

APOPTOSIS AND CELLULAR AGEING

Apoptosis :- programmed cell death.

Enzymatic degradation of cell's own DNA, nuclear and cytoplasmic proteins

- No Inflammation.
- It is both physiological & pathological.

Causes

- Physiological :- during embryogenesis.
- Turnover of proliferative tissue. (intestinal epithelium, lymphocytes in bone marrow, thymus).
- Involution of hormones dependant tissues (eg. endometrium)
- Decline in leukocyte numbers at the end of immune response.
- Elimination of potentially harmful self-reactive lymphocytes.
- Pathological :-
 - DNA damage
 - Accumulation of misfolded proteins
 - Infections, especially certain viral infections.

Mechanism

Biochemical pathway

Enzyme involved - (caspases)
Initiators and executioners

Mechanisms of Biochemical pathway.
→ The mitochondrial pathway (intrinsic)
→ The death receptor pathway (extrinsic).

Mitochondrial Pathway

→ Anti-apoptotic / BCL2 family proteins.

BCL2 / BCL-XL.

→ sensors - BH3 only proteins.

→ pro-apoptotic BAX & BAK.

Viable cell

survival signal.

↓
Production of anti-apoptotic proteins.

↓
No leakage of cytochrome c.

Apoptosis

lack of survival signal / Irradiation

Activation of sensors.

↓
Antagonism of BCL2.

↓
Activation of BAX / BAK.

↓
leakage of cytochrome c.

(1) ↓ APOPTOSIS.

Death receptor pathway

Case 8.

Binding of ligand of death receptor.

Refer flow chart.

Cleavage of apoptotic cells.

Phosphatidyl serine

→ related with cleavage of apoptotic cell when exposed to the
→ interact with phagocytes.

Morphology

→ No inflammation

Normal cell → condensation of chromatin → membrane blebs, cellular fragmentation
→ apoptotic body → phagocyte.

Necroptosis (MCQ)

→ features similar to necrosis.
* swelling of cells & organelles.
(release of lysosomal enzymes, rupture of plasma membrane, loss of ATP).

* Loss of ATP.

* Generation of ROS.

→ features similar to apoptosis.
* Genetically programmed process.

Pyroptosis (MCQ)

→ Inflammation + Apoptosis

Necroptosis
→ cellular level of ROS.

Autophagy

→ self eating
→ lysosomal degradation of cells own components.

Autophagolysosome. formation of autophagosome. Autophagy signal.

Cytoplasmic organelles

↓
Formation of autophagic vacuole with lysosomes.
↓
Enzymatic digestion of contents used as source of nutrients.

Cellular Aging

All normal cells have a limited capacity for replication and after a fixed no. div. cells become senescent.

MCQ. TTAGGG repeats increasing in telomere

Telomere reactivation → cancerous cells.

Telomeropathies

→ aplastic anemia.
→ pulmonary & liver fibrosis.
→ skin & nail abnormalities.
→ Premature greying of hair.

X "Smearing pattern" MCQ

(2). DNA ladder → age of leukocytes

Mechanisms of Cell Death

Mechanism of cell death caused by different agents may vary. However, certain biochemical events are seen in the process of cell necrosis.

- ATP depletion
- Mitochondrial damage
- cytoskeletal damage
- Damage to DNA
- loss of homeostasis and free cytosolic calcium.
- Free radicals, superoxide anion, hydroxyl radicals, hydrogen peroxide.
- defective membrane permeability
- Defective plasma membrane

Necrosis (6 mark)

- Irreversible form of cell death characterized by denaturation of intracellular proteins and enzymatic digestion of lethally injured cell.

leaked out contents

(hint: - karyolysis, pyknotic, Autolysis or On seen)

Pattern of necrosis in tissues or organs

- ① Coagulative necrosis
MCA - tooth like appearance → solid organ
- typically seen in

hypoxic environment
eg: myocardial infarction.

② Liquefactive necrosis

- the dead cells undergo disintegration of affected tissue as liquefied
eg: cerebral infarction.
- usually associated with cellular destruction and pus formation
eg: pneumonia.

Types of Necrosis

* Caseous necrosis

- surrounded by granuloma
- specific form of coagulation necrosis caused by mycobacteria (tuberculosis).
- combined features of coagulative and liquefactive necrosis (cheese like)
eg: Tuberculosis lesions.

* Fat Necrosis

- Enzymatic digestion of fat
eg: Necrosis of fat by pancreatic enzymes.

* Focal Gangrenous Necrosis

- Necrosis (secondary to ischemia).
- usually with superadded putrefaction.
eg: necrosis of distal limbs, usually foot and toes, no shallos.

Granuloma (Important)

→ heals chronic inflammation.

Other types.

- Gummatous necrosis - Es
resembled to necrosis involving
spirochetal infection (syphilis).
- Hemorrhagic necrosis
eg. hemorrhagic liver.
- Fibrinoid necrosis: caused
by immune related vascular
damage.

Morphology

necrosis to

- ↑ eosinophilia.
- glassy homogeneous
appearance.
- Myelin figure
- Vacuolated, with
eaten cytoplasm
- Pyknotic, karyolytic
karyorrhectic.

Apoptosis

- cell shrinkage
- chromatin
condensation
- nuclear
fragmentation
- cytoplasmic bleb
- apoptotic bodies.

Major features of Necrosis and Apoptosis. (4 mark)

Necrosis.

- cell enlarged
- Nuclear features:
pyknosis,
karyorrhexis,
karyolysis.
- Disrupted cell
membrane.
- leakage of cellular
contents
- frequent adjacent
inflammation.

Apoptosis.

- cell shrinkage.
- intact all
membrane.
- Nuclear fragment
into nucleosome
- No inflammation
- cellular
contents
intact.