Pathology

3rd Stage
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Lecture 3

Morphologic Patterns of Tissue Necrosis

Coagulative, liquefactive, caseous, fatty, gangrenous and fibrinoid necrosis

*** Coagulative necrosis:** is a form of necrosis in which the underlying tissue architecture is preserved for at least several days after injury (presumably the injury denatures not only structural proteins but also enzymes, thereby blocking the proteolysis of dead cells), e.g. myocardial infarction. Coagulative necrosis is mainly caused by sudden cessation of blood flow and is characteristic of infarcts (areas of ischemic necrosis) in all solid organs except the brain. **Gross examination:** In early stages, the affected tissue is pale, firm. and slightly swollen, later becomes more yellowish, softer and shrunken. **Microscopical examination:** Tissue architecture is preserved but with loss of nucleus and intra cellular details with the presence of deep eosinophilic cytoplasm. Leukocytes reach site of necrosis and remove cellular debris by phagocytosis.

***Liquefactive necrosis:** type of necrosis seen in focal bacterial and, occasionally, fungal infections (because microbes stimulate rapid accumulation of inflammatory cells, and the enzymes of leukocytes digest (liquefy) the tissue). It is also type of necrosis seen in hypoxic death of cells within the central nervous system.

Dead cells are completely digested, transforming the tissue into a viscous liquid mass. If the process is initiated by acute inflammation, as in bacterial infection, the material is frequently creamy yellow called pus . Tissue details and architecture are lost.

***Gangrenous necrosis:** is not a distinctive pattern of cell death. Gangrene is death of tissue caused by prolonged interruption of the blood supply.

Types of gangrene: Dry and wet (gas gangrene is a variant of wet gangrene)

Dry gangrene is due to lack of blood supply (progressive ischemia due to mainly arterial occlusion), often occurs in the extremities (e.g. atherosclerosis and diabetic vascular disease affecting lower limb). Grossly, the diseased part may at first be

discolored dry and cold, later it becomes black and dry (line of separation from viable tissue) . Microscopically shows features of coagulative necrosis.

Wet (moist) gangrene occurs when there is superimposed bacterial infection in addition to interruption of blood supply (vessel occlusion is predominantly venous) e.g. diabetic patients, generally it has poorer prognosis than dry gangrene due to septicemia . Grossly: the effected part is swollen , foul smell blisters form and may rupture and pus may appear, no sharp line of demarcation from normal tissue. Microscopically, the coagulative necrosis is modified by the liquefactive action of bacteria and the attracted leukocytes.

Gas gangrene: caused by infection with clostridium perfringens and other species, that produce exotoxins and cause presence of gas in subcutaneous tissue

***Caseous necrosis: is most often seen in tuberculous infection. Grossly, the lesion is soft, friable yellow-white in appearance (caseous means cheese-like)**

Microscopic examination: the necrotic area has an amorphous granular eosinophilic appearance, with obliteration of the tissue architecture and cellular outlines. Caseous necrosis is often surrounded by macrophages and other inflammatory cells that is characteristic of a nodular inflammatory lesion called granuloma.

***Fat necrosis: refers to focal areas of fat destruction, is of 2 types: traumatic (e.g. trauma to female breast) and enzymatic fat necrosis**

Enzymatic fat necrosis results from the release of activated pancreatic lipases into the substance of the pancreas and the peritoneal cavity, mainly in acute pancreatitis (pancreatic enzymes leak out of acinar cells and ducts, lipases will cause the release of fatty acids that will combine with calcium (fat saponification)).

Gross examination: visible chalky white areas (fat saponification)

Microscopical examination: Shadowy outlines of necrotic fat cells with basophilic calcium deposits, surrounded by an inflammatory reaction.

***Fibrinoid necrosis: special form of necrosis, usually occurs in immune reactions in which antigens and antibodies complexes are deposited in blood vessels walls, but also may occur in severe hypertension. Deposited immune complexes and plasma**

proteins that leaked out of damaged vessels, produce a bright pink, amorphous appearance ,on hematoxylin and eosin preparations, called fibrinoid (fibrin-like).

Mechanisms of cell injury and cell death

-The cellular response to injurious stimuli depends on the type of injury, its duration and severity. The consequences of injury depend on the type of cell and its metabolic state, adaptability and genetic makeup.

.Cellular function may be lost long before cell death occurs, and the morphologic changes of cell injury (or death) lag far behind loss of function and viability

The principal targets and biochemical mechanisms of cell injury are:

***. Mitochondria and the ability to generate ATP and reactive oxygen species (ROS)**

***. Disturbances in calcium homeostasis**

***. Damage to cellular (plasma and lysosomal) membranes**

***. Damage to DNA and misfolding of protein**

1. Mitochondria Damage: will result in:

1.ATP depletion which causes:

***Reduction in the activity of the plasma membrane energy-dependent pump resulting in water accumulation, cell swelling and ER dilation.**

***Increase anerobic glycolysis, depletion of glycogen stores, lactic acid accumulation, decrease intracellular pH resulting in decreased activity of many cellular enzymes.**

***Influx of calcium with its damaging effects *Prolonged or worsening depletion of ATP, causes disruption of the protein synthetic apparatus (detachment of ribosomes with reduction in protein synthesis). There may also be increased protein misfolding.**

•Finaly, irreversible damage occurs to mitochondrial and lysosomal membranes

2. Abnormal oxidative phosphorylation also leads to the formation of ROS.

Reactive oxygen species are oxygen derived free radicals with harmful effects (damage to DNA, proteins and lipids).

3. Leakage of mitochondrial proteins into the cytoplasm, thus initiating apoptosis.

THANK YOU