Chronic inflammation and wound repair

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Relationship between acute and chronic inflammation

Overview of Lecture
• Causes of chronic
• Key features of chronic
• Role of macrophages in chronic inflammation
• Fibrosis in chronic inflammation
• Granulomatous inflammation
• Wound healing
What causes chronic inflammation?

• Persistent infections
  – Intra-cellular pathogens
  – Extra-cellular pathogens
• Prolonged exposure to non-infectious pro-inflammatory materials
  – External material – inhaled particulates
  – Internal material – necrotic [dead] tissue
• Immune-mediated inflammatory disease *

* This will be covered in a later lecture

Key features of chronic inflammation. I.

• Swelling, pain
  – Redness and heat is typically less prominent as compared to acute inflammation
• Neutrophils are less common cf. acute inflammation
• Cell infiltrates comprise significant numbers of lymphocytes, plasma cells and macrophages
• Fibrosis – affected tissue often firm (indurated)
• Angiogenesis = growth of new capillaries
• Tissue destruction and deformation

Key features of chronic inflammation. II.

Chronic keratitis  Chronic ileitis  Chronic [rheumatoid] arthritis

Chronic dermatitis  Sheep chronic lymphadenitis  Chronic hepatitis C infection
Key features of chronic inflammation. III.

Mycardial infarct = [tissue death due to loss of blood supply]

- Acute = neutrophils
- Chronic = macrophages

Key features of chronic inflammation. IV.

- Chronic pneumonia
  - Macrophages and lymphocytes
  - Loss of normal tissue structure
  - Fibrosis

- Acute pneumonia
  - Congestion
  - Neutrophils fill alveoli

The roles of macrophages in chronic inflammation. I.

- Macrophages are bone marrow derived cells – like neutrophils and megakaryocytes

- Macrophages, unlike neutrophils, can divide locally in tissues
**The roles of macrophages in chronic inflammation. II.**

Macrophages

- Promote killing of microorganisms by mechanisms similar to neutrophils
- Regulate inflammatory response by releasing pro-inflammatory proteins (cytokines) and lipids (prostaglandins)
- Produce growth factors that promote tissue fibrosis
- Produce growth factors that promote angiogenesis

**Fibrosis and chronic inflammation. I.**

- Inflammation/necrosis destroys and weakens tissue. May result in rupture [e.g. intestine, heart, bladder]. Scarring strengths weakened tissue, but also impairs its function
- May help to isolate persistent infection e.g chronic abscess

**Fibrosis and chronic inflammation. II.**

Fibrosis – the deposition of collagen in the extracellular matrix by fibroblasts

Abnormal fibrosis may result in:

- Loss of tissue elasticity e.g. lungs, heart.
- Shrinkage (constriction) of tissue resulting in compression of key structures e.g. nerve and blood vessels.
- Walling off of an abscess entrapping bacteria
- Replacement of normal tissue limiting its regeneration
- Tissue weaker than originally e.g. tendon injuries
Granulomatous Inflammation.

I. Definition: Inflammation in which macrophages are the dominant cell type
- A specific type of chronic inflammation
- Associated with a small number of infectious agents
- Not usually preceded by acute inflammation
- Rarely may have non-infectious cause
- Macrophages are activated
  - Large amount of cytoplasm
  - May fuse to form multinuclear giant macrophages

II. Focal granulomatous inflammation [granuloma] without necrosis
- Caseating granuloma

III. Granulomatous inflammation with multinuclear cells
- Caseating granuloma = granulomatous inflammation with central necrosis; a feature of tuberculosis.
Infectious causes of granulomatous inflammation

- Mycobacterial infections
  - M. tuberculosis, M. bovis, M. avium
- Brucellosis, e.g. Brucella abortus
- Systemic fungal infections, e.g. Blastomycosis

Wound Healing

Considerations with wounds

- Has there been significant blood loss?
  - Hypovolemic shock – insufficient blood volume
- Where is the wound located? Vital structures?
  - Nerves, arteries, airways?
- Is the wound infected?
  - Infection interferes with the healing process
- Is there a foreign body?
- Is the wound gaping?
- Tissue damage is present in all wounds
  - Inflammation will always develop even if no infection

Skin as an example of wound healing

Types of trauma

Incisional injuries - caused by sharp objects

Excisional injuries - caused by blunt objects, often tissue is lost (defect)

Blunt trauma
Phases of the wound healing process

Healing of wounds by primary and secondary intention

Granulation tissue I

- Immature fibrovascular tissue – often forms within a gaping wound – fills gap
- Requires signals mainly from macrophages to stimulate
  - Proliferation of fibroblasts
  - Proliferation of endothelial cells
- As healing progress, granulation tissue matures into dense collagenous scar.
Granulation tissue II

Mechanisms of angiogenesis

Granulation tissue

Dense scar

Local factors that delay wound healing

- Infection results in persistent tissue injury and inflammation
- Mechanical factors – motion, compression
- Foreign bodies - steel, glass, bone
- Size, location, and type of wound.

Systemic factors that delay wound healing

- Nutrition – poor nutrition slows healing process
- Age – wound healing is slower with older age
- Drugs – some drugs inhibit fibrosis
- Concurrent disease
  - Diabetes slows healing process
  - Poor circulation is associated with slower healing
Regeneration as part of the tissue healing process

- Regeneration: replacement of damaged tissue by proliferation and differentiation of tissue stem cells
- High regenerative capacity is found in liver and lymphoid organs.
- Liver trauma may result in healing by a combination of regeneration and fibrosis (repair)
- Low regenerative capacity is found in central nervous system, skeletal muscle and heart muscle. Damage of these tissues / organs results in primarily a scarring-type of response

Regeneration of the human liver in living donor-transplantation

Example Questions

- What cell types are common in chronic inflammation?
- Protein factors produced by macrophages promote what processes? (name two)
- Name one pathogen or disease that is often associated with granulomatous inflammation?
- Why is there inflammation during the healing process – even when infection is absent?
- Name two features of granulation tissue
- Under what circumstances is granulation tissue most likely to form?