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Named Cells and Bodies in Blood, Skin and Neural Diseases Along with Metabolic & Storage Disorders

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Abstract

The visual specialty of oral pathology guides a pathologist into the world of minute details in complex tissues. When we see certain sick cells or bodies, we can become locked in a state of flux because our eyes are more used to seeing normal morphology in cells and structures. Despite the fact that they may be misleading in appearance, they help the pathologist make a diagnosis because they are pathognomonic for a number of diseases and ailments. Hence, the present article is an attempt to compile different histopathological bodies seen in various diseases associated with blood, skin and neural diseases along with metabolic and storage disorders with special emphasis on pathogenesis, microscopic and stains used to highlight features of the same.

Keywords: Inclusion bodies, Cells, Disease, Disorder, Named cells.

INTRODUCTION

When a foreign gene (the infectious agent) is introduced into a cell, the complementary DNA that results from the translation of a messenger RNA may code for a protein that does not go through additional modification and transport, leading to precipitation in the cell and the formation of an inclusion body.

Cells can change in specific illnesses or pathological states, and these changed cells may end up being pathognomonic for that particular disease [1].

Cells that bear the names of the researchers who initially discovered and characterized them are known as named cells. These cells have a distinctive shape and show particular staining reactions [2].

Present articles tires to give a complied data regarding different types of cells and bodies associated with blood, skin and neural diseases along with metabolic & storage disorders

DISEASES OF BLOOD

A. Fessas bodies

Pathogenesis: The oxidation of the chains results in the formation of hemichromes. Early in erythroid maturation, denatured chains and irreversible hemichromes precipitate as inclusion bodies and continue to do so. Red cell hydration, stability, and deformability are impacted by the structural and functional alterations brought on by these chains' instability and inability to maintain a stable tetrameric configuration [3,4].

Morphology: Precipitates are irregular in shape along with filamentous or loose structure seen close to the nucleus [5].

Stain: Methyl violet stain

Associated conditions: β Thalessemia

B. Anitschkow cells

Pathogenesis: Monocyte/ macrophage in origin

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Morphology: Elongated nuclei with a linear bar of chromatin along with radiating processes of chromatin [6].

Stain: Hematoxylin and eosin (H&E)

Associated conditions: Rheumatic heart disease, recurrent apthous ulcers, Iron deficiency anemia, Sickle cell anemia, Megaloblastic anemia [6].

C. Howell jolly bodies

Pathogenesis: It represents chromosomes that have separated from the mitotic spindle during the process of abnormal mitosis.

Morphology: Round, solid staining, dark-blue to purple inclusions, 1-2 µm in size. Mostly seen in mature erythrocytes that lack a nucleus & represent nuclear remnants mainly composed of DNA [7].

Stain: Wright stain, Feulgen reaction [8]

Associated conditions: Hyposplenism [9], Postsplenectomy [7], Hereditary spherocytosis, Haemolytic anemias, Pernicious anemias.

D. Cabot's ring

Pathogenesis: It may be obtained either from nuclear remnants or abnormal histone biosynthesis [7].

Morphology: Ring shaped, figure-eight or loop shaped structures

Stain: Wright stain

Associated conditions: Lead poisoning, Pernicious anemia [7]

E. Pappenheimer bodies

Pathogenesis: Due to abnormal accumulation of non-haem iron contained in lysosomes

Morphology: Aggregates of mitochondria mainly ferric (Fe3+) ions in ribosomes and iron particles infrequently seen in peripheral blood smears. Nucleated RBCs containing the bodies are called sideroblasts and non-nucleated RBCs containing the bodies are called siderocytes [10].

Stain: Wright Stain

Associated conditions: Iron loading anaemia, Hyposplenism, Haemolytic anaemia.

F. Dohle bodies

Pathogenesis: Lamellar aggregates of rough endoplasmic reticulum [11].

Morphology: Faint, pale blue cytoplasmic area representing endoplasmic reticulum, near the periphery of the neutrophil that becomes prominent during an infectious episode [12].

Stain: Romanovsky dyes

Associated conditions: Chediak-Higashi's syndrome, Severe burns, Wissler's disease, Pregnancy, Patients undergoing cancer chemotherapy [7].

G. Downey cells

Pathogenesis: Activated (due to constant antigenic stimulation) T lymphocytes produced as part of the immunological response to EBV-infected B lymphocytes.

Morphology: Resemble pleomorphic monocytes or immature cells

There are 3 types of Downey cells

Downey type I- Small cells with scanty basophilic cytoplasm with indented or lobulated nuclei.

Downey type II – Presence of round to oval nucleus, moderately clumped chromatin and absent or indistinct nucleoli in an abundant grey-blue cytoplasm.

Downey type III -Larger cells with round to oval nuclei with moderately dispersed chromatin and one or more prominent nucleoli [13].

Stain: Romanovsky stain

Associated conditions: Infectious Mononucleosis [13]

H. Basophilic stippling

Pathogenesis: Precipitation of ribosomes and RNA during the process of staining of a blood smear.

Morphology: Fine or coarse evenly dispersed bluish or bluish black granules found in erythrocytes. Appears as tiny, round, solid staining, and dark-blue granules, evenly distributed throughout the cell [10].

Stain: Wright stain - the RNA remnants cause the cell to have a diffuse blue color, orange and blue mottled appearance, or punctate fine & coarse granules [14].

Associated conditions: Disturbed erythropoiesis, lead poisoning and severe anemias [7].

I. Heinz bodies/ Schumach body /Erythrocyte refractile body

Pathogenesis: Any endogenous or exogenous factor that inhibits glutathione reduction within the erythrocyte could lead to denaturation of haemoglobin [15].

Morphology: Precipitate or clump of denatured haemoglobin

Stain: Brilliant cresyl blue or crystal violet stain

Associated conditions: G6PD deficiency [1], Diabetes mellitus, Hyperthyroidism, Lymphoma [15].

J. Russell bodies

Pathogenesis: Precipitation of immunoglobulins within the plasma cell [16].

Morphology: Homogenous, elliptical, eosiniphilic, intracytoplasmic inclusions, 20-40µm in size, two or three in number, seen within plasma cells [17].

Stain: Hematoxylin and eosin (H&E), Periodic acid Schiff stain, Gram stain, Millon reaction, Phloxine-tartrazine stain.

Associated conditions: Multiple Myeloma

K. Mott cell

Pathogenesis: Mott cell formation has been linked to a genetic locus-microsatellite marker.

Morphology: Plasma cells that have spherical inclusions packed in their cytoplasm [18].

Stain: Hematoxylin and eosin (H&E), Periodic Acid-Schiff (PAS) and May-Grünwald-Giemsa (MGG) stain.

Associated conditions: Reactive plasmacytosis, Burkitt's lymphoma, Large B-cell lymphoma, Multiple myeloma, Wiskott -Aldrich syndrome [][18].

DISEASES OF SKIN

A. Civatte bodies/ Cytoid bodies/Hyaline bodies/ Colloid bodies

Pathogenesis: Derived either from apoptosis of keratinocytes caused by epithelial damage or from the destruction of the thickened basement membrane [19].

Morphology: Rounded, homogenous, eosinophilic bodies, 10-25 µm in size, found in deeper parts of epithelium and upper connective tissue [20].

Stain: Hematoxylin and eosin (H&E), Periodic Acid-Schiff (PAS)

Associated conditions: Although civatte bodies are associated with mostly immune mediated and inflammatory disorders such as lichen planus, lupus erythematosus, bullous pemphigoid, erythema multiforme, Sweet's syndrome, they are also seen in few other conditions. These includes drug related disorders, viral infections such as herpes simplex and zoster and some of the genetic conditions such as Toxic epidermolysis bullosa [21].

B. Corps ronds and Grains

Pathogenesis: Abnormal keratinisation.

Morphology: They are miniature epithelial pearls, found in the granular layer, often containing a single large cell with a degenerated nucleus at the centre [22].

Stain: Hematoxylin and eosin (H&E)

Associated conditions: Darier's disease or keratosis follicularis [23,24].

C. Tzanck cells

Pathogenesis: Pemphigus is a condition brought on by antibodies to desmogleins 3 and 1, which disrupt the desmosomes in the lower layers of the squamous epithelium. As a result, fluid-filled blisters, vesicles, or bullae form, causing acantholysis and the free-floating clusters of cells known as tzanck cells.

Morphology: Large, clear nuclei containing large nucleoli that are usually single or may be multiple.

Stain: Hematoxylin and eosin (H&E), Giemsa stain, Papanicolaou stain (PAP), Wright stain, Methylene blue stain, Toluidine blue stain.

Associated conditions: Pemphigus group of lesions.

D. LE cell and bodies

Pathogenesis: Phagocytic leukocyte (blood neutrophil or macrophage) that has engulfed the denatured nucleus of an injured cell [24].

Morphology: LE Body-Homogenous pale blue to deep purplish material

LE cell- LE cell contains within its cytoplasm the LE body, with the nucleus of the phagocyte being pushed to one end [17].

Stain: LE body – Wright stain, Giemsa stain [17]; LE cell- Romanowsky stain [25].

Associated conditions: Systemic lupus erythematous (SLE)

E. Pustulo-Ovoid bodies

Pathogenesis: Gradual accumulation of granules in the interior of the lysosomes, which, because of their maturity, have lost mitochondria and the endoplasmic reticulum [26].

Morphology: Large eosinophilic intracytoplasmic granules surrounded by a clear halo, found in the cells of granular cell tumor.

Stain: Periodic acid Schiff stain

Associated conditions: Granular cell tumor of the tongue

DISEASES OF NEURAL TISSUES

A. Verocay bodies

Pathogenesis: Presumably the overexpression of laminins in portions of schwannomas prompts the alignment of cells into a tight pattern of rows [27].

Morphology: Stacked arrangements of elongated palisading nuclei alternating with anuclear zones containing cell processes. Found in the more densely packed Antoni A regions, rather than in the loose or microcystic Antoni B areas.

Stain: Hematoxylin and eosin (H&E)

Associated conditions: Schwannomas

B. Negri bodies

Pathogenesis: Rabies virus infection induces the formation of cytoplasmic inclusion bodies.

Morphology: Round or oval, eosinophilic, intracytoplasmic inclusions with central basophilic granules located in the cytoplasm of infected nerve cells [28].

Stain: Hematoxylin and eosin (H&E)

Associated conditions: Rabies

METABOLIC AND STORAGE DISORDERS

A. Gaucher cells

Pathogenesis: Accumulation of glucocerberoside in the lysosomes of macrophages due to absence of the enzyme, glucocerberosidase [29].

Morphology: 20–100 µm in diameter, and have small, usually eccentrically placed nuclei and cytoplasm with characteristic 'wrinkled tissue paper' appearance [29].

Stain: Wright stain, Periodic acid Schiff stain, Iron stains

Associated conditions: Gaucher's disease

B. Gargoyle cells

Pathogenesis: Excessive accumulation of intracellular mucopolysaccharides in many tissues and organs throughout the body.

Morphology: Large oval or polygonal cell, 20 µm in diameter, with a pale central nucleus, the cytoplasm appearing clear (H and E) or granular (toluidine blue).

Stain: Hematoxylin and eosin (H&E), Toluidene blue stain, Alcian blue stain

Associated conditions: Hurler syndrome

C. Niemann Pick cells

Pathogenesis: Increased sphingomyelin deposition within the cells of the reticuloendothelial system due to variable deficiency in the enzyme sphingomyelinase [30].

Morphology: Large histiocytic cells, 20-90 µm in size with small, bland centrally located or eccentric nuclei, clear to pale blue cytoplasm, that is vacuolated [31].

Stain: Giemsa stain, Wright stain, Periodic acid Schiff stain, Sudan black B stain, Oil red O stain.

Associated conditions: Niemann Pick disease type A and type B, Gangliosidosis, Fabry's disease

D. Reilly bodies

Pathogenesis: Lysosomes that stain abnormally due to their content of incompletely degraded mucopolysaccharides

Morphology: Round or comma shaped, are sometimes surrounded by a halo and tend to be clustered to one end of the cell [32,33].

Stain: Toluidene blue stain

Associated conditions: Hurler's Syndrome

DISCUSSION

The histopathological bodies are anomalies that are either intracellular or extracellular and are unique to particular diseases. These structures, which have distinctive staining characteristics, can be found either in the cytoplasm or the nucleus of the cell, or both. These are unusual morphological changes in a tissue that result in a very particular pattern.

The presence of histopathological bodies is often an important diagnostic-aid in identifying the underlying disease. These cells and bodies can either be pathognomic or not pathognomic to a particular condition. The term "pathognomonic" refers to a quality that is so distinctively or specifically associated with an illness that it aids in diagnosis. Whereas, a not pathogomic implies to quality that is seen in more than one condition.

Various routine and special stains have been utilized in order to view these cells and bodies under the microscope. Hematoxylin and eosin stain is most widely used stain. It is routinely used since it has a distinct ability to clearly demonstrate various nuclear and cellular components. Hematoxylin has the ability to stain intranuclear components imparting blue –black color whereas eosin stains the cell cytoplasm giving various shades of pink color. Examples of few cells and bodies stained using hematoxylin and eosin stain are Anitschkow cells, Russell bodies, Civatte bodies, Tzanck cells, Verocay bodies, Negri bodies and Gargoyle cells.

Romanowsky staining, often referred to as Romanowsky-Giemsa staining, is a classic staining technique that served as the basis for numerous other but related stains that are now frequently used in cytopathology and hematology. Stains that are related to or derived from the Romanowsky-type stains include Giemsa, Wright, Field, May–Grünwald and Leishman stains. It is considered to be one of the prototypical staining technique based upon Romanowsky effect / metachromatism. This stain is combination of eosin stain and aged solutions of methylene blue. This stains Dohle bodies, Downey cells and LE cells. One of most commonly used amongst these Romanowsky stain is Wright stain used to demonstrate Howell Jolly bodies, Carbot ring, Pappenheimer bodies, Tzanck cells, LE body, Gaucher cells and Niemann-Pick cells. Other stain includes Giemsa stain used for Tzanck cells, LE bodies and Niemann –Pick cells.

Sudan black B and Oil red O is used for staining mainly cells and bodies high with its lipid content such as Niemann Pick cells.

Periodic acid–Schiff (PAS) is a staining method used to detection of carbohydrates or glycoconjugates. Mechanism of PAS is based upon reactivity of free aldehyde groups within carbohydrates with Schiff reagent to form a bright red magenta end product. Cells and bodies stained using PAS technique include Russell bodies, Mott cells, Civatte bodies, Pustulo-Ovoid bodies, Gaucher cells and Niemann-Pick cells

Papanicolaou stain is a polychromatic stain that uses multiple dyes to differentially stain various components of the cells. It mainly contains a mixture of acidic and basic dyes that helps in defining nuclear details and helps in differentiation of different cells. It is mainly used for demonstration of Tzanck cells.

Howell Jolly bodies are demonstrated using Feulgen stain. This stain is mainly used to identify chromosomal material/DNA. Howell Jolly bodies are DNA inclusion bodies for a specific DNA or RNA located eccentrically and occur in mature or nucleated erythrocytes.

Staining using Perl's Prussian blue demonstrates Gaucher cells containing iron since there is excessive accumulation of iron deposits in macrophages and various other body systems.

Toluidine blue stain usually used for Tzanck cells, Gargoyle cells and Reilly bodies. It is a basic thiazine metachromatic dye which has high affinity for acidic tissue components thereby has potential to study tissues which are rich in DNA and RNA.

Conditions in which cells and bodies are pathognomic and not pathogonomic are enlisted as follows: (Table 1)

CONCLUSION

As the condition worsens, the body experiences a variety of metabolic alterations that result in cellular abnormalities. These cellular alterations are discernible at various stages of the development of disease. The absence of histopathological bodies is a sign that the disease is subsiding, just as the presence of these bodies indicates the presence of a disease. It may be helpful to stage the diseases based on the appearance of these histological entities at different points in the disease's progression.

In oral pathology, histopathological bodies are extremely important for disease diagnosis. These characteristics, some of which are pathognomonic, are frequently symptomatic of the origin of the disease.

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Table 1: Conditions with associated cells and bodies

Named cells/ Bodies	Disease	Diagnostic significance
Fessas bodies	β Thalessemia	Pathogonomic
Anitschkow cells	Rheumatic heart disease, Recurrent apthous ulcers, Iron deficiency anemia, Sickle cell anemia, Megaloblastic anemia	Not pathogonomic
Howell jolly bodies	Hemolytic anemias, Pernicious anemia, Hereditary Spherocytosis, Hyposplenism	Not pathogonomic
Cabot's ring	Lead poisoning, Pernicious anemia	Not pathognomic
Pappenheimer bodies	Sideroblastic anemia, Haemolytic anemia, Hyposplenism	Not pathognomic
Dohle bodies	Severe burns and infections, Chediak Higashi syndrome	Not pathognomic
Downey cells	Infectious Mononucleosis	Pathogonomic
Basophilic stippling	Disturbed erythropoiesis, Lead poisoning, β Thalessemia, Megaloblastic anemia	Not pathognomic
Heinz bodies	G6PD deficiency	Pathognomic
Russell bodies	Multiple Myeloma	
Mott cell	Reactive plasmacytosis, Burkitt's lymphoma, Large B-cell lymphoma, Lymphoplasmablastic lymphoma, Multiple myeloma	Not pathognomic
Civatte bodies	Lichen planus	Not pathognomic
Corps ronds and Grains	Darier's disease	Not pathognomic
Tzanck cells	Pemphigus group of lesions	Pathognomic
LE cell and bodies	Systemic lupus erythematous (SLE)	Pathognomic
Pustulo-Ovoid bodies	Granular cell tumor of the tongue	Pathognomic
Verocay bodies	Schwannomas	Pathognomic
Negri bodies	Rabies	Pathognomic
Gaucher cells	Gaucher's disease	Pathognomic
Gargoyle cells	Hurler syndrome	Pathognomic
Niemann Pick cells	Niemann Pick disease	Pathognomic
Reilly bodies	Hurler's Syndrome	Pathognomic