Short Comunications

Causality: autoimmunity and cancer

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SUMMARY

Introduction: The effectors of autoimmune diseases are the mechanisms of hypersensitivity. These processes also appear in cancer, which can give rise to autoinflammation.

Objective: To describe the causality between autoimmune diseases and cancer.

Methods: A literature review was performed using the Google Scholar and articles freely available on the basis of PubMed and Scielo January 2014 to February 2018. Data search terms were used as descriptors of the DeCS and MeSH.

Developing: Autoimmune diseases are chronic inflammatory processes caused by failures in tolerance. The mechanisms and specific processes that initiate the damage are still unknown. The activity of inflammatory cells and soluble pro-inflammatory mediators leads to a greater recruitment of endothelial cells and promotes angiogenesis. Persistent inflammation (chronic or low grade) can often promote tumor development, tumor progression and invasion. In the tumor environment there is release of molecular patterns associated with damage (DAMPs), which mimic a sterile lesion and recruit cells of innate immunity, which can promote an inflammatory environment and cause an autoimmune phenomenon.

Conclusions: Inflammatory responses can improve tumor growth and progression. Cancer can develop self-immunity or arise secondary to the genetic and epigenetic changes of autoinflammation. The causality between cancer and autoimmunity is bidirectional, they perpetuate themselves and are the product of inflammatory processes.

Keywords: autoimmunity; cancer; inflammation; autoimmune diseases.

INTRODUCTION

Autoimmune diseases occur due to failures in tolerance, originating autoreactive antibodies and lymphocytes. This hypersensitivity response constitutes the physiopathological mechanism that leads to the underlying inflammatory process. They affect a large part of the population, with predominance in the female sex.[1,2]

The specific mechanisms and processes that initiate the damage are still unknown. In living beings the complexity of interactions makes the cause-effect relationship not unidirectional.[1,2]

Although the adaptive immune system orchestrates the autoimmune response, the innate is vital to sustain the pathological response. The activation of the complement system and the secretion of inflammatory mediators can exacerbate tissue damage. These processes also appear in cancer, which can even give rise to autoinflammation. The mechanisms of hypersensitivity are basically the effectors in these entities.[3,4]

Taking into account the lack of integration of knowledge on this subject, the present work was carried out with the objective of describing the causality between autoimmune diseases and cancer.

DEVELOPING

Initially, in order to remove the cancer, macrophages and other innate immune cells produce and release proinflammatory factors, which stimulate the proliferation of local tissue and endothelium in order to replace dead cells during acute stages of neoproliferation.[5]

From autoimmunity to cancer

Chronic inflammation is the persistence over time and intensity of these factors can promote the development, progression and tumor invasion. The inflammatory environment is an essential component of all tumors and it is evident that autoimmunity is associated with chronic inflammation.[6]

The role of is primarily inflammation through two mechanisms in the projecting cells of the innate immune system: (a) secretion of cytokines, chemokines, growth factors and (b) the production of reactive oxygen species (ROS) and nitrogen (NO), capable of causing genetic or epigenetic damage. Where there is no pre-existing cancer, sustained and prolonged inflammation can recruit cells of the innate immune system, such as neutrophils, capable of effecting these mechanisms.[2,4,5]

The association between long-term alcohol abuse and inflammation correlates with different neoplasms. They can be mentioned as liver, pancreas; inflammatory bowel disease with increased risk of colon cancer, persistent pulmonary inflammation from exposure to asbestos or silica and lung cancer.[7]

Therefore, prolonged inflammatory responses may act as a driver of malignant transformation and, when inflammation occurs after a tumor has already been established, it may also promote tumor growth through the production of inflammatory cytokines.[4]

From cancer to autoimmunity

Do tumors cause a self-inflammatory response? The inflammatory environment can easily be exploited by tumors for the selection of cells capable of provoking an inflammatory response, by the recruitment of innate immune cells.[6]

Secondly, because, at some point during the formation of tumors, the blood supply becomes limiting due to the increase in size, so that a large amount of necrotic cell death will occur within the tumor, which will lead to the release of molecular patterns associated with damage (DAMPs). These patterns mimic the sterile lesion and contribute to the recruitment of innate immune cells in the tumor.[5]

In another scenario, where there is an established cancer, the production by the tumor of factors that recruit neutrophils and macrophages (LCR-1, CCL2, IL-8), can re-recruit innate immune cells to adapt to the range of mitogenic factors, repairers and angiogenic. These, in combination with ROS and NOS-producing neutrophils and macrophages, can help the tumor to progress and be more aggressive by acquiring new mutations and a more robust blood supply.[2]

In both scenarios, the cells of the innate immune system help protect the tumor from any T cell response through the creation of an immunosuppressive or tolerogenic environment in the tumor bed (see Table 1).[2,3,4]

Table1. Cytokines with pro-tumor functionsTNF-α: associated with direct DNA damage; regulates the expression of antiapoptotic gene products (members of the Bcl-2 family); mediates chronic inflammation; promotes malignant transformation in various organs; stimulates growth, angiogenesis, proliferation and tumor invasion.

IL-6: paracrine action in stromal cells, promotes angiogenesis, correlates with a worse prognosis in breast cancer.
IFN-γ: mediates chronic inflammation in the gastric epithelium, protects cancer cells from lysis by CTL by altering the expression of MHC.
TGF-β: induces tolerance, recruits' type 2 macrophages (M2) and neutrophils, promotes the differentiation and recruitment of Treg in the tumor microenvironment, promotes cancer cell metastasis and invasion, suppresses the antitumor response as it inhibits Th1 signaling.
IL-17 / IL-23: mediates chronic inflammation, in the liver, leads to the differentiation and proliferation of Th17 cells in the tumor microenvironment that are shown in favor of tumor growth and suppression the immune response, activates proliferation and survival tumor.
IL-4 / IL-13: leads to the tolerogenic differentiation of CD4 Th2 lymphocytes in the tumor microenvironment, recruit's tumor-associated macrophages (M2) and dendritic cells.
IL-8 (derived from tumors): promotes tumor infiltration by neutrophils and macrophages, stimulates production of other proinflammatory cytokines (IL-1β, TNF), promotes tumor growth, remodels the extracellular matrix, promotes tumor dissemination.

CONCLUSIONS

Chronic inflammatory responses can improve tumor growth and progression. Cancer can develop self-immunity or arise secondary to the genetic and epigenetic changes of autoinflammation. The causality between cancer and autoimmunity is bidirectional; they perpetuate themselves and are products of inflammatory processes.

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