

A Review Article: Hypersensitivity and its Disorders

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ABSTRACT

Hypersensitivity reactions are a set of reactions in which the immune system performs a protective function while also producing an inflammatory consequence. In most cases, both autoimmunity and sensitivities have been responsible for hypersensitivity reactions. In autoimmune contagion, the immune system reacts directly to tissues inside the body, while in sensitivities, the immune system reacts to parts of the environment that are shared. In general, allergic reactions have been put into four groups (Type I, Type II, Type III, and Type IV). This study focuses on hypersensitivity-related illnesses and the role of the immune system in these conditions.

Keywords- Hypersensitivity; Anaphylaxis, Allergies; Autoimmune reaction.

I. INTRODUCTION

The immune system's primary function is to defend the body against foreign organisms including bacteria, viruses, and fungi; however, an overactive immune response can cause illness. Hypersensitivity reactions is the common name for the overactive immune responses [1]. The human immune system has always been an important line of defense against pathogens, but its common defensive mechanisms can occasionally backfire and cause harm to the person [2]. Immunopathology is the study of such reactions, of which the most well-known is the allergic reaction. Those who have been exposed to an antigen in the past are thought to have shown late but noteworthy reactions to that antigen, and therefore are assumed to be well-informed [3].

It's possible to induce hypersensitivity reactions by either exposing yourself to your own self-antigens or to outside antigens. Autoimmune diseases are influenced by the immune system's reaction to endogenous antigens [4]. Exogenous antigens like bacteria and non-microbial components (such as drugs, foods, pollens, chemicals, and dust) can trigger an immune response that can take many forms. Sensitivity refers to the collection of illnesses caused by responses to exogenous antigens, and

its symptoms can range from itching and rash to fever and asthma to life-threatening anaphylaxis [5].

1.1. Types of reactions to hypersensitivity:

According to the original Gell and Coomb's categorization, there are four different types of hypersensitivity responses, each characterized by a distinct immune reaction and activation mechanism that causes cell and tissue harm [6].

1.1.1. Type I (immediate or IgE mediated):

Parasitic infections trigger the production of IgE antibodies, which coupled with eosinophil activation serve primarily protective purposes and aid in the elimination of the parasites. Atopic individuals may develop IgE antibodies specific to environmental, dietary, and medication [7], [8]. As a result, IgE antibodies are produced and bind to basophilic and mast cell surfaces that have high-affinity IgE receptors. When exposed again, IgE antibodies are linked to mast cells and basophils, which triggers these cells and causes an immediate hypersensitive response. In most cases, the immediate hypersensitive response is divided into two phases, which comprise the following:

1. A rapid reaction that takes place in a few minutes and is brought on by histamine, prostaglandin D₂, leukotriene D₄, and kinins (and tryptase).

2. A delayed reaction that takes place after four to eight hours and is caused by cytokines such as interleukin-1, tumor necrosis factor, interleukin-4, interleukin-5, and interleukin-13, as well as other colony-stimulating agents such as granulocyte monocyte colony-stimulating factor. Eosinophils and neutrophils may also play a role in the production of the full spectrum of the immediate hypersensitivity response, in addition to mast cells and basophils. [6]. Anaphylaxis, bronchial asthma, and urticaria are all examples of immediate hypersensitivity reactions. Anaphylaxis is characterized by dilatation of the blood vessels and constriction of the airways, and it can occur in response to allergens that are present in foods such as nuts and milk. Bronchial asthma can be caused by repeated immediate hypersensitivity and late-phase reactions in the lung tissue. Urticaria is a wheal and flare (erythema) [9] [10] [11].

1.1.2. Type II (cytotoxic or IgG/IgM mediated):

Immune reactions, which often serve to protect the body against infections and eliminate cancerous cells, have the potential to occasionally damage the tissues of the body. Antibodies of the IgG, IgM, and, to a lesser extent, IgA classes are typically involved in the immunological responses. Antibodies are typically targeted towards cell surface antigens such those found on RBCs, neutrophils, and platelets, as well as those found on the epithelial cells that line glandular and mucosal surfaces. There are generally three basic mechanisms that cause the tissue injury.

1. Coating or opsonizing cells with antibodies can be done in two ways: either directly through the antibody itself, or indirectly through the complement system, which can then produce activated complement components that can coat or opsonize the cells. These opsonized cells are taken in by phagocytes, which have receptors for antibodies and complement proteins and destroy them. A good example is the underlying cause of autoimmune hemolytic anemia and autoimmune thrombocytopenic purpura [12].

2. Antibodies that are deposited in tissues eventually attract neutrophils and macrophages, which ultimately results in damage to the tissue as well as inflammation. This is the process of damage that occurs in glomerulonephritis that is mediated by antibodies.

3. The third type of immunological reaction is called antibody-dependent cell mediated cytotoxicity, and it takes place when eosinophils connect to IgE-bound helminths and then liberate the granule elements that are contained in their bodies. In addition, there are two distinct subtypes that can be assigned to type II reactions: Type IIa reactions are distinguished by the production of cytolytic reactions by antibodies, which ultimately results in autoimmune hemolytic anemia. Type IIb reactions are distinguished from type I reactions by the presence of cell-stimulating antibodies in patients with Graves disease (long-acting thyroid stimulator, thyroid-stimulating hormone receptor

antibodies) or antibodies to the high-affinity mast cell receptor (FcRI) or IgE in patients with chronic idiopathic urticarial disease. [9].

1.1.3. Type III (IgG/IgM immune complex mediated):

The creation of IgG or IgM antibodies to self or foreign antigens, followed by the formation of complexes, is the process of tissue harm during a type II immune response [13]. With complex deposition and activation of the complement system, serum complement levels decrease. Inflammation and tissue damage arise when the activated complement components recruit and further stimulate neutrophils. The antigen's origin has no bearing on the constellation of symptoms, which is instead dictated by the location of immune complex deposition. Vasculitis, nephritis, and arthritis are common manifestations of the antigen-antibody complexes typically seen in tiny arteries, renal glomeruli, and synovial of joints. [14]. One such condition is one that resembles serum sickness and may have an acute course, or it may have a more protracted or chronic one instead. On the other hand, the first instances of this archetypal immune complex-mediated illness were found in people who had diphtheria infections. These patients were given serum from horses that had been inoculated with the diphtheria toxin in order to provide them with passive immunization [15]. The serum had antibodies against the diphtheria antitoxin. Tissue accumulation of antigen-antibody complexes has been linked to a number of autoimmune disorders. Systemic lupus erythematosus is an autoimmune illness that causes the body to develop a large number of antibodies against DNA and nucleoproteins. These antibodies form complexes with antigens, which subsequently deposit themselves in the tissues and cause an inflammatory reaction [16].

1.1.4. Type IV (delayed-type hypersensitivity or T-cell mediated):

The sensitized T cells are involved in type IV reactions. The type IV reaction that Gell and Coombs identified, also known as delayed-type hypersensitivity, is a Th1 type of response that is mediated by CD4+ T helper cells and is characterized by its delayed onset. At the moment, we refer to this answer as type Iva. Lysosomal enzymes, reactive oxygen intermediates, nitric oxide, and proinflammatory cytokines are the primary agents responsible for the damage to the tissue [17]. Activated macrophages are also a contributing factor. The formation of scar tissue is frequently caused by the release of cytokines and growth factors. There is some evidence that a delayed hypersensitivity reaction plays a role in the etiology of a variety of disorders. For example, in type I diabetes, lymphocytes and macrophages may be responsible for the destruction of insulin-producing islet cells. In multiple sclerosis, an autoimmune disease that affects the central nervous system, T cells react against myelin antigens. In rheumatoid arthritis, an inflammation may be caused by

T cells. By counting the T-cell subsets, the type IV immune responses can be put into even more groups. This grouping into four subtypes—IVa, IVb, IVc, and IVd—is based on the different cytokine profiles, cell types involved, and how the disease develops [18]. One example of a type IVa reaction is contact dermatitis, which can be caused by poison ivy Rhus antigen. This response is mediated by Th1 type T cells, which stimulate macrophages to become activated by producing high quantities of cytokines, such as interferon- and tumor necrosis factor. Following a Th2 type immune response, type IVb responses might occur. Keratinocytes can either undergo apoptosis or necrosis when activated CD8+ T lymphocytes are present, depending on the situation. Neutrophilic inflammation brought on by T cells characterizes reactions of the type IVd subtype. A common instance of this is found in patients with acute widespread exanthematous pustulosis, when there is sterile neutrophilic inflammation of the skin. The development of superficial pustules following the administration of a medicine or the introduction of an infection is a hallmark of acute

widespread exanthematous pustulosis [19]. In this condition, T-cell-derived CXCL-8 is responsible for recruiting neutrophils to the lesion, while granulocyte monocyte colony-stimulating factor produced by T cells is responsible for preventing neutrophils from going into apoptosis after being recruited. The synthesis of IgE from B cells, the deactivation of macrophages, and the responses of mast cells and eosinophils are all facilitated by Th2 cells, which are responsible for the production of the cytokines IL-4, IL-5, and IL-13. In the late phase of allergic inflammations of the bronchi or nasal mucosa, type IVb reactions may play a role (i.e., allergic rhinitis, and asthma). Cytotoxic CD8+ T lymphocytes are primarily responsible for mediating type IVc responses. Bullous skin reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis, appear to be mostly caused by type IVc reactions. In addition, IL-17 and IL-22 encourage the synthesis of IL-8, which helps to maintain an adequate number of neutrophils in areas of inflammation. There are also conditions such as Behcet illness and pustular psoriasis that are instances of type IVd reactions.

Table 1: Modern methods to classify allergic reactions

Classification/ Type	Immunologic Mechanisms	Clinical Examples
I	Activation of mast cells IgE-dependent (anaphylactic) (anaphylactic) not dependent on the immune system (gE-independent) (anaphylactoid)	Allergies can cause a wide variety of symptoms, including anaphylaxis, angioedema, urticaria, asthma, and rhinitis. Physiological Reactions to Iodinated Contrast Media and Many Biologicals
Ila	Cytotoxic reactions mediated by antibodies (IgG/IgM); complement is usually convoluted	Immune cytopenias
I Ib	Responses generated by antibodies that activate cells	The disease Graves as well as chronic idiopathic (natural) urticaria
III	Activation of the immune complex by the complement system	Vasculitis, serum sickness, and lupus that was triggered by medication
IVa	Stimulation of macrophages through the action of Th1 cells	Interaction dermatitis (with type Ivc), a positive tuberculin test reaction, and type 1 diabetes
I Vb	Eosinophilic infection that is mediated by Th2 cells	Exanthems maculopapulares, illness of the ovaries and testes, persistent asthma, and allergic rhinitis
IVc	mediated cytotoxicity by T cells responses	The SIS and/or TEN, bullions exathems
IVd	Neutrophilic infection mediated by T cells	Behcet's disease, and AGEP.

II. IMMUNOLOGICAL STUDY OF HYPERSENSITIVITY

Allergic IgE bound to the high-affinity Fc RI receptor on mast cells and basal cells has caused type I

immune responses. Cross-linking of these receptors by allergens releases mediators (such as histamine), which in turn cause symptoms including angioedema, urticaria, and/or a feeling of extreme nausea and vomiting[20]. IgG and IgM that are required to recognize self antigens on the surface of cells are considered to cause type II

responses, which can lead to tissue damage by the activation of phagocytosis, complement-immediate cytotoxicity, and/or antibody-dependent cell-mediated cytotoxicity[21]. Developments in the immune system, such as IgG/IgM and antigens, mediate type III responses, which involve the deposition of antibodies in tissues and the subsequent direct harm to organs[22]. As a late reaction driven by T lymphocytes, Type IV responses can be further subdivided into four subtypes [22].

In general, allergic disorders that are associated with eosinophilia are those in which an immediate-type hypersensitivity reaction is prominent. This refers to reactions that include mast cells that have been sensitized by IgE and are triggered by certain allergens. There is a growing interest in the involvement of the eosinophil, particularly eosinophil granule-derived enzymes, in eosinophilic endomyocardial illness and in the cardiomyopathy that is frequently encountered in connection with the hyper-eosinophilic syndrome [23].

III. CLINICAL STUDY

Different kinds of allergic reactions can be caused by different drugs, like penicillins. There are four different kinds of hypersensitivity reactions that can be caused by antibiotics: Type I reactions are caused by IgE and could cause anaphylaxis this is in concomitant with [24] study ; Type II reactions are caused by antibodies and can lead to low platelets, low neutrophils, or hemolytic anemia; Type III reactions, like vasculitis, involve the formation of an immune complex. Type IV reactions have four subtypes and usually involve a rash of varying severity, with or without other signs and symptoms in the body[25]. There is currently no medicine that has been discovered that can effectively prevent IgE-mediated reactions. Medicines such as H1 antihistamines and corticosteroids can only attenuate the effects of certain intermediaries, not all of them [26] . It is possible to prevent anaphylactic reactions to certain substances, such as iodinated contrast media, by treating patients in advance with corticosteroids and H1 antihistamines. These substances do not use the IgE protein as a mediator.

An excellent example of a temporary immune complex-mediated disorder is the condition known as serum sickness. An antibody response is triggered when a foreign protein or proteins are injected into the body. These antibodies join forces with the circulating foreign proteins to create immune complexes. These complexes are what cause fever and the symptoms of vasculitis, nephritis, and arthritis. They are deposited in small capillaries, where they stimulate complement and phagocytes and cause deposition in the vessels. All of these symptoms are very temporary and will disappear after the foreign protein has been eliminated[27]

IV. DISCUSSION

Immunology play an important role in pathogenesis of hypersensitivity disorders. Diseases characterized by hypersensitivity are the result of normal immune systems that are directed against harmless antigens, this is in concomitant with [28] study. They can be mediated by IgG antibodies that are coupled to changed cell surfaces, or they can be caused by complexes of antibodies that are bound to inadequately catabolized antigens, like what happens in serum sickness this is in concomitant with [17] study. T cell-mediated hypersensitivity reactions are triggered either by injected proteins like those found in the mycobacterial extract tuberculin, or by modified self proteins. Delayed-type hyper-sensitivity refers to T cell-mediated responses that develop more slowly because they require the stimulated production of effector molecules. An allergic reaction to food, insecticide, spores, or medication is not unprecedented. Several clinical studies, including the HLA Quadruple and microarray methods, have shown promise in facilitating clinical presentation for hypersensitive response. Anaphylaxis, the most severe reaction to a food allergen, is caused by a two-stage process: an initial, rapid response to the allergen followed by a delayed, more gradual reaction many hours later, this is in concomitant with [29] study. The symptoms experienced during the acute phase of a reaction are caused by the release of preformed mediators, while the symptoms experienced during the late phase of a reaction are caused by the infiltration of inflammatory cells. In the clinic, patients' responses vary widely; some have only the acute phase, while others experience it along with the late phase, this is in concomitant with [30] study. Anaphylactic reactions can be triggered in a variety of ways, adding to the already-varied clinical contexts in which they occur, this is in concomitant with[31] study.

V. CONCLUSION

An excessive immune reaction to a foreign substance that leads in inflammation and organ malfunction is referred to as hypersensitivity. In general, hypersensitivity disorders can be broken down into two categories: antibody-mediated reactions and T-cell-mediated reactions. The inflammatory pathways that result in disease are activated in an antigen-specific manner through Fab sections of antibodies or the T-cell receptor. This causes the up-regulation of effector mechanisms that are supposed to eliminate the offending substance.

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