IRREVERSIBLE CELL INJURY (CELL DEATH)

Cell death is a state of irreversible injury. It may occur in the living body as a local or focal change (autolysis, necrosis and apoptosis) and the changes that follow it (gangrene and pathologic calcification), or result in end of the life (somatic death). These pathologic processes involved in cell death are described below

AUTOLYSIS

Autolysis (self-digestion) is disintegration of the cell by its own hydrolytic enzymes liberated from lysosomes. Autolysis can occur in the living body when it is surrounded by inflammatory reaction but the term is generally used for postmortem change in which there is complete absence of surrounding inflammatory response. Autolysis is rapid in some tissues rich in hydrolytic enzymes such as in the pancreas, and gastric mucosa; intermediate in tissues like the heart, liver and kidney; and slow in fibrous tissue. Morphologically, autolysis is identified by homogeneous and eosinophilic cytoplasm with loss of cellular details and remains of cell as debris

NECROSIS

Necrosis is defined as a localized area of death of tissue followed by degradation of tissue by hydrolytic enzymes liberated from dead cells it is invariably accompanied by inflammatory reaction. Necrosis can be caused by various agents such as hypoxia, chemical and physical agents, microbial agents,

immunological injury, etc. Two essential changes characterise irreversible cell injury in necrosis of all types

1.Cell digestion by lytic enzymes. Morphologically this change is identified as homogeneous and intensely eosinophilic cytoplasm. Occasionally, it may show cytoplasmic vacuolation

2.Denaturation of proteins. This process is morphologically seen as characteristic nuclear changes in necrotic cell. These nuclear changes may include: condensation of nuclear chromatin (pyknosis) which may either undergo dissolution (karyolysis) or fragmentation into many granular clumps (karyorrhexis)

Types of Necrosis

Morphologically, there are five types of necrosis: coagulative, liquefaction (colliquative), caseous, fat, and fibrinoid necrosis

1. COAGULATIVE NECROSIS

This is the most common type of necrosis caused by irreversible focal injury, mostly from sudden cessation of blood flow (ischaemia), and less often from bacterial and chemical agents. The organs commonly affected are the heart, kidney, and spleen.

Grossly foci of coagulative necrosis in the early stage are pale, firm, and slightly swollen. With progression, they become more yellowish, softer, and shrunken. Microscopically the cell type can still be recognised but their cytoplasmic and nuclear details are lost. The necrosed cells are swollen and appear more eosinophilic than the normal, along with nuclear changes described above., the necrosed focus is

infiltrated by inflammatory cells and the dead cells are phagocytosed leaving granular debris and fragments of cells

2. LIQUEFACTION (COLLIQUATIVE) NECROSIS. Liquefaction or colliquative necrosis occurs commonly due to ischaemic injury and bacterial or fungal infections. It occurs due to degradation of tissue by the action of powerful hydrolytic enzymes. The common examples are infarct brain and abscess cavity

Grossly the affected area is soft with liquefied centre containing necrotic debris. Later, a cyst wall is formed.

Microscopically the cystic space contains necrotic cell debris and macrophages filled with phagocytosed material.

3. CASEOUS NECROSIS. Caseous necrosis is found in the centre of foci of tuberculous infections. It combines features of both coagulative and liquefactive necrosis.

Grossly foci of caseous necrosis, as the name implies, resemble dry cheese and are soft, granular and yellowish.

Microscopically the necrosed foci are structureless, eosinophilic, and contain granular debris The surrounding tissue shows characteristic granulomatous inflammatory reaction

4. FAT NECROSIS. Fat necrosis is a special form of cell death occurring at two anatomically different locations but morphologically similar lesions. These are: following acute pancreatic necrosis, and traumatic fat necrosis commonly in breasts. In the case of pancreas, there is liberation of pancreatic lipases from injured or

inflamed tissue that results in necrosis of the pancreas as well as of the fat depots throughout the peritoneal cavity, and sometimes, even affecting the extraabdominal adipose tissue Fat necrosis hydrolyses neutral fat present in adipose cells into glycerol and free fatty acids. The damaged adipose cells assume cloudy appearance. The leaked out free fatty acids complex with calcium to form calcium soaps (saponification)

Grossly fat necrosis appears as yellowish-white and firm deposits. Formation of calcium soaps imparts the necrosed foci firmer and chalky white appearance. Microscopically the necrosed fat cells have cloudy appearance and are surrounded by an inflammatory reaction.

5. FIBRINOID NECROSIS. Fibrinoid necrosis is characterised by deposition of fibrin-like material which has the staining properties of fibrin. It is encountered in various examples of immunologic tissue injury (e.g. in immune complex vasculitis,autoimmune diseases, Arthus reaction etc), arterioles in hypertension, etc

Microscopically fibrinoid necrosis is identified by brightly eosinophilic, hyaline-like deposition in the vessel wall. Necrotic focus is surrounded by nuclear debris of neutrophils (leucocytoclasis). Local haemorrhage may occur due to rupture of the blood vesse