrombosis (RVT) and nephrotic syndrome, the finding of RVT at autopsy should prompt consideration of ancillary studies upfront.

Histologic examination requires systematic evaluation of the four anatomic compartments on H&E stain, namely the glomeruli, tubules, interstitium, and vasculature. Injuries simultaneously involving several anatomic compartments are common in adult kidneys. If abnormalities are detected, additional histochemical stains can be performed as necessary including periodic acid-Schiff (PAS), Jones methenamine silver (JMS), trichrome, and Congo red stains. Thorough examination of both cortex and medulla is imperative, as some diseases can be focal or selectively involve certain regions of the kidney. Well-preserved and nonischemic glomeruli should be evaluated for diffuse and/or nodular mesangial expansion, mesangial hypercellularity (>3 cell nuclei per peripheral mesangial area in a 4-μm thick tissue section), endocapillary hypercellularity, crescents, fibrinoid necrosis, glomerular basement membrane (GBM) thickening and/or duplication, and thrombi. The tubulointerstitial compartments will show varying degrees of interstitial fibrosis and tubular atrophy with accompanying nonspecific inflammation that may correlate with the degree of arteriosclerosis. Notable findings in the tubulointerstitium include tubular epithelial cell attenuation/necrosis, interstitial inflammation and tubulitis, atypical or pigmented casts, viral inclusions, and crystals. Arteries and arterioles should be evaluated for intimal fibrosis, hyalinosis, fibrinoid necrosis and/or vasculitis, thrombi, atheroemboli, and mural deposition of amorphous material.

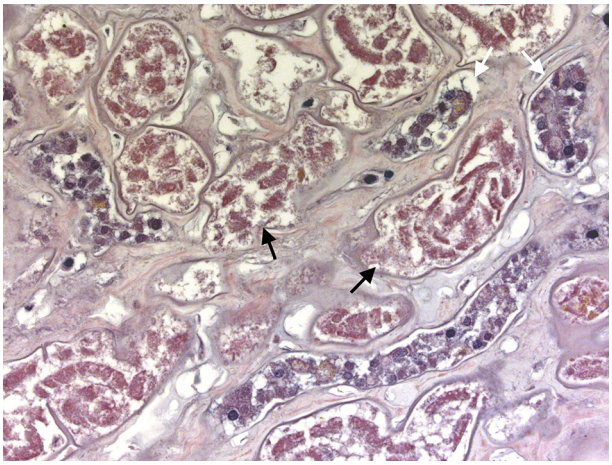

Figure 1 Autolysis is characterized by tubular epithelial cell degeneration, nuclear loss, and detachment from the underlying tubular basement membranes uniformly affecting all tubular segments, including the proximal (black arrows) and distal (white arrows) convoluted tubules (H&E).

One of the challenges in assessing autopsy kidney specimens is that postmortem changes of autolysis are invariably present, characterized by tubular epithelial cell degeneration with pyknosis and detachment from the underlying tubular basement membranes (Figure 1). These changes can mimic acute tubular injury (Figure 2), so correlation with pre-mortem renal function is sometimes necessary to differentiate between the two. Distinguishing histologic features are discussed below. In our experience, varying degrees of postmortem autolysis does not preclude assessment of medical renal disease in the vast majority of cases. Specifically, the evaluation of anatomic structures including glomerular and tubular basement membranes, mesangial matrix, and vasculature is unaffected by autolysis (Figure 3).

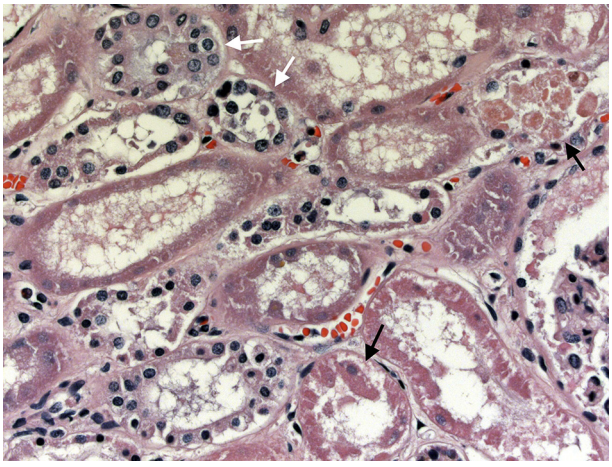

Figure 2 Findings of acute tubular injury in a patient with acute renal failure. There is attenuation of the proximal tubular epithelial cells with cytoplasmic sloughing and nuclear loss (black arrows), while the distal convoluted tubules (white arrows) are relatively well-preserved (H&E).

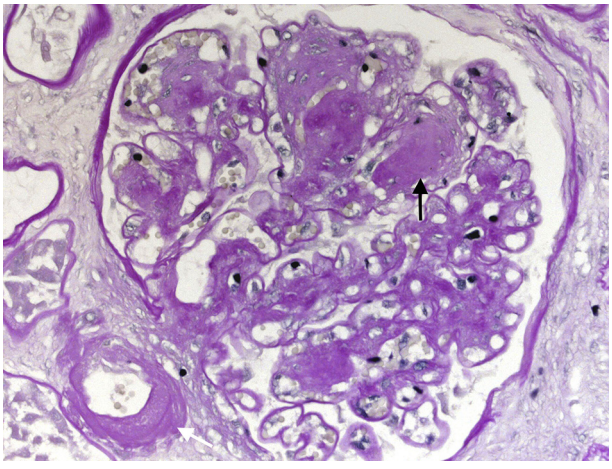

Figure 3 Features of diabetic nephropathy are easily recognizable despite extensive autolytic changes. This glomerulus demonstrates prominent nodular mesangial sclerosis (Kimmelstiel-Wilson nodules, black arrow), thickened glomerular basement membranes, and marked arteriolar hyalinosis (white arrow). There are few viable cells in the glomerulus or tubulointerstitium (PAS).

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