RENAL BLOCK

LECTURE SIX – PATHOLOGY OF RENAL TRANSPLANTATION

BY

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INTRODUCTION:

Organ transplantation is increasingly being used to treat irreversible diseases of the kidney, liver, heart, lung and bone marrow. Unfortunately, the action of the immune system can lead to the transplanted tissue being destroyed, a process termed **transplant rejection**. For the best chance of survival, antigens in the graft and recipient must be alike.

After **blood group** identity, the most important set of antigens in transplantation immunology are the histocompatibility antigens, **human leukocyte associated antigens (HLA antigens).** The endothelial cells that line the blood vessels of the graft are particularly rich in both HLA antigens and blood group antigens, and so blood vessels are an important target of the host's immune response to a transplanted allograft.

There are three patterns of rejection seen in transplanted organs.

The patterns of rejection seen in post-transplant organs are:

- **Hyperacute –** due to preformed host antibodies.

- **Acute** – associated with necrosis of vessels in the graft (acute vascular rejection) and an infiltration of the graft tissues by CD4-positive T lymphocytes (acute cellular rejection).
- **Chronic** – slowly progressive destruction of graft structure and function, mainly as a result of vascular occlusion with an infiltrate of lymphocytes, plasma cells and eosinophils.

The most detailed work on transplantation pathology and the greatest experience, has been obtained by observation in kidney transplantation, but bone marrow, liver, heart and lung transplant are now very common.

RENAL TRANSPLANTATION:

Renal transplantation is increasingly being performed as a treatment for end-stage renal failure. After transplantation, several complications may occur, including **thrombosis** of the surgical vascular anastomosis leading to **ischemia in the graft, transplant rejection or recurrence of disease** in transplanted kidney, e.g. membranoproliferative glomerulonephritis.

Four patterns of renal transplant rejection are recognized.

The four patterns of rejection seen after renal transplantation are hyperacute rejection, acute rejection, accelerated acute rejection and chronic rejection.

(1) **Hyperacute rejection** occurs within a very short time of the organ being perfused by the host's blood. It takes that form of widespread intravascular thrombosis in small vessels, with focal necrosis and neutrophil infiltration. It is the result of performed host antibodies reacting instantly with antigens in the graft, and in the past was almost entirely due to host antibody against donor blood group substances, it was therefore nearly always the result of blood-group incompatibility. More recently, it is due to performed anti-HLA antibodies in recipient blood, formed by prior exposure to blood transfusions, or form previous grafts. Although, a common problem in the earlier days of renal transplants: Testing of recipients for the presence of antibodies to donor

lymphocytes now became a routine practice and for this reason, hyperacute rejection is now almost never seen.

(2) **Acute rejection** occurs within a week or so of the graft being inserted, but may also appear after cessation of immunosuppressive therapy. It is termed "acute" because it typically progresses rapidly, being mediated by both **humoral** and **cell-mediated** mechanisms.

A] The **cellular** component of acute rejection is mediated by T-cells reacting against donor HLA antigens, particularly class II. The graft becomes infiltrated by lymphocytes, most of which are T cells and the lymphocytes destroy various components of the graft, including tubules **(acute cellular rejection).**

B] The **humoral** component of acute rejection is characterized by vasculitis with endothelial necrosis, neutrophil infiltration of vessel walls and damage to the

intima and elastic lamina of the larger arteries in the graft **(acute vascular rejection).**

Parenchymal damage caused by the cellular acute rejection usually responds rapidly to immunosuppressive therapy, whereas damage caused by vascular pathology associated with the humoral component may be permanent. A typical case of acute rejection has a mixture of both components.

(3) **Accelerated acute rejection** can occur in a patient who has had a previous unsuccessful graft and is therefore already sensitized to donor antigens.

(4) **Chronic rejection** occurs slowly and progressively over some months. The result of slow breakdown of the host's tolerance to the graft, it may be due to inadequate immune suppression. Histologically, there is minimal fibrosis in arteries in the graft, leading to secondary ischemic damage to the parenchyma. The interstitium is infiltrated by plasma cells and lymphocytes.

Key facts and summary - Renal transplantation complications:

- Thrombosis of vascular graft.
- Recurrence of original renal disease.
- Hyperacute rejection (now rare) happens immediately after transplant. Caused by blood-group incompatibility or performed anti-HLA antibodies.
- Acute rejection happens 2-3 weeks after transplant or after stopping immunosuppression. Caused by humoral and cell-mediated mechanisms.
- Chronic rejection occurs over a period of months, causing permanent loss of nephrons.