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REVIEW ARTICLE

Allergies: diseases closely related to cancer

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Abstract Allergies are hypersensitivity reactions that occur through specific type Th2 immunological mechanisms characterized by different soluble mediators, as well as specific cells of the immune system. In recent decades, evidence has emerged relating this disease with cancer development. However, most of the results of epidemiology studies have been controversial and contradictory. There are mainly two trends. While the first indicates that allergies can reduce the risk of cancer, the other indicates that they may increase this risk. The first trend can be explained by the immunosurveillance hypothesis, which states that the increased immune surveillance after the immune hyper-responsiveness can inhibit or exert a protective effect against the development of cancer. Similarly, the prophylaxis hypothesis suggests that the physical effects of allergy symptoms can prevent cancer by removing potential carcinogens.

In contrast, the opposing hypothesis propose that there is a deviation of the immune response toward Th2, which favors the development of cancer, or that the process of chronic inflammation favors the generation of mutations, and therefore the development of cancer.

With the purpose of understanding more about these two hypotheses, the main soluble and cellular factors of allergic diseases that could be playing a key role in the development or inhibition of cancer were considered in this review.

PALABRAS CLAVE
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Alergias: enfermedades estrechamente relacionadas con el cáncer

Resumen Las alergias son reacciones de hipersensibilidad que ocurren mediante mecanismos inmunológicos específicos de tipo Th2. Se caracterizan por distintos mediadores solubles, así como células específicas del sistema inmune. En las últimas décadas ha surgido evidencia que asocia esta enfermedad con el desarrollo de cáncer. Sin embargo, los resultados obtenidos, en su mayoría de estudios epidemiológicos, han sido controversiales y contradictorios. Lo anterior se debe a que existen dos principales tendencias. Mientras algunos estudios han demostrado que las

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alergias pueden reducir el riesgo de cáncer, otros estudios muestran que puede aumentarlo. Lo primero puede explicarse por la hipótesis de inmunovigilancia, que establece que el aumento de la vigilancia después de la hiperreactividad inmune puede inhibir o ejercer un efecto protector contra el desarrollo de cáncer. Del mismo modo, la hipótesis de la profilaxis sugiere que los efectos físicos de síntomas de las alergias pueden prevenir el cáncer mediante la eliminación de los carcinógenos potenciales. Las hipótesis opuestas proponen que existe un desvío de la respuesta inmune hacia Th2 lo cual favorece el desarrollo del cáncer, o que el proceso de inflamación crónica favorece la generación de mutaciones, y por tanto el desarrollo del cáncer. Con el propósito de entender más acerca de estas dos hipótesis, en esta revisión se consideraron los principales factores solubles y celulares de las enfermedades alérgicas que pudieran estar desempeñando un papel clave en el desarrollo o inhibición del cáncer.

1. History of allergic diseases

Allergic diseases have been present throughout human development, and are the reason why it has been vital to continue the study and research of a large bouquet of diseases that conform to allergies.

In 1913, Charles Richet and Paul Portier discovered allergies, or anaphylaxis, when they tried to immunize a dog with actinia extracts several times. The animal showed some tolerance and maintained good physical condition after four injections. However, 25 min after the final exposure (22 days later), the dog suddenly deteriorated and died. This fact gave rise to the discovery of anaphylaxis because it showed that immunization could acquire, not only protection, but also induce detrimental effects. A significant advancement in understanding anaphylaxis was made through the experiments of Dale and Laidlaw, who showed that histamine was able to induce very similar symptoms.[1]

At the beginning of the 21st century, both the European Academy of Allergy and Clinical Immunology (EAACI) and the World Allergy Organization (WAO) defined the concepts of anaphylaxis based on a clinical symptom-independent mechanism due to many outstanding contributions.[2] Therefore, it is now possible to distinguish between an allergy, and immune anaphylaxis, formerly called 'pseudo-allergic' reactions.

Currently, anaphylaxis prevalence appears to be increasing worldwide, perhaps due to pollen, food allergies, and the increasing prevalence of atopic diseases. Since anaphylaxis describes a syndrome of clinical symptoms involving multiple organ systems with greater or lesser intensity, attempts have been made to classify the severity of this reaction using the severity scales, such as the Mueller[3] and the Messmer.[1]

Asthma is defined as a chronic allergic airway inflammation disease leading to various degrees of inflammation. This disease affects millions of people worldwide. Airway Inflammation in asthma is mediated by T-helper type 2 (Th2) cytokines, basophils, eosinophils, and mast cells.[4] IL-4, IL-5, and IL-13 cytokines have a prominent role in the inflammatory asthma cascade. Also, they have chemoattractant properties for rapid accumulation of macrophages, granulocytes and other cells to the site of inflammation.[5]

2. AllergoOncology

For several decades, the biological relationship between cancer and allergies has brought epidemiological, oncological and immunological interest to researchers. Numerous studies show a complex association, which has not been fully elucidated so far due to the varied results. Allergy, or atopy, is considered a hypersensitivity reaction initiated by specific immunologic mechanisms, which involve various soluble mediators such as cytokines, chemokines, specific immunoglobulins (IgE, IgG), as well as the activation and effects of the immune system cells as Th2, Th17, eosinophils, mast cells and others.

Immune hyper-responsiveness is usually assumed to reflect a change in T cell response away from Th1 type to a principal activity of Th2. Even diseases mediated by Th1 and induced Th2 disorders coexist in different pathologies such as diabetes and cancer.[6,7]

Theoretically, the hyper-reactive state atopy might be accompanied by enhanced immune surveillance, leading to a better detection and destruction of malignant cells, and therefore, a decreased risk of cancer. In contrast, an increased incidence of cancer might result from repeated tissue inflammation in atopic patients, which in turn could be linked to repeatedly damaged tissues.[8] To better understand the mechanisms involved in the relationship between cancer and atopy, several studies have suggested various and often contradictory epidemiological findings. On this basis, the following four different immunologic hypotheses have been proposed:

1. *Chronic inflammation or antigen stimulation hypothesis*. This hypothesis suggests that the inflammatory conditions associated with—and often secondary to—allergic disease may promote cancer development by inducing oxidative damage, resulting in mutations of tumor