Transplant rejection
Learning objective: At the end of lecture, the students should be able to:
1-Define transplant rejection.
2-Mention the mechanisms of transplant rejection.
3-Mention the mechanisms of T cell-mediated graft rejection(celullar rejection).
4-Explain the direct pathway of allorecognition by the recipient’s T cells.
5-Explain the indirect pathway of allorecognition by the recipient’s T lymphocytes.
6-Discuss the mechanisms of antibody-mediated reaction in graft rejection.
7-Classify the morphology of rejection reactions (renal transplant).
8-Describe the morphology of hyperacute rejection (renal transplant).
9-Describe the morphology of acute celullar rejection of a renal allograft.
10- Describe the morphology of acute humoral rejection (rejection vasculitis).
11-Describe the morphology of chronic rejection in a kidney allograft.
Transplant rejection
Transplant rejection
-Definition.
-Examples.
Mechanisms of transplant rejection(kidney grafts)
-Mechanisms:
1-Cell-mediated immunity.
2-Humoral-mediated immunity.
Mechanisms of T cell-mediated graft rejection(celullar rejection)
-Mechanisms:
1-T cell mediated cytotoxicity induced by CD8+ CTLs.
2-Delayed hypersensitivity reaction triggered by activated CD4+ helper cells.
Direct pathway
Recipient’s T cells(CD4+ T cells and CD8+ T cells.
-Allogenic(donor) MHC(ALA) molecules on the surface of an antigen presenting cell(APC)such as dentritic cell in the graft.
-Cytokines(IL-2) from CD4+ helper cells.
-Role of CD4+ helper cell in activation of APC and the differentiation of CTLs-----graft injury.
CD8 helper T cell differentiated into TH1.
Delayed hypersensitivity
-reaction:
*Increased vascular permeability.
*Accumulation of mononuclear cells(Lymphocytes and Macrophages)
*Graft injury.
Indirect pathway
-Recipient’s T lymphocytes.
-Antigens of the graft donor(MHC molecules).
-Recipient’s own antigen presenting cells(APC).
-Delayed hypersensitivity reaction(CD4+ T cell-----graft rejection.
-CD8+ CTLs----Kill graft cells.
Antibody-mediated reaction(humoral rejection)
-In recepients previously sensetized to transplantation antigens(performed antidonor antibodies are present in the circulation of the recipient.
*Hyperacute rejection.
-In recipients not previously sensitized to transplantation antigens(HLA antigens [class I and class II]-------antibodies-------injury by several mechanisims including:
1-Complement-dependent cytotoxicity, inflammation.
2-Antibody-dependent cell-mediated cytotoxicity.
*Acute humoral rejection(rejection vasculitis).
-Chronic rejection(present clinically with increased serum creatinine).
Concept and morphology of hyperacute rejection
-Concept.
-Morphology.
*Antibody + Antigen-----deposition on vascular endothelium of the grafted organ-------complement fixation-----thrombosis-----ischemic death of vessels in the graft.
Concept and morphology of hyperacute rejection
-Concept.

-Morphology.
*Antibody + Antigen-----deposition on vascular endothelium of the grafted organ-------complement fixation-----thrombosis-----ischemic death of vessels in the graft.
Concept and morphology of acute rejection
1-Acute celullar rejection.
-Concept.
-Morphology.
1-extensive interstitial mononuclear cell infiltration.
2-Presence of mononuclear cells in glomerular and peritubular capillaries.
3-endothelitis(by CD4+ cells)
4-The affected vessels have swollen endothelial cells and infiltration of lymphocytes.
5-edema.
6-mild interstitial hemorrhage.
2-Acute humoral rejection(rejection vasculitis).
-Concept.
-Morphology:
1-necrotizing vasculitis with endothelial cell necrosis.
2-neutrophilic infiltration.
3-deposition of immunoglobulin,complement, fibrin and thrombosis.
4-extensive necrosis.
5-thickining of the intima(proliferation of fibroblast, myocytes,and foamy macrophages).
6-narrawing of the arterioles---infarction----cortical atrophy.
*Chronic rejection:
-Concept.
-Morphology:
1-Vascular changes(intimal fibrosis).
2-interstitial fibrosis, and interstitial mononuclear cell infiltration(plasma cells and eosinophils).
3-Tubular atrophy and loss of renal parenchyma.
Questions:
Q1)Discuss the concept of Graft Versus Host(GVH) disease.
Q2) Identify the methods of increasing graft survival.
References:

1-MacSween R.N.;and Whaly K.(Murs Textbook of pathology); 13th edition,Arlond.1997.
2-Kumar V.;Abbas A.; and Fausto N.(Robbin and Cortan, Pathologic basis of disease).7th edition. Elsevier Sounder. 2004.
3-Rosal J. (Ackerman's surgical pathology); 9th edition.Mosby.2003.

4-Walts J.B.,Talbot L.c.(general pathology); 7th edition ,Churchill Livingstone; 1996 .

5-Krishna V.(Text book of pathology);Orient Longman Private limited. 2004 .