Pathology

3rd Stage
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Lecture 2

Cellular adaptation, cell injury and cell death

Reversible and irreversible cell injury

Cell injury results when cells are exposed to stress that exceeds the adaptative capability of the cell or the stimulus is inherently damaging. Cell injury could be reversible or irreversible cell injury (cell death)

***Reversible injury:** **is the stage of cell injury at which the deranged function and morphology of the injured cells can return to normal if the damaging stimulus is removed (injury has not progressed to severe membrane damage and nuclear dissolution).**

Morphology: The 2 most consistent forms of reversible cell injury are cellular swelling and fatty change

1. Cellular swelling (hydropic change or vacuolar degeneration): is commonly seen in cell injury (cells {and intracellular organelles} become swollen because of sodium and water influx due to failure of energy-dependent ion pumps in the plasma membrane i.e. inability to maintain ionic and fluid homeostasis).

Gross (macroscopical examination): When it affects many cells, it causes pallor (due to compression of capillaries) and increase in organ weight.

Microscopic examination: Small, clear vacuoles within the cytoplasm; these represent distended and pinched-off segments of the endoplasmic reticulum.

2. Fatty change: It is manifested by the appearance of cytoplasmic lipid vacuoles. It is principally seen in organs that are involved in lipid metabolism.

Other ultrastructural changes of reversible cell injury (seen by electron microscopy):

(1)Plasma membrane changes like blebbing

(2) Mitochondrial swelling with phospholipid-rich amorphous densities

(3) Dilation of the ER with detachment of ribosomes

(4) Nuclear changes (clumping of chromatin)

(5) Myelin figures (collections of phospholipids resembling myelin sheaths, that are derived from damaged cellular membranes).

***Irreversible cell injury (cell death):** **With persistent or excessive harmful exposures, irreversible cell injury and cell death develop.**

Irreversible cell injury is consistently characterized by three phenomena:

***the inability to restore mitochondrial function** **(oxidative phosphorylation and ATP generation) even after resolution of the original injury; *the loss of structure and functions of the plasma membrane and intracellular membranes; and *loss of DNA and chromatin structural integrity.**

Necrosis and apoptosis are the two main forms of cell death that differ in causes, mechanisms, morphology and functional consequences.

•Necrosis refers to the morphological changes that accompany cell death in living tissue due to loss of membrane integrity and leakage of cellular enzymes that ultimately digest the cell (effects group of cells). Necrosis stimulates local host response called inflammation, due to leakage of cell contents through damaged plasma membrane. The inflammatory response serves to eliminate the debris and start the subsequent repair process.

The enzymes responsible for digestion of the cell are derived from lysosomes of the dying cells themselves or from leukocytes recruited as part of the inflammatory reaction.

Morphology: Necrosis is characterized by changes in the cytoplasm and nuclei of the injured cells.

***Cytoplasmic changes: By light microscope, necrotic cells show**

1. Increased eosinophilia (due *to increased binding of eosin to denatured cytoplasmic proteins and *to loss of basophilic ribonucleic acid (RNA) in the cytoplasm).

2. The cell may have a glassy, homogeneous appearance, mostly due to the loss of glycogen particles.

3. Vacuolated cytoplasm (moth-eaten)

By electron microscopy, necrotic cells are characterized by discontinuities in plasma and organelle membranes, marked dilation of mitochondria with large amorphous densities, disruption of lysosomes, and intracytoplasmic myelin figures (that are more prominent in necrotic cells than in reversibly injured cells).

***Nuclear changes: Nuclear changes assume one of three patterns, all resulting from a breakdown of DNA and chromatin (pyknosis, karyorrhexis and karyolysis).**

Pyknosis: is characterized by nuclear shrinkage and increased basophilia; the DNA condenses into a dark shrunken mass.

Karyorrhexis: When the pyknotic nucleus undergoes fragmentation

Karyolysis: Nucleus undergoes dissolution (basophilia fades due to DNase activity)

In 1 to 2 days, the nucleus in a dead cell may completely disappear.

Fates of necrotic cells: Necrotic cells may persist for some time or may be digested and disappear. Dead cells may be replaced by myelin figures, which are either phagocytosed or degraded into fatty acids that bind to calcium salts resulting in calcified dead cells.

THANK YOU