Chronic Inflammation

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Chronic Inflammation….. continue2

Eosinophils

Eosinophils are related to neutrophils; both display a segmented nucleus; both are polymorphonuclear leukocytes. Eosinophils comprise about 3% of the circulating wbcs and are recognized by the bright red granules within their cytoplasm. These granules are filled with a substance called "major basic protein" that can destroy some parasites and some cells. These cells are not seen in all chronic inflammatory reactions. Rather, they appear in parasitic infestations, hypersensitivity reactions, and some autoimmune conditions.

Multinucleated Giant Cells

Huge cells with many nuclei may appear in chronic inflammatory reactions. These cells are formed from the fusion of several macrophages and are called "multinucleated giant cells." They are often seen associated with foreign particulate matter (splinters, talc, debris). They may also accompany reactions to certain microorganisms of low virulence (e.g. tuberculosis).

Fibroblasts and Collagen

Fibroblasts and the collagen they produce are prominent features of chronic inflammation. In fact, overexuberant collagen formation may permanently deform inflamed tissues; this circumstance in known as "fibrosis." Fibroblasts are recruited to enter an area of tissue injury by lymphokines and monokines. Once in the area, they produce collagen to replace that which has been destroyed. In the inflammatory reaction does not resolve in a reasonable time, the collagen can build up to scar tissue proportions (fibrosis).

The Microscopic Features of Chronic Inflammation

The presence of lymphocytes (and often, macrophages) and collagen are the two constant microscopic features of chronic inflammation. While plasma cells, eosinophils, and giant cells may appear in certain situations, lymphocytes are always present and if the reaction lasts more than a week or two collagen is always present as well. Dilated blood vessels so characteristic of acute inflammation are usually absent in chronic inflammation.

The Clinical Features of Chronic Inflammation

The redness, warmth, swelling, pain, loss of function, and fever associated with acute inflammation are absent or greatly suppressed in chronic inflammation.

Examples of chronic inflammatory diseases:

- Tuberculosis.
- Chronic cholecystitis.
- Bronchiectasis.
- Rheumatoid arthritis.
- Hashimoto's thyroiditis.
- Inflammatory bowel disease (ulcerative colitis and Crohn's disease).
- Silicosis and other pneumoconioses.
- Implanted foreign body in a wound.

Other examples of chronic inflammatory diseases:

- Allergy — Inflammatory cytokines induce autoimmune reactions
- Alzheimer's — Chronic inflammation destroys brain cells
- Anemia — Inflammatory cytokines attack erythropoietin production
- Aortic valve stenosis — Chronic inflammation damages heart valves
- Arthritis — Inflammatory cytokines destroy joint cartilage and synovial fluid
- Cancer — Chronic inflammation causes many cancers
- Congestive heart failure — Chronic inflammation contributes to heart muscle wasting
- Fibromyalgia — Inflammatory cytokines are elevated
- Fibrosis — Inflammatory cytokines attack traumatized tissue
- Heart attack — Chronic inflammation contributes to coronary atherosclerosis
- Kidney failure — Inflammatory cytokines restrict circulation and damage nephrons
- Lupus — Inflammatory cytokines induce an autoimmune attack
- Pancreatitis — Inflammatory cytokines induce pancreatic cell injury
- Psoriasis — Inflammatory cytokines induce dermatitis
- Stroke — Chronic inflammation promoted thromboembolic events
- Surgical complications — Inflammatory cytokines prevent healing

Outcome of chronic inflammation

- Resolution/regeneration/restitution of normal structure.
- Repair/organization/healing by connective tissue/ fibrosis/ scarring.
- It can continue indefinitely--some disease processes are capable of continuing indefinitely such as rheumatoid arthritis..

Complications of Chronic Inflammation.

Unlike acute inflammation where the reaction itself may be life-threatening (e.g. cellulitis), the adverse effects of chronic inflammation are not so dramatic. Two complications are rather common: fibrosis and persistence.

Scarring in Chronic Inflammation

Much tissue can be destroyed during a long-standing chronic inflammatory reaction. This missing tissue is usually replaced by continual production of collagen by fibroblasts. If the inflammatory reaction persists for a long time, collagen build up can be significant. If this occurs, scars may form causing permanent distortion of the tissue and interfere with its function. Also, the presence of scar tissue may hinder regeneration of parenchymal cells.

Persistence of Chronic Inflammation

Substances with low antigenic properties may not be eliminated quickly. If these persist, the chronic inflammatory reaction may be continually stimulated for years. Similarly, reactions to one's own cells (autoimmunity) may also produce long-standing chronic inflammation due to continual cellular destruction and, therefore, the unending supply of antigen.

Granulomatous Chronic Inflammation

Under certain circumstances a chronic inflammatory reaction will acquire features so special that they will narrow a diagnosis to a group of conditions called "granulomatous diseases." These conditions include tuberculosis, syphilis, leprosy, and most fungal (mycotic) infections. The microorganisms that produce these granulomatous diseases are low-virulence ones that produce persistent chronic inflammatory reactions. The lesion of granulomatous chronic inflammation is the "granuloma." It is a little mass of tissue composed of chronic inflammation with a background of reparative tissue consisting of new capillaries, new fibroblasts, and new collagen. This reparative tissue is called "granulation tissue." It is the

presence of granulation tissue that gives the granuloma its name. When macrophages become activated they acquire special morphologic features. These cells acquire large, round nuclei that remind pathologists of epithelial cell nuclei. It is this feature that gives rise to their designation as “epithelioid cells.” Epithelioid cells are diagnostic of granulomatous chronic inflammation.

Chronic Granulomatous Inflammation

Definition: a type or pattern of chronic inflammation defined by the presence of **granulomas** which are small, 0.5 to 2 mm collections of modified "epithelioid" histiocytes/macrophages and (***Langhan's***) giant cells (***fused histiocytes***), with a background of new capillaries, fibroblasts, and new collagen, usually surrounded by a rim of lymphocytes.

Granulomas occur in response to various diseases:

- Foreign body
- Tuberculosis (Tb)
- Fungal (mycotic) infections
- Sarcoidosis
- Schitosomiasis
- Leprosy

Two factors necessary for granuloma formation

- Presence of ***indigestible*** organisms or particles (Tb, mineral oil, etc)
- Cell mediated immunity (T cells)

Subacute Inflammation

Pathologists do not speak of subacute inflammation often because it is so ill-defined that its microscopic appearance cannot be described. However, clinicians sometimes use the term to refer to a clinical situation in which the signs and symptoms displayed by the patient are neither “acute” nor “chronic”—they seem to be somewhere in between. In these cases, the reaction is neither “clinically acute” nor “clinically chronic.”

Resolution

Definition: Resolution is the return of tissue to its normal state.

Factors necessary for resolution

- Removal of the offending agent
- Regenerative ability if cells have been destroyed
- Intact stromal framework

Categorization of cells based on regenerative ability

- Labile cells: cells which continue to proliferate throughout life (gut, skin, bone marrow)
- Stable cells: cells which retain the capacity to proliferate throughout life but usually do not unless stimulated (liver, kidney, pancreas, bone)
- Permanent cells: cells which cannot reproduce themselves after birth (neurons, and cardiac)

Stromal framework: It is not enough to be able to regenerate. There must be an adequate stromal framework.