

PATHOLOGY OF INFECTIOUS RENAL DISEASES IN SOUTH AMERICA

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The kidney parenchyma may be involved by diverse injuries affecting particularly tubulo-interstitial areas, but also glomeruli resulting in abnormal decline in renal function. Determining to the clinician the different causes and to prevent chronic or acute renal failure, appropriate and timely identification of a particular infectious disease may allow a specific treatment. In certain situations the pathologist is first in the diagnostic team to alert about infections.

Universally, pathogens can get access to the kidneys as an ascending infection from the urinary tract, or by the blood stream in systemic infections caused by bacteria, fungi or viruses. Epidemiologic data in Latin America are uncertain.

Escherichia coli is the most common infectious agent leading to acute pyelonephritis as well as enterococcus.

From the pathologist point of view, chronic pyelonephritis and / or Reflux nephropathy are characterized by varying extent of tubulo-interstitial nephritis, frequently associated with glomerular sclerosis and fibrous scars. The affected tubules may content Tamm-Horfall protein. (1-2)
The gross and microscopic features of these condition is well-known and will not be discussed here.

XANTHOGRANULOMATOUS PYELONEPHRITIS (XP)

XP is characterized by accumulation of foamy macrophages intermingled with plasma cells, lymphocytes, polymorphs and occasional giant cells. It is often associated with *Proteus* infection and obstruction is the usual cause. Grossly, the kidney is enlarged unlike other types of pyelonephritis and the lesions are seen as yellowish orange nodules. These findings, together with numerous foamy histiocytes, may be taken as renal cell carcinoma (3-4).

TUBERCULOUS PYELONEPHRITIS (TP)

TP results from blood dissemination from pulmonary disease or as an ascending infection from genital lesions. The kidney presents one or several nodular caseous foci, with ucerative destruction of the renal parenchyma. The histology shows granulomas with epithelioid histiocytes containing acid-alcohol resistant bacilli as well as necrosis. A few cases were reported in kidney transplant patients.(5-6)

Syphilis

Membranous or diffuse proliferative GN-Syphilitic nephropathy is usually observed in secondary syphilis because this phase is associated with high levels of immune complexes. A few reports, indicate *treponema pallidum* antigens may be located in the glomerular deposits. On electron microscopy, glomerular subendothelial, subepithelial or mesangial deposits are observed.

LISTERIOSIS

is produced by *Listeria monocytogenes*, may affect the kidney with different histologic patterns, commonly, with a tubulo-interstitial nephritis.

PARASITIC INFESTATIONS

Malaria

Even though falciparum malaria can cause acute tubular necrosis due to acute hemolysis, hemoglobinuria and hypotension, a chronic progressive nephropathy is observed with *Plasmodium malariae* infection. In comparison with falciparum malaria, *P. malariae* infection is a more indolent form of infection, which affects only 25% of erythrocytes. However, it is also associated with chronic progressive immune complex-mediated (Membranous GN) glomerular disease.(7).

Schistosomiasis

Mesangial proliferative GN, focal segmental glomerulosclerosis, membranoproliferative GN, and membranous GN have all been reported in patients with this infestation. On occasion, if schistosomiasis is associated with co-infection with *Salmonella* species, treatment of the *Salmonella* infection improves the nephropathy. The antigen for schistosoma has been localized within the glomerular immune complexes. The following are glomerular lesions reported in various parasitic infections:

- Leishmaniasis - Mesangial or focal proliferative GN
- *Stroglyoides Stercoralis*: Mesangial or Membranous or membranoproliferative GN
- Hydatidosis - Mesangiocapillary GN, membranous GN
- Toxoplasmosis - Mesangioproliferative GN

FUNGI

Fungal: *Aspergillus*, the zygomycetes, *Cryptococcus* and *Blastomyces* are the most common fungi involving the kidney including *Candida* spp.

A number of histologic stains are available that are routinely used to visualize fungi in tissue sections. Hematoxylin and eosin (H&E) stain, on the other hand, is very useful to observe the host response but is not a special fungal stain. Grocott methenamine silver (GMS), Gridley's fungus (GF), and periodic acid-Schiff (PAS) are very effective to identify the fungi, as Kinyouin or Gram stains are used for acid-alcohol resistant bacilli. Occasionally Best Mucicarmine or Fite-Faracco stains are also useful.

ASPERGILLUS AND ZYGOMYCETES: present as hyaline, septate, dichotomously branched hyphae of uniform diameter and branching at acute angles. In cavitory lesions, conidial heads are occasionally observed. Purulent, necrotizing inflammation may occur. Calcium oxalate crystals, probably originating from fungal oxalic acid, are present near hyphae in necrotic tissue if the infecting species is *Aspergillus niger*.

SOUTH AMERICAN BLASTOMYCOSIS: this fungi presents as a spherule containing endospores. Yeast-like cells with multiple buds are typical. The buds are attached to the mother cell with narrow necks. The appearance resembles a "steering-wheel". The transition form may be observed in necrotic nodules and misdiagnosed as one of the fungi in zygomycetes group, when spherules are not yet evident.

CRYPTOCOCCUS NEOFORMANS: This shows as pleomorphic yeast-like cells and formation of narrow-based buds are typical. The encapsulated strains have capsular material detected with mucin stain.

CANDIDA shows as budding yeast cells (blastocidia), pseudohyphae and septate hyphae are observed.(8).

VIRAL INFECTIONS

The incidence of CMV, HIV, BK/JCV, HBV and HCV infections are similar to the rest of the world. In Hantavirus Infection and Argentinean Hemorrhagic Fever-BOLIVIAN hemorrhagic Fever infections may affect the kidney.

ADENOVIRUS INFECTION

Virus can be isolated from the majority of tonsils/adenoids surgically removed, indicating latent infections. It is not known how long the virus can persist in the body, or whether it is capable of reactivation after long periods, causing disease. The virus is reactivated during immunosuppression, e.g. in AIDS and transplant patients. Pre-existing adenovirus infection is a major problem in the rejection of transplanted heart/ lung grafted patients. Several reports show that it has to be considered in kidney grafts as well when BK/JC infection diagnosis has failed. The inclusions are morphologically similar in H-E stained slides. However, often this is accompanied by necrotizing features and neutrophilic infiltrate. Immunohistochemistry is confirmatory.

A characteristic feature of adenovirus infection is the ability to subvert the host immune response by using the early E3 protein. The E3 membrane proteins are able to down regulate critical recognition structures for the host immune system from the cell surface.(9-10)

HERPES SIMPLEX INFECTION.

Herpes simplex virus (HSV) infection usually occurs in immunocompromised or severely debilitated patients. It is not so common in patients with renal transplants. The diagnosis can be made histologically.

HSV mainly affects tubular cells causing necrosis, a major reason for functional deterioration.

Peculiar nuclear inclusions are present in the tubular cells. IHC demonstration is essential for diagnosis.

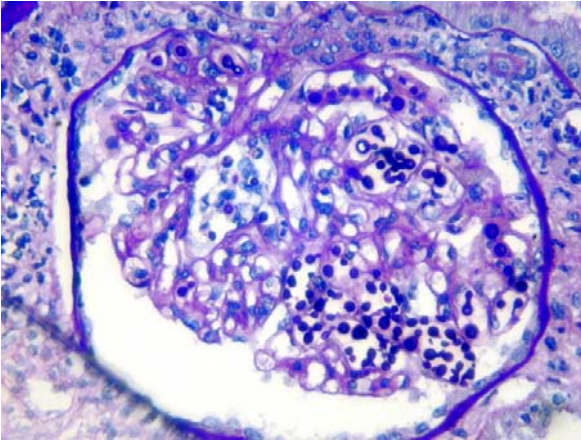
Recently several reports refer kidney lesions by Parvovirus (B 19), sometimes associated with collapsing glomerulopathy. Differential diagnosis should include early stages of BK/JC infections.(10)

Most glomerular diseases associated with infection are mediated by the immune complexes. The classic example observed in poststreptococcal GN involves an antigen-antibody reaction, which may develop in the circulation or in the glomeruli. Deposition in the glomerulus results in activation of the complement cascade, which may involve either the classic or alternative pathway. The immune complexes may activate endogenous glomerular cells, especially endothelial cells. The production of chemotactic factors results in the accumulation of leukocytes and platelets within the glomerulus and, consequently, in the development of the inflammatory response and an exudative form of proliferative glomerulonephritis.

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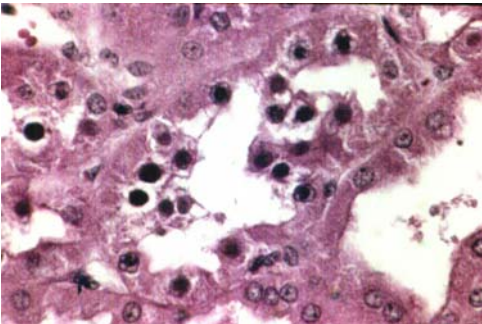
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Fungal

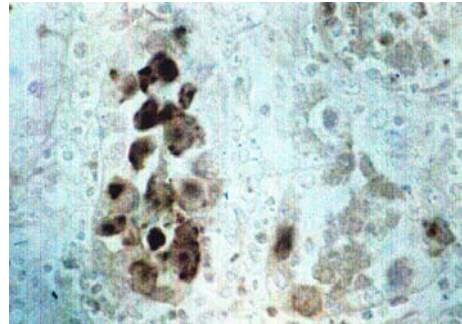


Cryptococcus neoformans in glomerulus

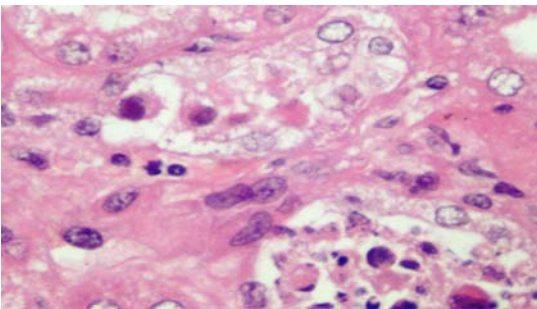
Viral



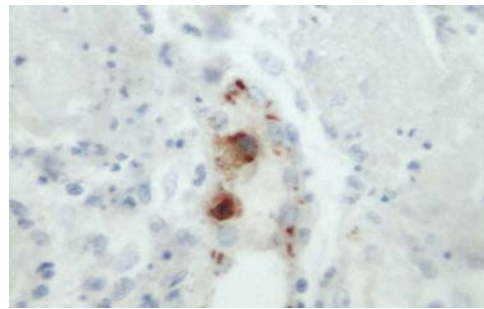
Intranuclear adenoviral inclusions H&E



Adenovirus IHC



Herpes viral inclusion 400x H&E



Nuclei with Herpes viral inclusions 400x H&E