

Immune Complexes and Type III Hypersensitivity

Main Points

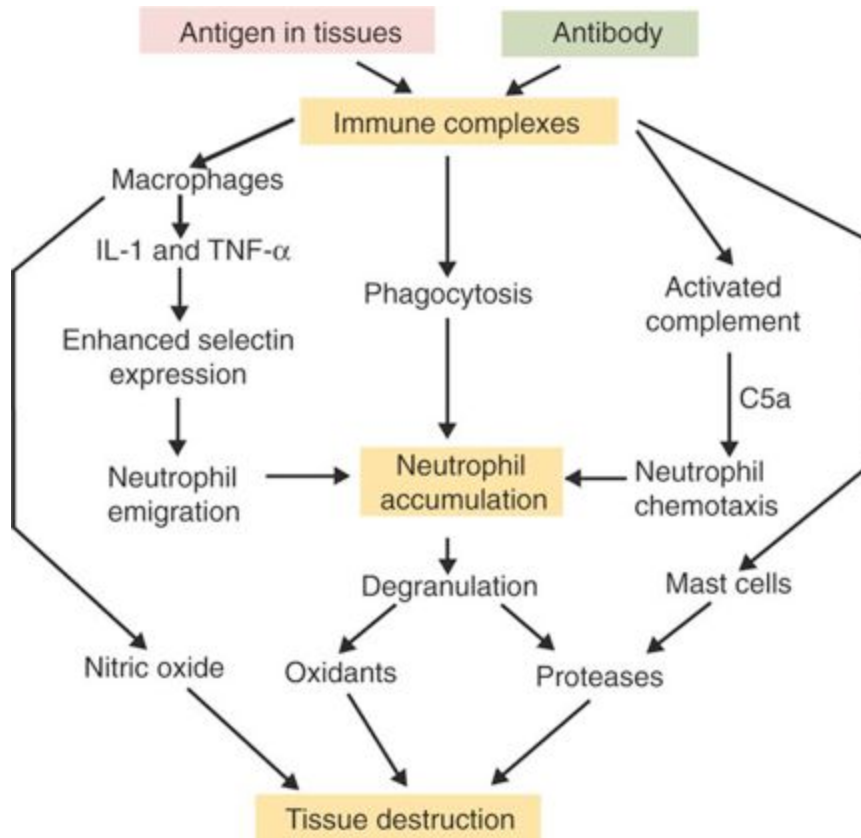
- Membranoproliferative glomerulonephritis can be caused by immune complex deposition in the kidney
- Type III hypersensitivity can be common with viral diseases
- Immune complexes activate complement, which leads to inflammation at the site of deposition and chemoattraction of neutrophils

Classification

- Local formation of immune complexes within tissue
- Systemic formation of immune complexes with blood and subsequent deposition
 - Deposition will occur in kidneys
 - Only pathological when there is an excessive amount produced

Local formation

- If antigen is injected subcutaneous into animal with precipitating antibodies in bloodstream, acute inflammation will develop at injection site within several hours.
 - First neutrophil infiltration, then monocyte
 - Complement (via the classical, antibody dependent pathway) and antibodies will bind their Fc receptors to macrophages stimulating production of nitric oxide, leukotrienes, prostaglandins, cytokines and chemokines
 - Will also bind to mast cells causing release of vasoactive molecules



- Further accumulation and degranulation of neutrophils
- Examples of local type III hypersensitivities
 - Blue Eye
 - Dogs infected or vaccinated with live canine adenovirus type 1 (we vaccinate with type 2)
 - Deposits of antigen antibody complexes in anterior uvea leading to corneal edema and 'blue eyes'
 - Resolves after virus is eliminated in 1-3 weeks
 - Hypersensitivity Pneumonitis
 - Cows and horses

Generalized Type III Hypersensitivity Reactions

- If antigen is intravenous in animals with high level of circulating antibodies, immune complexes form in blood stream
 - Typical removal is after binding to RBCs or platelets and removal by mononuclear phagocyte system of liver, spleen or lungs
 - Overproduction leads to accumulation in walls of blood vessels and vessels where there is physiological outflow
 - Glomeruli
 - Synovia

- Choroid plexus
- Glomerulonephritis
 - Immune complex deposition in the glomeruli causing proliferation of glomerular cells and thickening of basement membrane
 - “Membranoproliferative” glomerulonephritis
 - There are 3 subtypes, but likely out of our scope
 - Clinical features
 - Patients with proteinuria without evidence of infection should be suspicious for chronic inflammation from antigen stim by:
 - Infectious canine hepatitis
 - Leishmaniasis
 - Lyme
 - Ehrlichia
 - Dirofilaria immitis
 - Poymetra
 - Chronic pneumonia
 - Distemper
 - Acute pancreatic necrosis
 - Bacterial endocarditis
 - Feline leukemia
 - Lymphoma
 - Osteosarcoma
 - Lupus (SLE or Discoid)
 - Generalized demodicosis
 - Recurrent staph pyoderma
 - Presence of immune complex lesions within glomeruli stimulates neutrophils, mesangial cells, macrophages, and platelets to release thromboxanes, nitric oxide, platelet activating factor
 - Increases membrane permeability to macromolecules and thus causes proteinuria
 - Compensatory increase in secretion of antidiuretic hormone, increased sodium retention, and worsening edema
 - Decreased blood volume results in drop in renal blood flow, reduction in GFR, retention of urea, creatinine, azotemia, hypercholesterolemia

Questions

1. Draw out the pathway of an immune mediated glomerulonephritis, making sure to include stimulating event, formation of immune complexes, and inflammatory pathways