

Named Cells in Oral Pathology: A Brief Review

¹NJ Naziya, ²Jayanthi Palani, ³S Sunil, ⁴R Rathy, ⁵RK Harish, ⁶M Nivia

ABSTRACT

Named cells refer to cells that are associated with the name of the scientist who first described them. These cells can be either seen in normal tissues or may be noticed in pathological conditions, including infections, inflammatory conditions, neoplasms, and in certain metabolic disorders. This article lists some named cells seen in routine histopathological practice with a brief description about their morphology and staining reactions.

Keywords: Infections, Named cells, Neoplasm.

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INTRODUCTION

Named cells refer to cells that are named after the scientists who first identified and described them. These cells have a characteristic morphology and exhibit specific staining reactions. A variety of these cells can be identified in pathological conditions, including infections, metabolic disorders, and neoplasms, while some of them are also noticed in normal tissues. These cells are broadly divided into physiological and pathological cells.

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 - Merkel cells
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 - Tzanck cells
 - Langerhans giant cells
 - Downey cells
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 - Mikulicz cells
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- Seen in inflammatory conditions
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- Seen in neoplasms
 - Paget cells
 - Sézary cells
 - Reed–Sternberg cells
 - Touton giant cells
- Seen in metabolic disorders
 - Gargoyles cells
 - Gaucher cells.

Physiological Cells

Langerhans Cell

Langerhans cell, named after the scientist Paul Langerhans, is a pale-staining nonkeratinocyte with a convoluted nucleus. The cytoplasm contains vimentin intermediate filaments and small rod- or racket-shaped structures called Birbeck granules. These cells are distributed in the epidermis (especially in the supra basal position), oral mucosa, esophagus, and vagina. They are the antigen processing and presenting cells. They are reduced in the epidermis of patients with diseases like psoriasis, sarcoidosis, and contact dermatitis. Increased Langerhans cells are seen in Langerhans cell histiocytosis. The markers used to demonstrate Langerhans cell include CD 1a, S-100, and Langerin (CD 207).^{1,2}

Merkel Cells

Merkel cells are named after German anatomist, Friedrich Sigmund Merkel. Merkel referred to these cells as Tastzellen or “touch cells.” Most often, they are associated with sensory nerve endings, when they are known as Merkel nerve endings. They are oval-shaped nonkeratinocytes having a pale-staining cytoplasm, with bundles of intermediary filaments and osmiophilic granules. The nucleus is large and lobulated and the margins of these cells project cytoplasmic “spines” toward the keratinocytes.¹ It has been reported that Merkel cells are derived from neural crest cells, but more recent experiments in mammals have indicated that they are of epithelial origin.³

Merkel cells are found in the skin and in some parts of the mucosa of all vertebrates. In mammalian skin, they are clear cells found in the stratum basale. They also occur

¹Postgraduate Student, ^{2,5}Reader, ^{3,4}Professor, ⁶Senior Lecturer
^{1,2,4,6}Department of Oral Pathology and Microbiology, Azeezia College of Dental Sciences & Research, Kollam, Kerala, India
³Department of Oral Pathology and Microbiology, Pushpagiri College of Dental Sciences, Tiruvalla, Kerala, India

Corresponding Author: NJ Naziya, Postgraduate Student Department of Oral Pathology and Microbiology, Azeezia College of Dental Sciences & Research, Kollam, Kerala, India, e-mail: dr.naziya.nj@gmail.com

in epidermal invaginations of the plantar foot surface called rete ridges.⁴

The stains/markers used to demonstrate Merkel cells include silver impregnation technique, CAM 5.2 or AE1/AE3, CK 20, and Neuron-specific enolase (NSE).¹

Cells seen in Pathological Conditions

Cells seen in Infections

Tzanck cells: These cells are named after French dermatologist, Arnault Tzanck. These are large, round keratinocytes with an enlarged hyperchromatic nucleus, hazy or absent nucleoli, and abundant basophilic cytoplasm. The basophilic staining is deeper peripherally on the cell membrane ("mourning edged" cells) due to the cytoplasm's tendency to get condensed at the periphery, leading to a perinuclear halo. Stains/markers used to demonstrate Tzanck cells include Giemsa, Papanicolaou stain, Wright stain, methylene blue, and toluidine blue.¹

Tzanck cells are found in pemphigus vulgaris and viral infections, induced by herpes simplex, varicella and herpes zoster, and Cytomegalovirus.⁵

In contrast to pemphigus vulgaris, the acantholytic Tzanck cells in pemphigus foliaceus and pemphigus erythematous often have a hyalinized cytoplasm that corresponds to dyskeratosis seen in tissue sections.⁶

Langhans giant cells: Langhans giant cells (LGC) are named after Theodor Langhans, a German pathologist. They are formed by the fusion of epithelioid cells and contain multiple nuclei arranged in a horseshoe-shaped pattern in the cell periphery or are arranged circumferentially.¹

When activated, the CD4+ T cells and monocytes come in close contact with each other, resulting in interaction of CD40-CD40L between these two cells. There is subsequent secretion of IFN γ by the T cells causing upregulation and secretion of fusion-related molecule DC-STAMP (dendritic cell-specific transmembrane protein) by the monocytes, which results in LGC formation.⁷

Although traditionally their presence was associated with tuberculosis, they are not specific for tuberculosis or even for mycobacterial disease. In fact, they are found in nearly every form of granulomatous disease, regardless of etiology. They are reported to be seen in tuberculoid leprosy, gumma of syphilis, and sporotrichosis.¹

Downey cells: Downey cells, named after Hal Downey, are atypical lymphocytes, which show extreme variability in size and shape. They have abundant pale blue cytoplasm and irregular nucleus with lightly staining chromatin. Their cytoplasmic edges may be indented by other blood cells, leading to a scalloped appearance called Dutch skirting. These cells stain positively with Giemsa stain.¹

Downey cells are seen in the peripheral blood of patients with infectious mononucleosis. The detection of at least 10% atypical lymphocytes on a peripheral blood smear in a patient with mononucleosis has a sensitivity of 75% and a specificity of 92% for the diagnosis of infectious mononucleosis.⁸

Virchow cells: Virchow cells are named after the scientist Rudolph Virchow. They are observed in lepromatous leprosy and are referred to as lepra cells. Their protoplasm, which forms the greater part of the cell, is filled with vacuoles and contains enormous numbers of lepra bacilli. The nucleus is usually single and is usually pressed to one side by the vacuoles and bacilli that crowd the cell body.^{9,10} In some instances, these vacuoles are so numerous that there is little actual protoplasm remaining, the cell body having the appearance of foam. They resemble xanthoma cells and, on staining with fat stains, are shown to contain lipid, largely neutral fat, and phospholipids rather than cholesterol. These cells stain positively with Modified Fite Faraco stain.¹

Mikulicz cells: Mikulicz cell is a large histiocyte with pale, vacuolated cytoplasm.¹¹ The cell stains positively with Giemsa, Gram's stain, Warthin–Starry silver stain, and periodic acid–Schiff (PAS) stain.¹ Mikulicz cells are characteristic of rhinoscleroma, a disease caused by *Klebsiella* bacilli. The vacuoles observed in the Mikulicz cells were considered to be phagosomes containing principally bacterial mucopolysaccharide and a few bacteria and, to a lesser extent, swollen mitochondria.^{11,12}

Wright cells: Wright cells are large macrophages that contain numerous protozoa grouped together in a typical "swarm of bees" fashion within the weakly basophilic cytoplasm. These cells are demonstrated using May Grunwald and Giemsa stain. These cells are seen in cutaneous and mucosal leishmaniasis.¹

Warthin–Finkeldey cells: Warthin–Finkeldey cell is a type of giant cell that vary in size, but can contain as many as 100 nuclei per cell along with cytoplasmic and nuclear inclusions. These cells are pathognomic for measles infection. They are found within the exanthem, Koplik spots, and respiratory secretions of infected persons. These cells are also found in hyperplastic lymph nodes early in the course of measles, HIV infection, Kimura's disease, and rarely in a number of neoplastic (e.g., lymphoma) and non-neoplastic lymph node disorders.¹

Their origin is uncertain, but they have previously been shown to stain with markers similar to those of follicular dendritic cells, including CD21. Under the light microscope, these cells consist of a large, grape-like cluster of nuclei.¹²

Greenblatt and Pund cells: They are large mononuclear cells measuring 25 to 90 μ m in diameter. The nucleus is

eccentrically placed and is either vesicular or pyknotic. They are seen in granuloma inguinale and stain positively with Giemsa, Leishman, and Wright stains. They have intracytoplasmic vacuoles containing Donovan bodies in either young noncapsulated or mature capsulated forms.¹

Cells seen in Inflammatory Conditions

Pekin cells: In 1967, Pekin, Malinin and Zvaifler described macrophages with one or more phagocytosed granulocytes. These Pekin cells contain one or more intact polymorphonuclear leukocytes and basophilic globular structures within their cytoplasm. They are characteristic cells seen in Reiter's syndrome. Besides in Reiter's syndrome, these cells are also seen in other inflammatory joint diseases like juvenile rheumatoid arthritis.¹³

Pekin cells play a regulatory part in preventing autolysis of polymorphonuclear neutrophils (PMN) and thus inhibit local tissue damage. These cells express both CD36 and CD14 adhesion molecules. CD36 expression on Pekin cells seems to support the notion of the involvement of this receptor in the clearance of apoptotic PMN during synovial inflammation.¹⁴

Von Hansemann cells: Named after David Paul Von Hansemann, they are large macrophages with abundant foamy eosinophilic cytoplasm and a prominent eccentric, hyperchromatic round nucleus. Variable numbers of concentrically laminated, round-ovoid, basophilic inclusions are noticed within the cytoplasm and are referred to as Michaelis-Gutmann bodies.¹⁵ They are found in malacoplakia, which is a rare inflammatory condition presenting clinically as a papule, plaque, or ulceration which usually affects the genitourinary tract.¹⁶

Cells seen in Neoplasms

Paget cells: Paget cells are round or oval cells that appear larger than keratinocytes. They have a vacuolated amphophilic, cytoplasm with a hypertrophic nucleus, scanty nuclear chromatin, and a large nucleolus. No desmosomal attachments are seen between Paget cells and the adjacent keratinocytes. They are PAS positive and are found in Paget's disease of the breast. The occurrence of Paget cells is not limited to Paget's disease, but they are also found in trachoma, psoriasis, lichen planus, pemphigus, Bowen's disease, and nongonorrheal endometritis.¹

Paget cell develops from the normal epithelial cell. The process occurring in the Paget cell is a normal response of the epithelial cell towards different kinds of animate and inanimate stimuli like tar, X-rays, sunlight, and viruses.¹⁷

Sézary cells: Sézary cells were first described by Albert Sézary, and they are also known as Mycosis cell, monster cells, or cerebriform lymphocytes. They are atypical lymphocytes with a grooved or cerebriform nucleus with a

condensed nuclear chromatin. The cytoplasm is sparse and appears as a narrow rim around the nucleus. These cells can be demonstrated with Wright stain, Giemsa stain, and PAS stain.¹ Three variants of Sézary cell are identified based on its size. The "small cells" are less than 12 microns in diameter, "large cells" are more than 12 microns, and the "very large cells" are more than 14 microns.¹⁸

Although Sézary cell is the pathological hallmark of cutaneous T cell lymphoma, its significance has been brought into dispute as similar atypical mononuclear cells have been described in a variety of other skin disorders.¹⁹ The conditions include lichen planus, discoid lupus erythematosus, psoriasis, vasculitis, actinic keratosis, dilantin hypersensitivity syndrome, and erythrodermic follicular mucinosis. Recently, CD158k marker has been demonstrated on Sézary cells.²⁰

Reed-Sternberg cells: They are named after Dorothy Reed Mendenhall and Carl Sternberg, who provided the first definitive microscopic descriptions of Hodgkin's disease. They are large cells that either are multinucleated or have a bilobed nucleus (having an "owl's eye" appearance) with prominent eosinophilic nucleoli.¹

Reed-Sternberg cells are giant cells found in Hodgkin's lymphoma (HL). The presence of these cells is pathognomonic for the diagnosis of classical HL.¹ Other than HL, cells resembling Reed-Sternberg cells may be present in other B and T cell lymphomas, carcinomas, melanomas, and sarcomas. Although these cells are derived from B lymphocytes, they are CD30 and CD15 positive and are usually negative for CD20 and CD45.^{21,22}

Touton giant cells: Touton giant cells are named after Karl Touton. Karl Touton first observed these cells in 1885 and named them "xanthelasmatic giant cells."²³ Touton giant cells are extremely large and sometimes contain more than 10 nuclei. They contain a ring of nuclei surrounding a central homogeneous cytoplasm, while foamy cytoplasm surrounds the nuclei. These cells have a peripheral wreath-like arrangement of nuclei.²⁴

Touton giant cells are formed by the fusion of macrophage-derived foam cells. It has been suggested that cytokines, such as interferon gamma, interleukin-3, and monocyte colony stimulating factor may be involved in the production of Touton giant cells. They are seen in xanthoma, disseminated xanthoma, juvenile xanthogranuloma, necrobiotic xantho granuloma, and dermatofibroma.¹

Cells seen in Metabolic Disorders

Gargoyle cell: Gargoyle cell is a large oval or polygonal cell with a pale central nucleus and the cytoplasm appearing clear on Hematoxylin and Eosin staining. When stained with toluidine blue, metachromatic granules are seen in

the cytoplasm. On electron microscopy, the cytoplasm of the clear cells is seen to be filled with large irregular clear vacuoles. The membranes of the vacuoles are often broken and the ruptured ends curl. Occasionally, mitochondria and cisterns of endoplasmic reticulum are interspersed between the vacuoles. The stains used to demonstrate Gargoyle cells are toluidine blue and Alcian blue.¹

Gardner has reported the presence of "gargoyle cells" in the gingival tissues of patients with Hurler's syndrome, a disease characterized by disturbance of mucopolysaccharide metabolism.²⁵

Gaucher cells: Gaucher cells are glucocerebroside-laden macrophages measuring 50 to 60 μm in diameter. On electron microscopy, they contain tubular cytoplasmic inclusions that are considered to be transformed secondary lysosomes. The fibrillar ceramide accumulations are extensive enough to give the cytoplasm a distinctive "crinkled blue tissue paper" appearance. These cells are visualized using Wright stain, PAS stain, and iron stains. Gaucher cell is the pathological hallmark of Gaucher disease. Gaucher's disease is an inherited disorder of ceramide metabolism in which an enzyme deficiency leads to the accumulation of glucocerebroside in macrophages of the bone marrow and reticuloendothelial system.²⁶

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