General Internal Medicine and Clinical Innovations

Mini Review

ISSN: 2397-5237

The neutrophil

Clyde Schultz[1,2*]

[1]Department of Biology, The University of Calgary, Alberta, Canada

[2]BioGram Inc., Ponte Vedra, USA

Abstract

The neutrophil is one of the first cells drawn to a site of inflammation or infection. It can arrive in an activated state within minutes of the presence or stimulus of infection, or an allergen which might cause inflammation. It is a diverse cell capable of inducing cytokine production which activates other immune cells. This complex cell is an essential piece to the non-specific immune response, and the ability to ward off infection and inflammation in its' early stages. Conversely, under, or overproduction of neutrophils can lead to disease states.

Introduction

The neutrophil is a type of "white" cell found in the blood in the range of 2.5 X 10^3 to 7.5 X10^3 cells/microliter of blood. They comprise about 60-70% of the white cells in humans and other animals [1]. Neutrophils a part of the polymorphonuclear leukocyte cell family along with eosinophils and basophils. Neutrophils become "activated" during the early stages of infection or inflammation due to allergens or some other type of environmental exposure, and are one of the first cell types to arrive "on scene" [2,3]. They are recruited to sites of injury or trauma within minutes. They are activated or recruited to do so by chemokines such as IL-8 and C5a. Neutrophils have a maximum life span of under 140 hours [4]. They are continually replenished in healthy individuals.

Structure

Neutrophils show an increased segmentation as they mature, having 3-5 segments which are visible under the light microscope. This lobbed appearance is facilitated by chromatin which tends to hold the segments together in a somewhat loose fashion. The average neutrophil has a diameter of about 9.0 micrometers when in suspension and just under double that when adhered to an object. They are formed in the bone marrow in response to cytokine stimulus [5].

As the neutrophil matures the nucleolus is reduced in size and eventually disappears. Mitochondria and ribosomes are few, and the Golgi are small. Since the life span is a maximum of about 140 hours there is no need for complex structures. This may be a function of evolution. Anti-microbial products produced by neutrophils tend to be tissue destructive so a shorter life span may limit the damage. This also implies that neutrophils are constantly being produced [5]. They are more numerous than macrophages which have a longer life span. They are circular when in suspension in the blood but when activated tend to be more amorphous, and can extend themselves as they seek antigens to destroy.

Neutrophils are removed from a site of activation by macrophages. This is performed by PECAM-1 and phosphatidylserine at the surface of the cells [6].

Function

Neutrophils will migrate rapidly to a site of "irritation" by amoeboid movement which occurs via chemotaxis [6,7]. They migrate by the interaction of interleukins 8 and 6, complement factors. They have receptors for complement and cytokines as well as interferon. They can adhere to Fc receptors on antibody molecules and the endothelium. It has been shown in mice that neutrophils have the ability to "swarm" to a site of inflammation. This swarming action has also been seen in the human eye. Neutrophils will migrate to a site of irritation in the cornea and once there burst. This burst will cause an "ulcer" to appear on the cornea, with associated pain, photophobia, exudate production, redness and general irritation [8]. Steroids are used to successfully treat the condition.

Because they are motile, neutrophils congregate at the sites of microbial infection quickly when attracted by cytokines from macrophages, endothelium, and especially in the case of allergic reactions mast cells [9,10]. The major ways neutrophils attack microorganisms are by phagocytosis and the release of soluble substances that act directly with the invading microbe.

Neutrophils release proteins by de-granulation. There are several types of granules that have anti-microbial properties. Azurophilic granules contain groups of defensins, BPI or bactericidal/permeability increasing protein [11]. Secondary granules contain lysozyme, lactoferrin and NADPH oxidase, and tertiary granules contain collagenase and gelatinase as members of this sub-group [12].

Significance in the body

Since neutrophils are one of the initial cells recruited to a site of injury or infection, their significance is obvious. Should these cells not be recruited, significant disease related events would occur, or be

Correspondence to: Clyde Schultz, Department of Biology, The University of Calgary, Alberta, Canada, Tel: 4032205278; E-mail: schultzc@ucalgary.ca

Key words: *neutrophil, immune cell, cytokine, PMN*

Received: August 14, 2020; **Accepted:** August 28, 2020; **Published:** September 01, 2020

exacerbated as one of the initially recruited cell types would not be present. Neutropenia is a condition in which an individual will have low neutrophil counts. The condition may be congenital, or it may be a side effect of certain medications, such as cancer treatment. The ANC or absolute neutrophil count is used for diagnosis. An individual with an ANC < 1500 cells/mm^2 is considered to have neutropenia. An individual with and ANC < 500 cells/mm^2 is considered to be a more serious condition as a major part of the acute phase immune response is compromised. Decreases in neutrophil function can lead to hyperglycemia.

Alpha 1-antitrypsin deficiency is a condition where the enzyme elastase is not inhibited by alpha 1-antitrypsin [13]. As a result, there is tissue damage during inflammation reactions. Elastase is essential in the control of neutrophils when activated. Lack of control may lead to pulmonary emphysema, and acute lung injury.

Symptoms of another condition Familial Mediterranean Fever include fever, arthralgia, peritonitis and amyloidosis [14]. This is caused by a genetic mutation in the pyrin which is contained in granulocytes. This leads to an excessive acute phase response.

Neutrophils are also implicated in the development of cancer as they are one of the initial cells recruited to an area of inflammation Evidence suggests that neutrophils are involved in tumor growth and spread [15].

References

1. Edwards S (2005) The development and structure of mature neutrophils, In: Edwards SW, editor. Biochemistry and Physiology of the neutrophil, Cambridge Univ Press; New York, pp: 33-76.
2. Mantovani A, Cassatella MA, Costantini C, Jaillon S (2011) Neutrophils in the activation and regulation of innate and adaptive immunity. *Nat Rev Immunol* 11: 519-531.
3. Amulic B, Cazalet C, Hayes GL, Metzler KD, Zychlinsky A (2012) Neutrophil function: from mechanisms to disease. *Ann Rev Immunol* 30: 459-489.
4. Pillay J, den Braber I, Vrisekoop N, Kwast LM, de Boer RJ, et al. (2011) Response: the in vivo half-life of human neutrophils. *Blood* 117: 6053-6054.
5. Borregaard N (2010) Neutrophils, from marrow to microbes. *Immunity* 33: 657-670.
6. Ley K, Laudanna C, Cybulsky MI, Nourshargh S (2007) Getting to the site of inflammation: the leukocyte adhesion cascade updated. *Nat Rev Immunol* 7: 678-689.
7. Muller W (2013) Getting leukocytes to the site of inflammation. *Vet Pathol* 50: 7-22.
8. Schultz C (2000) Cytokines in the ocular environment, in Allergic Disease in the Eye. Simon and Schuster Publishers. Ed: Abelson M. pp 21-42.
9. Vieira OV, Botelho RJ, Grinstein S (2002) Phagosome migration: aging gracefully. *Biochem J* 366: 689-704.
10. Sheppard FR, Kelher MR, Moore EE, McLaughlin NJ, Banerjee A, et al. (2005) Structural organization of the neutrophil NADPH oxidase: phosphorylation and translocation during priming and activation. *J Leukoc Biol* 78: 1025-1042.
11. Choi K-Y, Chow LN, Mookherjee N (2012) Cationic host defense peptides: multifaceted role in immune modulation and inflammation. *J Innate Immun* 4: 361-370.
12. Lande R, Gregorio J, Facchinetti V, Chatterjee B, Wang Y-H, et al. (2007) Plasmacytoid dendritic cells sense self-DNA coupled with antimicrobial peptide. *Nature* 449: 564-569.
13. Kawabata K, Hagio T, Matsuoka S (2002) The role of neutrophil disease in acute lung injury. *European J Pharma* 451: 1-10.
14. Ozen S (2003) Familial Mediterranean Fever: revisiting an ancient disease. *European J Peds* 162: 449-454.
15. Nicolas-Avila JA, Adrover JM, Hidalgo A (2017) Neutrophils in homeostasis, immunity and cancer. *Immunity* 46: 15-28.