Pathology

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Inflammation

Fifth Lecture

Fate of Acute Inflammation (Outcomes)

1. Resolution.
2. Suppuration.
3. Organization and Scarring (Fibrosis).
4. Chronic Inflammation.

1-Resolution:

- ✓ Complete restoration of inflamed tissue to normal structure and function. Usually seen when there is No or minimal tissue damage and in tissue that is capable of regenerating.
- ✓ Lymphatic drainage of inflammatory exudate.
- ✓ Phagocytosis and clearance of cellular debris, necrotic tissue and microorganisms by macrophages.
- ✓ Regeneration of damaged cell.
- ✓ Restoration of normal structure and function.
- ✓ E.g. lobar pneumonia.

2-Suppuration :

☒ Pus formation, due to secondary infection by pyogenic bacteria. Pus may be:

☒ Diffuse in tissue.

☒ Localized in tissue (Abscess).

☒ On surface of a skin wound.

☒ In serous cavity (Empyema).

3-Organization and Scarring (Fibrosis) :

✓ Replacement of necrotic tissue by granulation tissue which mature into fibrous tissue (scar formation) by ingrowth of blood vessels (angiogenesis) and proliferation of fibroblasts.

✓ It is seen in:

- Chronic inflammation.
- Excessive tissue damage.
- Excessive fibrin deposition (Organization).
- Non-regenerating tissues.

4-Chronic inflammation :

✓ Acute inflammation may progress into chronic inflammation

✓ When there is:

- Persistent causative agent or infection.
- Presence of foreign body, etc.

Chemical Mediators

- ✓ Substances which play a role in inflammatory reactions.
- ✓ They are responsible for:
  1. Vasodilation.
  2. Increased vascular permeability.
  3. Emigration of WBC (Chemotactic agents).
  4. Humoral response (Signs and Symptoms).

Types of chemical mediators

1. Plasma-derived mediators (Plasma Proteins).

   They are synthesized by liver → circulate in plasma as inactive proteins → they are activated at site of inflammation.

2. Cell- derived mediators (produced or formed by cells).

Plasma Protein - Derived Mediators

- ❖ Activation of Four interrelated plasma systems (Kinin, Complement, Clotting and Fibrinolytic systems) → Inflammatory Chemical Mediators (plasma proteases) (circulating plasma proteins).
- ❖ All are activated by initial Activation of Clotting Factor XII (Hageman Factor) → protein is synthesized by liver and circulate in plasma as inactive protein.
- ❖ Activation of Hagmen factor is done by → contact of plasma in exudate with (-ve) negative charged surface such as Collagen, Basement Membranes, Bacterial Lipopolysaccharides, Foreign-body and Proteolytic enzymes.

Kinin system Activation : Results in

✓ Bradykinin (Potent factor) : It causes

1. Increased vascular permeability.
2. Vasodilation.
3. Bronchospasm.
4. Pain.

Complement system Activation :

✓ Complement system consists of 20 cascade proteins that play an important role in Immunity and Inflammation.

✓ Complement components numbered (C1 – C9) are present in plasma in Inactive proteins. Activation by Two pathways : classical and alternative pathways, results in:

✓ C5b – C9 = formation of Membrane Attack Complex.

- Cytolysis: lysis of microbe or bacteria.

✓ C3a and C5a = Anaphylatoxins (Anaphylaxis)

- Increase vascular permeability and vasodilation by inducing the mast cells to release Histamine.

✓ C5a = Potent Chemotaxin for leukocytes.

✓ C3b and iC3b = Opsonins help in phagocytosis.

Clotting and Fibrinolytic systems Activation :

☒ Fibrinolytic system activation → Plasmin

☒ Clotting system activation → Thrombin

↓

Soluble Fibrinogen → Insoluble Fibrin clot

Plasmin

↓

Insoluble Fibrin clot → Fibrinopeptides (Fibrin-split products)

Soluble Fibrinopeptides cause :

1. Increased vascular permeability.
2. Vasodilation.
3. Chemotaxis.

Cell – Derived Mediators

1. Vasoactive Amines : Histamine + Serotonin.

- Sources : Mast cells, basophils and platelets.
- Vasodilation and increased vascular permeability.
- Histamine ➔ Immediate Transient Vascular Response.

2. Prostaglandins and Leukotrienes :

☒ They are Arachidonic Acid Metabolites .

☒ Play a role in :

- Inflammation
- Hemostasis

☒ Sources : Mast cells, platelets and leukocytes.

☒ Prostaglandins → Vasodilation, Pain and Fever.

☒ Thromboxane A_2 → Vasoconstriction.

☒ Leukotrienes (C_4, D_4 & E_4) → Increased vascular permeability.

☒ Leukotriene B_4 → Chemotaxis and Leukocyte Adhesion.

☒ Anti – inflammatory effect of Aspirin and Non-Steroidal anti-inflammatory drugs, inhibit prostaglandin production and relieving the pain and fever.

3. Platelet – Activating Factor (PAF) :

❖ Sources : Leukocytes, mast cells, endothelial cells and platelets.

❖ Vasodilation, increased vascular permedility, leukocyte adhesion, chemotaxis and platelet activation.

4. Cytokines :

- ❖ Sources : Lymphocyte and Macrophage.
- ❖ Interleukins (IL-1 and IL-6).
- ❖ Tumor Necrosis Factor (TNF).
- ❖ Chemokines (IL-8) = Chemotaxis.
- ❖ Interferon- gamma (ɣ) = Chronic Inflammation.

Functions of IL-1 and TNF :

- ✓ Activation of endothelial cells.
- ✓ Activation of fibroblasts.
- ✓ Induce systemic acute-phase reactions (fever and leukocytosis).

5. Nitric oxide :

- ☒ Sources : Endothelial cells and macrophages.
- ☒ Soluble Free- Radical gas.
- ☒ Vasodilation.
- ☒ Tissue damage.
- ☒ Microbial killing.

6. Oxygen - Free Radicals :

- ✓ Sources : Neutrophils and Macrophages
- ✓ H_2O_2, Superoxide $\bar{O}_2$ and ·HO Hydroxyl group.
- ✓ Microbial killing.
- ✓ Tissue damage.
- ✓ Vascular permeability.
- ✓ Very Very destructive agents.

- ✓ Protective Anti – oxidant in serum and tissue to prevent toxicity of these oxygen metabolites (glutathione peroxidase, catalase and transferrin).

7. Lysosomal Enzymes of Leukocytes :

- ❖ Sources : Neutrophils and Macrophages.
- ❖ They release during phagocytosis and after cell death (elastase, collagenase and myeloperoxidase).
- ❖ Microbial killing and Tissue Damage.
- ❖ Harmful effects of lysosomal enzymes are controlled by Anti- proteases in serum and tissue (α_1- Antitrypsin) .
- ❖ α_1-antitrypsin deficiency→tissue damage in lung (Emphysema).

Summary of Chemical Mediators

❖ Vasodilation :

Histamine, Prostaglandins, Nitric Oxide, PAF and Bradykinin.

❖ Increased vascular permeability :

Histamine, Serotonin, C3a and C5a, Bradykinin, Leukotrienes- C_4, D_4, E_4, and Platelet Activating Factor (PAF).

❖ Leukocyte activation and chemotaxis :

TNF, IL-1, C3a, C5a, Leukotriene-B_4, Chemokines (IL-8) and Bacterial Products.

❖ Fever : IL-1, TNF and Prostaglandins.

❖ Pain : Prostaglandins and Bradykinin.

❖ Tissue damage and Microbial Killing :

Lysosomal Enzymes, Nitric Oxide and Oxygen-Free Radicals.

Lymphatic and lymph node in Acute Inflammation

- Drainage of lymph and inflammatory exudate including cells and microorganisms to the regional lymph nodes.
- May get inflammation of lymph nodes → Lymphadenitis.
- Inflammation of lymphatic vessels → Lymphangitis.
- The inflamed lymph nodes are enlarged due to hyperplasia (Reactive Hyperplasia) or Lymphadenitis.