Intricate Network Between Inflammation; Immunity; Cancer- From Tumor Prevention to Tumor Initiation, Tumor Promotion and Tumor Progression

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ABSTRACT

Inflammation is a reaction to noxious stimulants. During acute inflammation release of inflammatory mediators are cytokines, growth factors, and proteolytic enzymes by immune cells such as neutrophils are predominant cells, NK cells, DCs, and macrophages result in cellular repair and regeneration. If the same inflammation is aggravated chronically by immune cells such as macrophages are predominant cells followed by T cells, and B cells, releasing immune mediators such as cytokines, growth factors, and enzymes results in offensive action against epithelial cells, immune cells, vascular tissue, and resulting in pro-tumoral activities. Inflammation has a dual role in cancer it can prevent or promote cancer mainly driven by transcription factors such as NF-KB, and key transcription factors activated in the development of immune cells to tumor progression in all the stages of cancer. This article highlights the inflammatory mediators in acute and chronic inflammatory-microenvironments involved in various cellular-immunologic and vascular changes.

Key Words: *Nuclear factor-kappa beta, Signal transducer and activator of transcription-3, Epidermal growth factor, Transforming growth factor-beta, Vascular endothelial growth factor, Regulatory T cells*

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INTRODUCTION

Cancer is an uncontrolled, progressive, persistent, proliferation of cells even after the removal of stimulus such as external environmental factors are physical, chemical agents (Methyl mercaptan, Benzene, lead, carbon monoxide, etc.), infectious agents (HPV, EBV), and chronic psychological stress account 90% of all cancers. Lung cancer is the most common and common cause of death worldwide, followed by other cancers oral cancers, cervical cancer, breast, colorectal cancer, etc. 25% of all cancers are preceded by chronic inflammation or infection [1-3].

This article highlights the inflammatory mediators in acute and chronic inflammatory- microenvironments involved in various cellular-immunologic and vascular changes.

MATERIALS AND METHODS

Articles regarding inflammation including acute and chronic inflammation, inflammatory and immune cells and inflammatory mediators, cancer prevention, and cancer progression were searched on Pubmed, Medline, Scopus, Elsevier, and Google Scholar. This article includes studies, reviews, Clinical trials, and key findings of my research were included in my manuscript.

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RESULTS AND DISCUSSION

Inflammation is the defensive action against any noxious stimuli. During acute inflammation release of inflammatory mediators such as cytokines, growth factors, and enzymes by inflammatory cells such as neutrophils, DCs, NK cells, etc results in tissue repair and regeneration. Whereas if the inflammation is aggravated chronically, smoldering, dysregulated resulting in cell injury, tissue damage, immunomodulation, by inflammatory mediators such as cytokines, growth factors, and proteolytic enzymes released by chronic inflammatory cells such as macrophages, T cells, and B cells leading to tumor initiation, tumor promotion, and tumor progression by constitutive activation of key transcription factors such as NF-KB and STAT3.

Interactions between inflammatory mediators; Immune cells; Epithelial cells; and connective tissue in acute inflammatory tumor microenvironment

Inflammation is the human body's response to noxious stimulating agents. During initial inflammation predominantly neutrophils, followed by DCs, NK cells, macrophages, and mast cells [4, 5]. Chemokines generated by leucocytes attracted these inflammatory cells to the site of inflammation. Immune cells including neutrophils, macrophages, and epithelial cells are involved in cell regeneration, repair, and antibacterial activity by releasing low doses of H2O2 [6, 7].

Growth factors such as EGF, FGF, VEGF, and PDGF, from immune cells involved in cell proliferation, angiogenesis, and collagen synthesis by fibroblast involved in cellular regeneration by activation of NF-KB and STAT-3 transcription factors [8, 9]. NK cells are natural killer cells involved in the release of opsonin, granzyme-B, and IFN-ϒ, without prior antigenic stimulation leads to apoptotic activity, anti-inflammatory, antiviral, and anti-tumor activity [10, 11].

DCs and macrophages are innate immune cells involved in long-lasting memory immunity and antibody release [12, 13].

Pro-inflammatory IL-1, TNF-α, and IL-6 cytokines are involved in the activation of NF-KB, a ubiquitous transcription factor of anti-inflammatory and immune stimulatory activity by releasing (IL-2, IL-12, IFN-ϒ) and also development, maturation of innate and adaptive immune cells [7-9].

Interactions between inflammatory mediators; Immune cells; Epithelial cells; and connective tissue in chronic inflammatory tumor microenvironment

If the inflammation is chronically aggravated, smoldering, constitutive, dysregulated, abnormal activation of NF-KB, a key transcription factor involved in the transcription of inflammatory mediators results in protumoral activities [10, 11, 14]. In chronic inflammation, predominant cells are macrophages later T cells and B cells involved in the release of growth factors, proteolytic enzymes, chronic inflammatory mediators - cytokines involved in cell and tissue injury, immunomodulation, genomic instability, cell proliferation, cell survival, and angiogenesis. Dysregulated constitutive activation of NF-KB along with STAT-3 key - transcription factors involved in cell proliferation (cyclin D, E), cell survival (BCL-2, BCL-XL), angiogenesis (IL-8, COX-2, HIF-1α, VEGF), genomic instability (ROS, RNS, AID, Arginase1), immune modulation (IL-3, IL-4, IL-5, IL-13, IL-15, IL-17) and invasion and metastasis (UPA, MMp's) [15-18].

Transformed induced T regulatory cells (A Tregs) are present in immunomodulation formed by Th1 cells mediated by IL-10 release through TGF-β. B cells producing IL-10 are called Bregs mediated by TGF-β involved in immunomodulation. NF-KB, transcription factor monitors up to 500 genes and above and also acts opposing to p53, an Onco suppressor gene mutated by NO, RNS, and ROS, inflammatory mediators [19-21].

CONCLUSION

Inflammation is defensive in an acute stage and offensive at a chronic stage. Intricate interaction between various inflammatory-immune-immune-epithelial cells involved in various changes from cell repair and regeneration to cellular injury, tissue injury, vascular changes, and immunomodulation leads to tumor progression. A thorough understanding of acute and chronic inflammatory microenvironment and their mediators and interactions with other epithelial cells and vascular tissue helps us to understand tumor prevention, therapeutic, and prognosis for better management of patients.

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REFERENCES

[1] Freddie B, Jacques Ferlay ME, Isabelle S, Rebella LS, Lindsey AT, Ahmedin J. Global cancer statistics 2018: globocon estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424.

[2] Shrihari TG. Dual role of inflammatory mediators in cancer. Ecancermedicalscience. 2017;23(11):1-9.
[3] Furman D, Campisi J, Verdin E, Carrera-Bastos P, Targ S, Franceschi C, et al. Chronic inflammation in the etiology of disease across the life span. Nat Med. 2019;25(12):1822-32.
[4] Zhao H, Wu L, Yan G, Chen Y, Zhou M, Wu Y, et al. Inflammation and tumor progression: signaling pathways and targeted intervention. Signal Transduct Target Ther. 2021;6(1):263.
[5] Glanben L, Marjorie DF, Peti T, Chanitra T, Marcela AH. Chronic inflammation and cytokines in the tumor microenvironment. J Immunol Res. 2014;6:1-20.
[6] Schmitt M, Greten FR. The inflammatory pathogenesis of colorectal cancer. Nat Rev Immunol. 2021;21(10):653-67.
[7] Greten FR, Grivennikov SI. Inflammation and cancer: triggers, mechanisms, and consequences. Immunity. 2019;51(1):27-41.
[8] Shrihari TG. Innate and adaptive immune cells in tumor microenvironment. Gulf J Oncol. 2021;1(35):77-81.
[9] Liu J, Zhang X, Cheng Y, Cao X. Dendritic cell migration in inflammation and immunity. Cell Mol İmmunol. 2021;18(11):2461-71.
[10] Su H, Kang Q, Wang H, Yin H, Duan L, Liu Y, et al. Fan changes in expression of p53 and inflammatory factors in patients with ulcerative colitis Exp. Ther Med. 2019;17(4):2451-6.
[11] Das D, Karthik N, Taneja R. Crosstalk between inflammatory signaling and methylation in cancer. Front Cell Dev Biol. 2021;9:756458.
[12] Nouri Z, Fakhri S, Nouri K, Wallace CE, Farzaei MH, Bishayee A. Targeting multiple signaling pathways in cancer: the rutin therapeutic approach. Cancers. 2020;12(8):2276.
[13] Shrihari TG. Inflammation related cancer-Highlights. J Carcinog Mutagen. 2016;7(269):2.
[14] Korniluk A, Koper O, Kemona H. Dymicka-Piekarska. From inflammation to cancer. Ir J Med Sci. 2016;10:45-52.
[15] Lippitz BE. Cytokine patterns in patients with cancer: a systematic review. Lancet Oncol. 2013;14(6):e218-28.
[16] Shrihari TG, Ramesh DN. Chronic inflammation induced immunosuppression in Tumor microenvironment of oral cancer. Global J Med Res: J Dentist Otolaryngol. 2016;16:1-8.
[17] Li Y, Huang H, Liu B, Zhang Y, Pan X, Yu XY, et al. Inflammasomes as therapeutic targets in human diseases. Signal Transduct Target Ther. 2021;6(1):247.
[18] Sharma BR, Kanneganti TD. NLRP3 inflammasome in cancer and metabolic diseases. NatImmunol. 2021;22(5):550-9.
[19] Hou J, Karin M, Sun B. Targeting cancer-promoting inflammation—have anti-inflammatory therapies come of age? Nat Rev Clin Oncol. 2021;18(5):261-79.
[20] Shrihari TG. Dual role of cytokines in tumor microenvironment. J Cancer Prev Curr Res. 2022;13(5):141-3.
[21] Liu J, Hong M, Li Y, Chen D, Wu Y, Hu Y. Programmed cell death tunes tumor immunity. Front Immunol. 2022;13:847345.