ZAPOROZHZHIAN STATE MEDICAL UNIVERSITY

The department of pathological anatomy and forensic medicine with basis of law

Critical Alteration Morphology of Cell Death Necrosis of Tissue and Organ

Lecture on pathological anatomy for

Critical Damage and Cell Death

Critical damage it is molecular-sub-cellular violation of metabolism and fading of function of specialized cells.

Cell death it is destruction of specialized cells in the living organism under action of critical damage factors.

Critical Damage and Cell Death

Objects of critical damage are structures of the cells:

1. mitochondria
2. genetical apparatus (nuclear DNA)
3. plasmatic membrane
4. biosynthetic system
5. cytoskeleton
6. lysosomes and peroxisomes

Changes in cells can't be determined by light microscope, it is recognized by molecular-cytochemical and autography methods.

Reasons of development:

I. Endogenous metabolic catastrophe:

1. bioenergetics insufficiency of cells (hypoxia of different genesis)
2. damage of the cells by the surplus of free oxygen (O^-) and oxide nitrogen (NO)
3. damage of the cells by the free radicals
4. increased of the ionized calcium in the cells
5. acid alteration of cells (pH 7)
6. damage of cells by the surplus of own mediators (exayto-toxical damage)
7. denaturation and/or proteolysis out of control
8. activating of hydroxy-oxidization of lipids

II. Exogenous factors of injury:

1. infectious aggression (viruses, bacteria, fungi's)
2. physical and/or chemical damages (gamma- and ultraviolet damage, hypo-/hyperthermia, poisons, mechanical, electric damages)
3. Immunological damages :
   a) at overloading of organism by foreign albumen
   в) iatrogenic damage (anesthetics, preparations of blood, solutions, medicines)
4. damage by enzymes and aggressive molecules of macrophages and leucocytes (factor of tumor necrosis, oxide of nitrogen, hydrolytical enzymes of lysosom - proteases, lipases,

Consequences of critical damage:

- partial necrosis of cell
- destruction of cells by necrosis
- pathogenic induction apoptosis
- immune elimination of cells
- reparative regeneration (renewal)
- stimulation of neighbors
- development of inflammation
- damage of genome and appearance of new tumor generations

NECROSIS

Necrosis - it is death of cells or tissues in living organism.

Other forms of organ destructions:

Autolysis – post mortem destruction of organs under action of enzymes, produced by the dead cells or bacteria.

Necrobiosis – protracted process of destruction of tissue (trophic

NECROSIS

CELL

1. Necrosis:
   -coagulative
   -colliquative
2. Apoptosis
3. Immune-mediated cell death:
   - phagocytosis
   - immune-cell killing
   - destruction by activated fragments of complement (C5-C9)

TISSUE

1. Coagulative:
   - fibrinoid
   - caseous
2. Colliquative
3. Fat necrosis

ORGAN

1. Infarction:
   - white
   - red
   - white with hemorrhagic hal
2. Gangrene:
   - wet
   - dry
3. Noma
4. Bedsores

NECROSIS of CELL

It is the premature death and destruction of cell's organelles in the living organism under action of critical damage factors

Phases of development

1. Critical damage
2. Destruction of cells and intercellular connections:
   - cytokaryolysis,
   - coagulative necrosis
3. Post-necrotic transformation of cells

Duration: 1 min – 24 hours

Classification of Cells Death, based on the mechanism of development:

- Necrosis of specialized cells
- Pathogenic inducted apoptosis
- Selective immunological elimination of cells

Morphology of cell destruction:

1. Karyolysis - the basophilic of the chromatin may fade, a change that reflects the activation of the DNA-ses.

2. Pyknosis - characterized by nuclear shrinkage and increased basophiles. Here the DNA apparently condenses into a solid, shrunken basophilic mass.

3. Karyorrhexis - the pyknotic or partially pyknotic nucleus undergoes fragmentation.

Post-necrotic transformation of cells in living organism

1. Autolysis – destruction of cells by ferments of the organism
2. Phagocytosis by macrophages
3. Destruction by free-radical molecules of leucocytes (at inflammation)
4. Destruction by ferments of bacteria (at infected injury)

Pathogenic inducted apoptosis

It is a "programmed by genes cell death" or cell suicide, that is initiated by internal or external factors of critical damage.

Features of apoptosis:

The process begins at activation of genes of apoptosis or inhibition of genes that can stop apoptosis

2. Duration of the process – 10-60min

Fragmentation of cell into apoptotic

Morphologic stages of apoptosis

1. Cell shrinkage. Cell is smaller in size; the cytoplasm is dense.

2. Chromatin condensation. The chromatin aggregates peripherally, under the nuclear membrane, into well-delimited dense masses of various shapes and sizes. The nucleus break up, producing two or more fragments

Morphologic stages of apoptosis

3. Formation of cytoplasmatical blebs and apoptotic bodies. The apoptotic cell first shows extensive surface blebbing, then undergoes fragmentation into a number of membrane-bound apoptotic bodies composed of cytoplasm and tightly packed organelles, with or without a nuclear fragment.
4. Phagocytosis of apoptotic cells or bodies by adjacent healthy cells, either parenchymal cells or macrophages.

Immune-mediated cell death

It is damage of cells by immunocytes and auto-antibodies with destruction of cells in living organism.

By this method can be destroyed:

1. Tumor cells
2. Transplanted cells
3. Infected cells
4. Normal cells (at autoimmune disease)

It is performed by:

- immunocytes
- activated fragments of complement (AB)

Immune-mediated cell death

Phases of process:

1. Recognition of damaged cells by IS
2. Destroying (killing) of cells

Types of Immune-mediated cell death:

1. Phagocytosis – it is absorbtion and destruction by macrophages after opsonization in phagolysosoms of phagocytes, performed by:
   - professional macrophages
   - leucocytes (neutrophils)
   - trombocytes (rarely)
2. Immune-cell killing
3. Destruction by activated fragments of

2. Immune-cells killing

Cells, that perform immune killing:

- T-lymphocytes killers
- natural killers (NK-cells)
- Zero-cells (K-cell)
- macrophages

Mechanisms of killing:

- Antibody-related killing – against the cell cytotoxical K-cell registers by antibodies, which causes elimination.
- AB-independent killing - elimination by killers (NK-cells, T-killers) without antibodies. Killers recognize the cells-targets in accordance with the main complex of histocompeabiality (HLA-1 or HLA-2)

NECROSIS OF ORGANS

It is destruction of all components of organs (specialized cells, vessels, stroma, intercellular matrix, nerves) in the living organism under action of critical alteration.

Reasons ofdevelopment of necrosis:

- protracted ischemia
- stopping of arterial blood supplying
- damage by the mechanical and chemical factors
- inflammatory-destructive action of infects – bacteria, fungi, viruses
- massive damage of organ by endogenous metabolites

CLASSIFICATION OF NECROSIS OF ORGANS

I According to morphology:

1. Dry necrosis (coagulative) – coagulations of proteins
   - caseouse – at syphilis, leprosis, tuberculosis
   - fibrinouse – in vessel's walls at hypertonic disease
2. Wet necrosis (colliquative) – lysis, hydrolysis of soft tissue
3. Fermented necrosis of fat tissue (fat necrosis) – destruction o fat tissue by ferments of pancreas

II According to spreading:

1. partial necrosis of specialized cells
2. total necrosis
3. selective hearth necrosis of specialized cells

III According to clinic-morphological picture:

1. gangrene
2. infarction (heart attack)
3. noma
4. bedsores

Clinic-morphological forms of necrosis of organs:

1. Gangrene – total necrosis of the organ, connected with the external environment:

a) dry – at the thrombosis of arteries, an organ acquires the black coloring

) moist (wet) – at the thrombosis of arteries and veins + influencing of putrid bacteria

) gas (anaerobic) – necrotic tissue is infected by Cl.perfingens

Clinic-morphological forms of necrosis of organs:

Infarction – localized necrosis of part of organ as a result of stopping of regional circulation of blood (thrombosis, embolism, pressuring of the vessel by tumor).

Morphological forms:

a) white (ischemic)

b) red (hemorrhagic)

c) white with hemorrhagic halo

Clinic-morphological forms of necrosis of organs:

Bedsores – necrosis of soft tissue from the local violation of blood circulation at immobilized patients

Noma – widespread necrosis of soft tissue under influence of bacterias (Bacterium fusiformis, spirocheta dentinum) or fungies at immune insufiency.

Morphological forms of tissue necrosis:

- Coagulative necrosis
- Liquefactive necrosis
- Caseous necrosis
- Fat necrosis

Stages of development of necrosis:

1. Before-necrotic changes – from the beginning of damage to stopping of implementation of the specialized functions (8-15 hours).
2. Stage of necrosis – destruction of components and structures of organ with formation of biological demarcation of dead tissue (it takes a few days).

   Microscopically: kariocytolysis, coagulative necrosis of cell, destruction of vessels.

   Clinic: functional insufficiency of organ, fever, leykocytosis.
3. The Postnecrotic changes – reparative regeneration (remodulation) with complete or not full regeneration of organ structures.

The outcomes of necrosis are the following:

- organization – the replacement of necrotic tissues by connective tissue
- incapsulation – formation of connective tissue capsula around necrotic area
- petrification – accumulation of calcium salts in the area of necrosis
- cyst formation
- hyaline change – the accumulation of hyaline masses in the area of necrosis
- sequestration – the formation of sequestrum
- ossification – the appearance of bone tissue in the area of necrosis
- regeneration – the restoration of necrotic tissues
- purulent fusion of necrotic tissues
- mutilation – spontaneous tearing away of the necrotic tissues