Renal Block

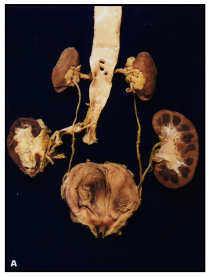
Lecture Seven

Renal Allograft

Objectives:

- Recognize the concept of renal allograft.
- Describe the pathology of rejection
- Differentiate between acute and chronic rejection.
- Recognize the principal infections inherent to renal transplantation.
- Recognize acute and chronic drug toxicity.

Introduction: Renal transplantation



Note the two end-stage native kidneys in normal position, the atrophic first donor kidney (lower left), and the larger second donor kidney (lower right).

- The major barrier to transplantation of organs from one individual to another of the same species (called allograft) is **immunological rejection** of the transplanted tissue.
- The word allograft refers to transplantation of organs within the same species while xenografts refer to transplantation between different species.
- **Rejection** is a complex phenomenon involving both cell and antibody mediated hypersensitivity reactions directed against the histocompatibility molecules of the foreign graft.
- The key to successful transplantation has been the development of therapies (drugs) that prevent or minimize rejection.

Mechanisms of graft (renal allograft) rejection:

→ Donor class I and class II major histocompatibility antigens on antigen-presenting cells in the graft (donor) are recognized by host (recipient) CD8+ and cytotoxic or suppressor T cells and CD4+ helper T cells respectively.

→ **CD4+ cells** proliferate and produce **cytokines** (like interferon gamma γ) which induce tissue damage to renal blood vessels and tubules by a local hypersensitivity reaction.

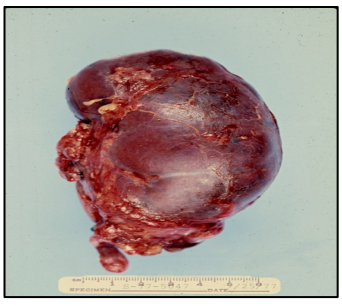
→ In addition, graft antigens are taken by the antigen presenting cells in the host (recipient).

→ These APC's activate CD4+ cells, which damage the graft (renal transplant) by a local delayed hypersensitivity reaction and stimulate B-lymphocytes to produce antibodies.

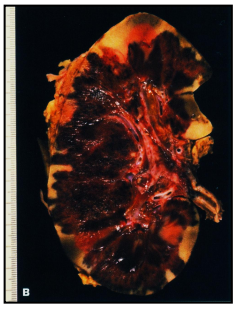
Renal allograft transplant rejections are divided into:

A. Normal

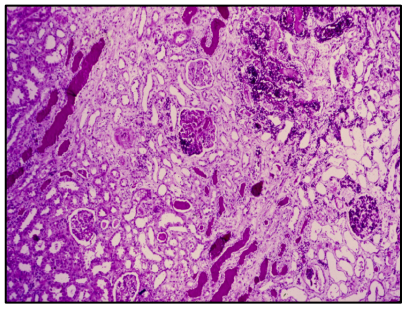
B. Hyperacute rejection: (antibody mediated endothelial damage)

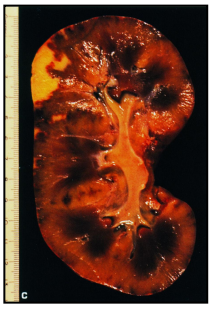


Occurs within minutes to a few hours after transplantation in a presensitized host and is typically recognized by the surgeon just after the vascular anastomosis is completed. Grossly, the kidney becomes cyanotic. Microscopically, there is widespread acute arteritis and arteriolitis, vessel thrombosis and ischemic necrosis.



Subtotal renal infarction due to **hyperacute (antibody-mediated) rejection.**

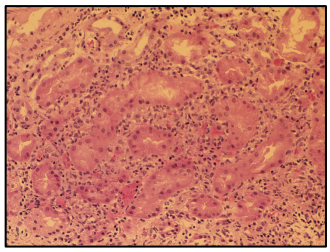




Severe acute rejection of donor kidney. Focal infarcts are present.

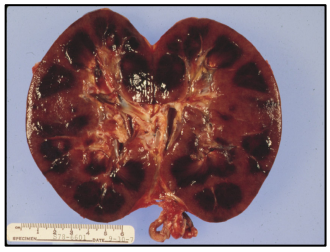
C. Borderline changes. (Very mild acute rejection)

D. Acute rejection: (T-cell mediated)

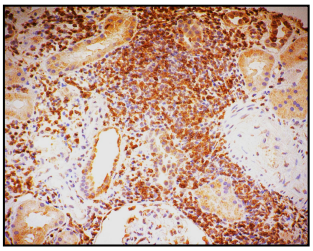


Acute rejection may occur within days to weeks of transplantation and sometimes after months or years later, this rejection is divided into:

1. Cellular rejection: interstitial edema and mononuclear (lymphocytic) infiltration of the renal interstitium.
2. Humoral rejection: associated with vasculitis.



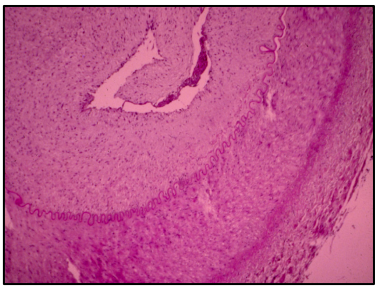
Acute Rejection with multiple infarcts.



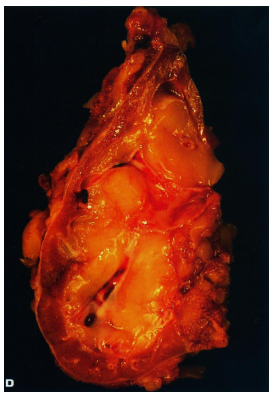
Acute rejection. The interstitial infiltrate consists of T cells mainly.

E. Chronic rejection:

Patients usually presents late after transplantation (months to years) with a progressive rise in serum creatinine levels. Chronic rejection is dominated by vascular changes, interstitial fibrosis and loss of renal parenchyma. Chronic rejection does not respond to standard immunosuppression treatment.



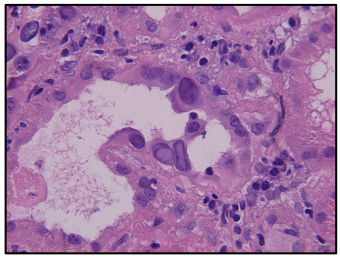
Severe rejection



Severe chronic rejection. (graft arteriopathy). Note the severe parenchymal atrophy and the thick-walled arteries.

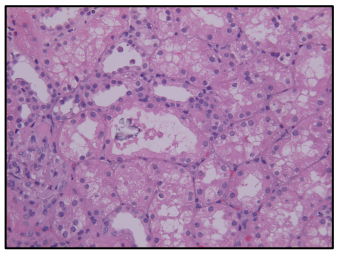
F. Others: changes not considered to be related to rejection.

Infections Recurrent or De Novo GN:

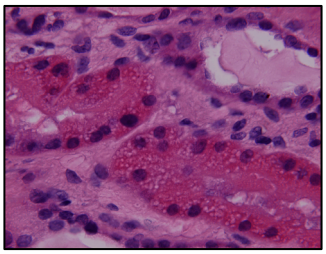


Intranuclear viral inclusion. Ground glass.

Drug Toxicity:

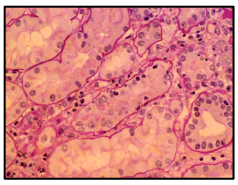
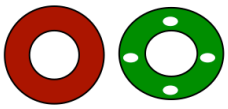
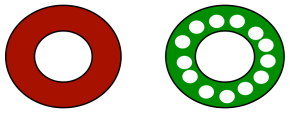
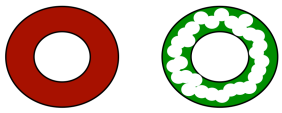
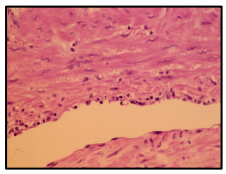
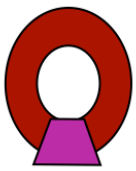


Acute Cyclosporine Toxicity: Isometric vacuolisation

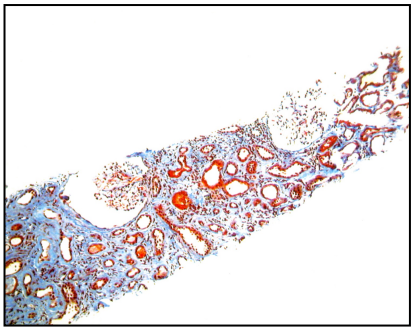


Acute Cyclo toxicity

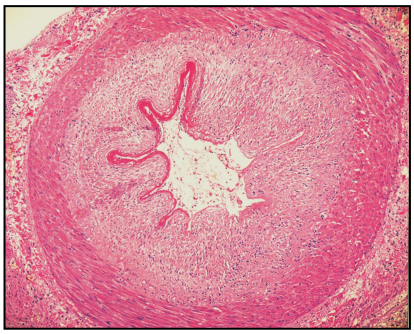
The Banff classification:

Class	Information	Morphology & Drawing
Borderline changes (Suspicious for Acute Rejection)	▪ No intimal arteritis ▪ Mild tubulitis (1-4/tubular cross section).	 
Grade IA Mononuclear interstitial	▪ Inflammation (>25%) ▪ + Moderate tubulitis (5 – 10)	
Grade I B: →	▪ Mononuclear interstitial ▪ Inflammation (>25%) ▪ +Severe tubulitis (>10)	
Grade II A	Mild to Moderate intimal arteritis	
Grade II B	▪ Severe intimal arteritis ▪ Mild arteritis (Microscopic Picture)	 
Grade III	Transmural arteritis and/or fibrinoid necrosis.	 

- Chronic Allograft Nephropathy:
  - Grade I (Mild)
  - Grade II (Moderate)
  - Grade III (Severe)
    - All is based on the tubular atrophy and interstitial fibrosis as well as on the transplant glomerulopathy (double contour).
    - Chronic allograft damage index.
    - Vascular :0 <25, >25,to 50, >50.
    - Mesangial matrix increase tubular atrophy, interstitial fibrosis.



Chronic/ sclerosing allograft nephropathy.
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.



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

Treatment based on Banff Classification:

- Normal, Suspicious → No Treatment
- Grade I → Treat **if** there are clinical signs
- Grade II → Treat
- Grade III → Treat or Abandon
- Cyclosporine toxicity → **Reduce** Cyclosporine
- Acute Tubular Necrosis → Await recovery or treat
- Chronic rejection → Temporize

Treat grade II with steroids and consider ALG/OKT3.

Conclusion:

The Banff classification has proposed a schema for interpretation and gradation of the histological findings in renal allograft biopsies that can be used as an indication for therapeutic consequences and expected graft survival.

Contact us: Pathology435@gmail.com

Team Members

Nouf Altwaijri

Aljohara Almazroua

Amjad Alduhaish

Budoor Julaidan

Deema Alfaris

Kayan Kaaki

Khawla Alammari

Lamees Altamimi

Nojood Alhaidri

Noura AlBulushi

Noura AlKharraz

Nouf Alabdulkarim

Reem AlAqeel

Khalid Aburas

Ahmad Taha Alkhiary

Ammar Saleh Almansour

Anas Baleegh Mohammad Ali

Faris Ibrahim Alwarhi

Hamzah Abdullah Alfiar

NaiF MoHaMMeD AlHaDi

Qusai Abdulbaqi Ajlan

Rayan Abdulrahman Almuneef

Zeyad Abdulaziz Alsalem

قال صلى الله عليه وسلم: (من سلك طريقًا يلتمس فيه علمًا سهّل الله له به طريقًا إلى الجنة).

دعواتنا لكم بالتوفيق.