Pathology

3rd Stage
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Lecture 5

Intracellular accumulations

In certain situations, cells may accumulate various substances, which may be harmless or cause injury. These substances may be situated in the cytoplasm, within organelles or in the nucleus, synthesized by the affected cells or produced elsewhere. The main pathways of abnormal intracellular accumulations are inadequate removal and degradation or excessive production of an endogenous substance, or deposition of an abnormal exogenous material.

Examples of intracellular accumulations (lipids, proteins and glycogen)

*Fatty change (steatosis): refers to any abnormal accumulation of triglycerides within parenchymal cells either due to excessive entry or defective metabolism and export. It is most often seen in the liver (because the liver is the major organ involved in fat metabolism) , but also may occur in heart, skeletal muscle, kidney, and other organs. Causes of fatty change include alcohol abuse, toxins, protein malnutrition, diabetes mellitus, obesity, or anoxia. Alcohol abuse and diabetes associated with obesity are the most common causes of fatty liver in industrialized countries.

Gross examination of fatty liver: Large, yellow, soft and greasy

Microscopical examination: Lipid droplets accumulate in hepatocytes, first in centrilobular area ranging from small to large vacuoles that then fill and expand the cell displacing the nucleus to the periphery of the cell, as steatosis become more extensive, changes extend to mid zone and finally to periportal zone.

*Cholesterol and Cholesteryl Esters:

Cholesterol is normally required for the synthesis of cell membranes without significant intracellular accumulation, thus its metabolism is tightly regulated. However, phagocytic cells may become overloaded with lipid in several pathologic processes, e.g. atherosclerosis (in which cholesterol and cholesterol esters accumulate in arterial wall smooth muscle cells and macrophages or extracellularly).

***Proteins: Protein accumulations are less common than lipid accumulations; and may occur due to excessive synthesis, absorption, or defects in cellular transport. e.g. in nephrotic syndrome, there is heavy protein leakage across the glomeruli filter, so more protein is reabsorbed and vesicles containing this protein will accumulate in proximal renal tubules.**

***Glycogen: Excessive intracellular deposits of glycogen are associated with abnormalities in the metabolism of either glucose or glycogen e.g. diabetes mellitus**

***Pigments : Pigments are colored substances that are either exogenous (coming from outside the body) like carbon or endogenous, (synthesized within the body itself), like lipofuscin, melanin, and certain derivatives of hemoglobin.**

Exogenous pigments: The most common exogenous pigment is carbon (e.g. coal dust), an air pollutant of urban life. When inhaled, it is phagocytosed by alveolar macrophages and transported through lymphatic channels to the regional tracheobronchial lymph nodes. Aggregates of the pigment blacken the draining lymph nodes and pulmonary parenchyma (anthracosis). Other e.g. tattooing.

Endogenous pigments:

•Lipofuscin (wear-and-tear pigment or pigment of aging): is an insoluble brownish-yellow granular intracellular material that accumulates in a variety of tissues (particularly the heart, liver and brain) with aging or atrophy. It is not injurious to the cell but is a marker of past free radical injury. The brown pigment when present in large amounts, imparts an appearance to the tissue called brown atrophy.

•Melanin: is an endogenous, brown-black pigment that is synthesized by melanocytes located in the epidermis and acts as a screen against harmful UV radiation. Excess melanin deposition occurs in:

1.Exposure to sun light 2.Addison disease (adrenal gland failure)

3.Chloasma (occurs during pregnancy, characterized by hyperpigmentation of the skin mainly of the face and other areas under hormonal influence)

4.Melanotic tumors (e.g. pigmented naevi and malignant melanoma)

•Hemosiderin: is a hemoglobin-derived golden yellow to brown granular pigment that accumulates in tissues when there is a local or systemic excess of iron. It

represents large aggregates of ferritin micelles. Excessive storage of hemosiderin (hemosiderosis) may be primary (hereditary haemochromatosis) or secondary (acquired) such as in chronic hemolytic anemias.

• Bilirubin: is a non-iron containing pigment that is present in bile. Elevated serum bilirubin causes yellow discoloration of skin and sclera (jaundice). Hyperbilirubinemia may be unconjugated (excessive destruction of red cells) or conjugated (transport defects within intrahepatic or extrahepatic biliary system) or biphasic.

Pathological calcification

Refers to abnormal deposition of calcium salts, together with smaller amounts of other minerals in tissues other than teeth and bone. It is of 2 types: Dystrophic and metastatic calcifications.

• Dystrophic calcification: is the type of pathological calcification associated with normal calcium metabolism (normal serum calcium) but it deposits in injured or dead tissue, such as *necrosis of any type, *atheromas of advanced atherosclerosis, *aging or damaged heart valves, *tumors and dead parasites. Dystrophic calcification may be an incidental finding indicating insignificant past cell injury, or it may cause organ dysfunction e.g. calcification in aging or damaged heart valves can severely compromise valve motion.

•Metastatic calcification :Is the type of pathological calcification that is associated with hypercalcemia and occur in normal tissues. The main causes of hypercalcemia:

1. Increased secretion of parathyroid hormone, e.g. primary parathyroid tumors

2. Destruction of bone due to the effects of accelerated turnover (Paget disease), immobilization, or tumors (e.g. multiple myeloma, leukemia or diffuse skeletal metastases due to increased bone catabolism)

3. Vitamin D–related disorders like vitamin D intoxication and sarcoidosis (in which macrophages activate a vitamin D precursor).

4. Renal failure (phosphate retention leads to 2nd hyperparathyroidism).

***Metastatic calcification can occur widely throughout the body but mainly affects the kidneys and lungs. Generally, It does not cause clinical dysfunction, however, extensive calcifications in the lungs and kidney may produce respiratory deficits and renal damage, respectively.**

Morphology of pathological calcification

Gross examination: Fine chalky white granules or clumps, with gritty sensation.

Microscopical examination: Intracellular and/or extracellular basophilic deposits.

GOOD LUCK