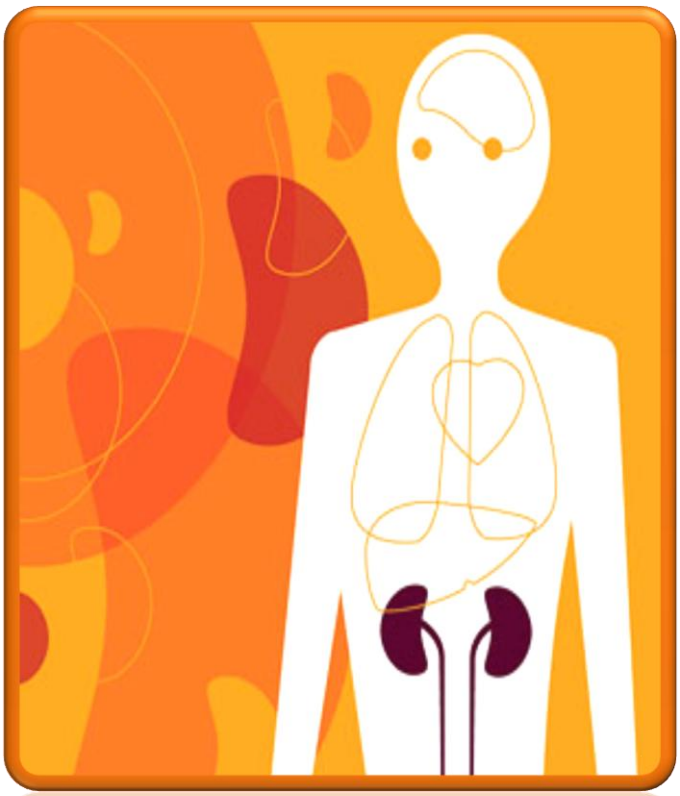

PATHOLOGY TEAM 431

(renal block)

Renal Transplant

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Renal Transplant

Objectives:

1. Recognize the concept of renal allograft.
   Describe the pathology of rejection and differentiate acute cell-mediated and antibody-mediated rejection.
2. Differentiate between acute and chronic rejection.
3. Recognize the pathology of the principal infections inherent to renal transplantation.
4. Recognize the pathology of acute and chronic drug toxicity.

Introduction:

An allograft refers to the organ transplantation within the same species while xenagrafts are between 2 different species (ex, animala and human)

The transplantation of organs from one individual to another of the same species is called allografts. The major barrier to it is immunological rejection of the transplanted and foreign tissue.

Rejection is a complex phenomenon involving both cell-mediated and antibody (humoral) hypersensitivity reactions directed against the hitocompatibility molecules if the foreign graft.

The key to successful transplantation is to minimize rejection by immunosuppressive therapy.

Renal transplant is an important topic to learn about because:

1. it is the most frequent internal transplantation done
2. the severity of the complications that can occur in cases of mismatch

Problems with Transplantation:

1- rejection
2- Surgical relating to anastomoses of the renal artery
3- Recurrence of an old disease like Focal Segmental Glomerulonephritis or Membranoprolifrative Glomerulonephritis

BEFORE:

Checking for HLA compatibility in the lab between the donor and recipient by PCR, MLR ..etc is required for good outcome , and blood group.

Best outcome ➔ the donor and recipient are relatives (higher chance of compatibility)

Cadaveric organs will not produce good results because of cold ischemia

cold ischemia time: In surgery, the time between the chilling of a tissue, organ, or body part after its blood supply has been cut off and the time it is warmed by having its blood supply restored. This can occur while the organ is removed from the body to be used for transplantation in another.

DURING:

The transplanted kidney is put anteriorly in the abdomen to be easily accessible in case the patient requires anther surgery or biopsy.

The old kidneys are not removed unless they are infected, malignant or if it results in hypertension.

AFTER:

Follow-up by serum creatinine measurement (to monitor GFR)

If it increases: 1. IMP: perfusion dopel to check if the problem is in the vascularization. If so a surgeon must interfere to restore adequate blood supply to the kidneys.

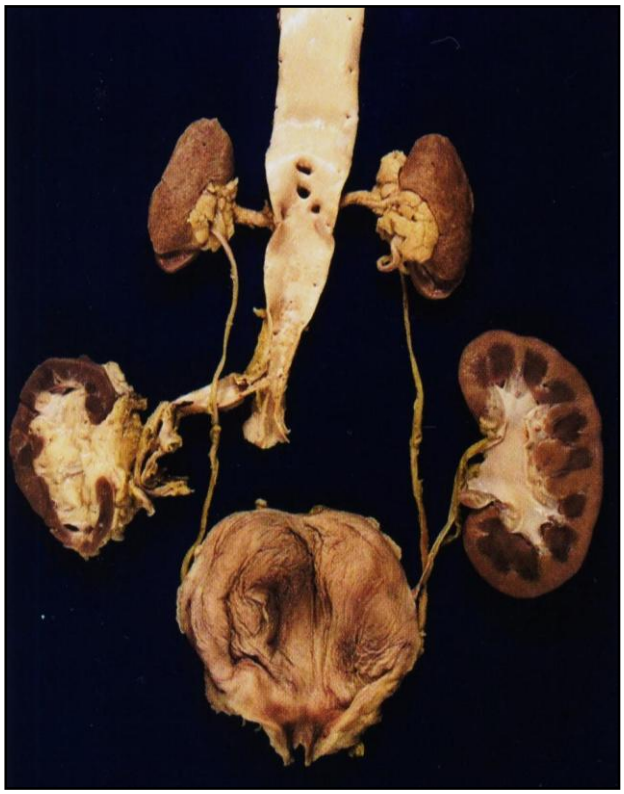
2. if vascularity is sufficient BIOPSY must be taken (sections of 10 glomeruli and 2 arteries). Two outcomes are possible:

Rejection of organ Classified into types and grades	Other: Drug toxcicity (cyclosporine), infection, recurrence of original disease, denovo, cancer

each with it's own management

Mechanism of rejection:

Donor class I and class II major histocompatibility antigens (MHC) on antigen presenting cells (APCs) in the graft (donor) are recognized by host (recipient) CD8 cytotoxic or suppressor T cells and CD4 helper T cells respectively. CD4 cells proliferate and produce cytokines (Interferone Gamma IF- Y) which induces tissue damage to renal blood vessels and tubules by a local hypersensitivity reaction. In addition, graft antigens are taken up by APCs in the host. These APCs activate CD4 cells which damage the graft (transplanted tissue or organ) by a local delayed hypersensitivity reaction and stimulate B lymphocytes to produce antibodies.



showing atrophic end stage kidneys (top) in normal position. Note that the biopsy of it's tissue cannot indicate the cause.

Here two kidneys were transplanted (bottom). This is when the patient is receiving from a child because their kidneys have less glomerular mass.

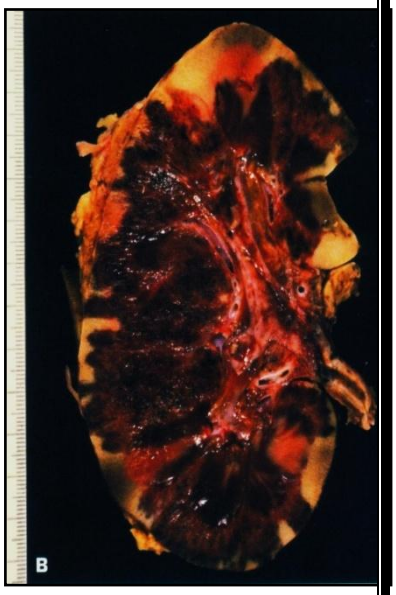
The Banff Classification of Rejection: {diagnostic catergories depending on the tissue biopsy}

1. Accelerated Acute Rejection
2. Hyperacute rejection
3. Borderline changed {very mild acute rejection}
4. Acute rejection {either T-cell or antibody mediated or both}
5. Chronic rejection (Sclerotic)
6. Others (listed above)

Accelerated Acute Rejection:

Happens when the patient has had a previous transplant that was rejected.

Hyperacute:



directly on the operating table usually by the surgeon after restoring the blood supply by vascular anastomosis. Could occur within a few hours to up to ONE day.
Grossly the kidney becomes cyanotic (pale blue-ish) instead of regaining it's pink color. It microscopically presents with heammorhage and ischemic necrosis. As well as arteritis, arteriolitis and vessel thrombosis.

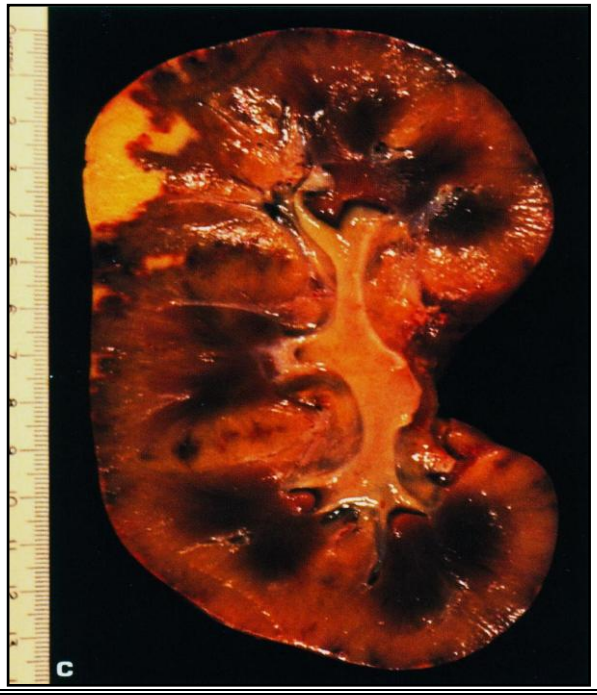
Result of circulating Ab that were not detected by cross matching in the lab.

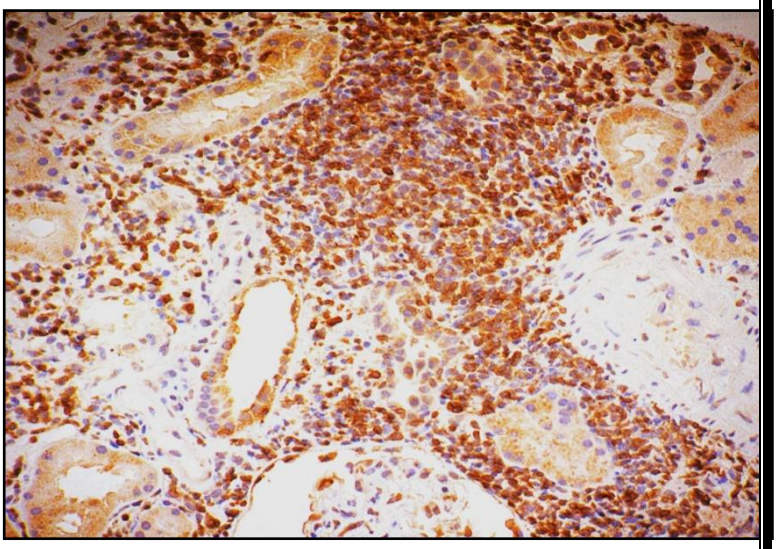
Not commonly seen nowadays because of the advanced technology and good testing ability.

Acute:

Occurs within days to week but sometimes months or years and can either be cellular (interstitial edema and mononuclear-lymphocyte infiltration) or humoral also called vascular (associated with vasculitis)

Predominantly T-cell mediated and subclassifieed into grades:

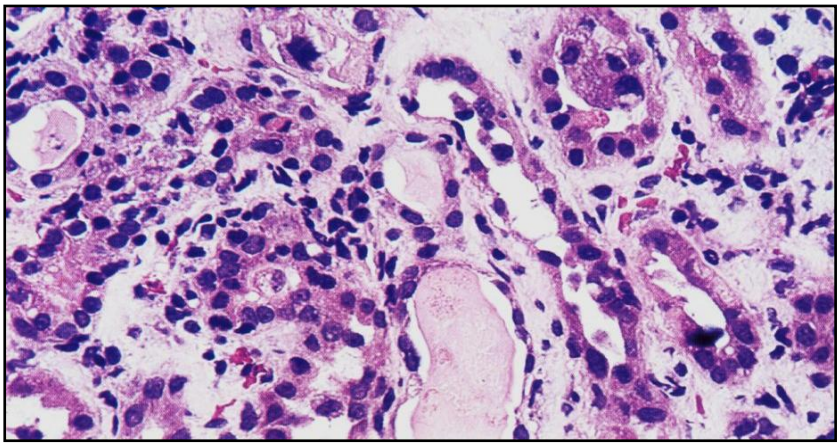




Focal Infarcts with interstitial infiltration of T-cells

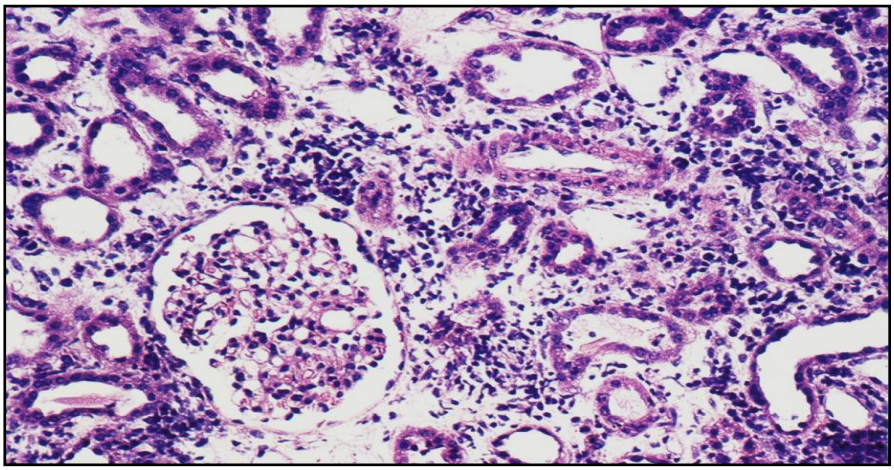
Grade I (cellular): tubulointerstitial inflammation (lymphocyte infiltration)

IA:



Arterioles show slight inflammation & Tubular lining shows lymphocyte infiltration – Moderate tubulitis

IB: more severe

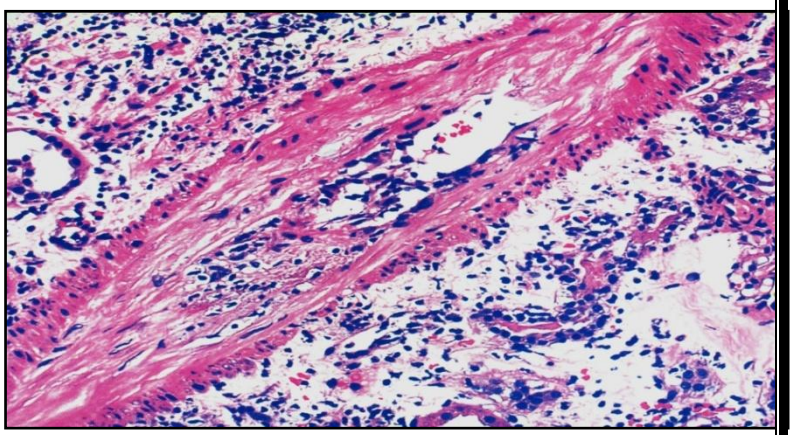


Arterioles show slight inflammation & Severe tubulitis

Grade II (humoral or vascular): artery endothelium is affected by the lymphatic infiltrate

Grade IIA: mild- t moderate intimal arteritis

Grade IIB: severe intimal arteritis ➔ ➔ ➔



Grade III: either T cells or Ab

T cell mediated ➔ transural arteritis

Ab mediated ➔ arteriolar fibrinoid necrosis

CD4 activates compliment which leads to deposition in capillary

Chronic (Sclerosing allograft):

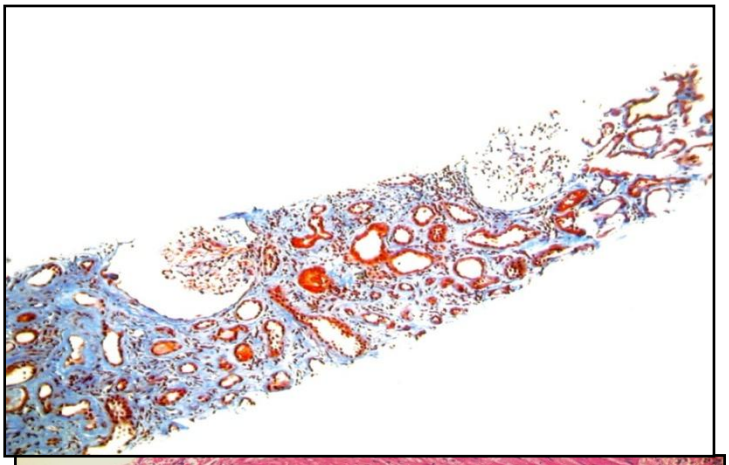
Usually presents late after transplant, by months to years.

There is a progressive rise in serum creatinine levels

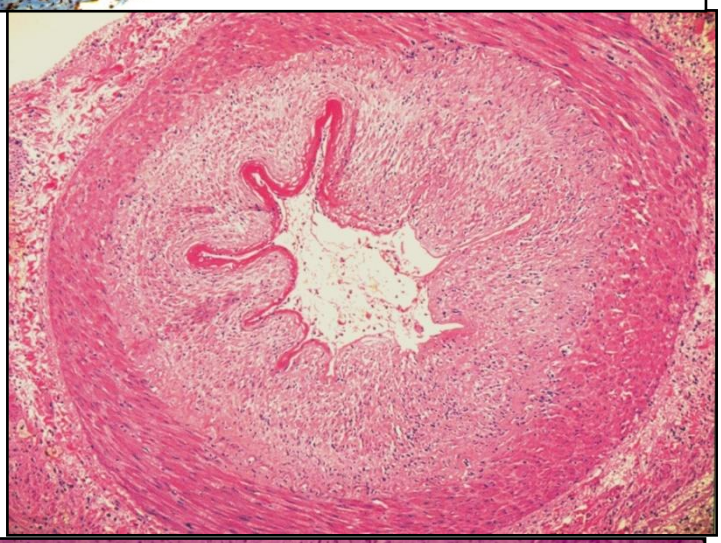
Charachterized by fibrosis and also classified into grades according to severity
Grade I: mild
Grade II: moderate
Gradde III: severe

Microscopicalley we see arteriolar sclerosis (occlusion of the artery by fibrous tissue sometimes to the extent of leaving only a tiny slit as lumen), and loss of renal parenchyma.

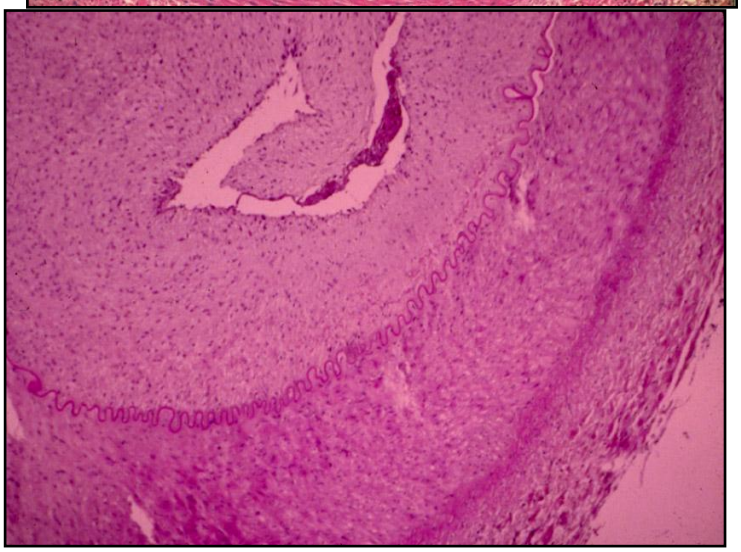
This type of rejection does not respond to standard immunosppressive treatment.



An example of Grade II-III is characterized by a diffuse increase in interstitial tissue and marked tubular atrophy as seen on this trichrome stain.



The classical lesion of chronic transplant vasculopathy is a circumferential proliferation of myointimal cells with an intact internal elastic lamina.

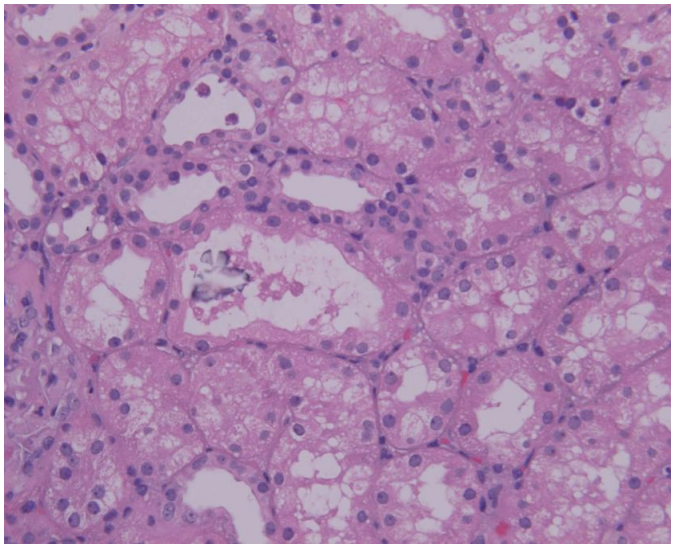


Occlusion of the vessel by fibrous tissue.

*note: different than appearance of hypertension in which there is also occlusion but as layers = multiplication of the elastic lamina

Other:

Infection: as a result of immunosuppression, most commonly cytomegalovirus (microscopically: enlargement of cells filled with cytoplasm) or polyoma (specific to renal transplants only)



Immunosuppreive drug toxicity (cyclosporine): resulting in isometric vaculization.

Here we switch the drug or lower the dose.

Summary:

An allograft refers to the organ transplantation within the same species while xenagrafts are between 2 different species (ex, animala and human).

The major problem in transplantation is rejection.

Before transplantation HLA typing must be done (MHC) and blood grouping

Mechanism of action is due to activation of the host CD4 , CD8 T cells which secrete IF-Y and activate B lymphocytes to produce antibodies leading to the damage of the graft by a hypersensitivity reactions.

Classification of rejection:

1- Accelerated Acute = happens after a previous rejected graft
2- Hyper acute = instantly right after surgery with hemorrhage and ischemic necrosis
3- Acute = cellular with tubulitis, and humoral affecting the vessels. Both T-cell infiltration
4- Chronic = fibrosis and sclerosis
5- Others = drugs (cyclosporine) and infections

Revision questions:

1- Pateint with a history of graft rejection (failed transplant), is admitted for a 2nd transplant which unfortunately was also rejected. According to Banff classification, what is the rejection type?
   a- Acute
   b- Chronic
   c- Accelerated acute
   d- Hyper acute

2- What cell causes local delayed hypersensitivity?
   a. CD4
   b. CD8
   c. B lymphocytes
   d. Macrophages

3- The type of rejection which has ischemic necrosis and vessel thrombosis due to circulating antibodies is:
   a. Acute
   b. Hyper acute
   c. Chronic
   d. Accelerated acute

4- A feature of acute rejection is the infiltration of which one of these cells?
   a. B cells
   b. T cells
   c. Macrophages
   d. Eosinophils

5- The type of rejection characterized by fibrosis and atrophy of tubules is,
   a. Cellular acute
   b. Humoral acute
   c. Hyper acute
   d. Chronic

1. C
2. A
3. B
4. B
5. D