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An insight into the little-known, menacing facts of autoimmune disorder

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Abstract

Autoimmunity is a misguided immune response that occurs when the immune system becomes disorganized and attacks the body. While autoimmunity is prevalent to some extent in most of us, it is often harmless. This immune response can sometimes cause a wide range of diseases known as autoimmune diseases. Autoimmune diseases start when there is a development from submissive autoimmunity to pathogenic autoimmunity. This progression is influenced by both genetic and environmental factors and mostly remains dormant for a period. A sudden recurrence of emergencies occurs with few options for survival. When T or B-cells or both get stimulated in the absence of infection, it results in a state where the immune system is unable to distinguish between self or non-self. This results in the efflux of immune cells leading to the destruction of self-molecules. The exact process governing this event is still inconclusive, but the research done so far predicts that genetics, habitat, and infections must be major causes of abnormal activation of the autoimmune reaction.

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INTRODUCTION

Autoimmune (AI) diseases are a combination of diseases occurring due to the disruption of the marginal safety line existing amidst immunity and tolerance. When T or B-cells or both get stimulated in the absence of infection, it results in a state where the immune system is unable to distinguish between self or non-self [1]. The deranged immune cells create a dangerous situation for self-molecules leading to severe destruction. The exact process governing this event is still inconclusive, but the research done so far predicts that genetics, habitat, and infections must be major causes of abnormal activation of the autoimmune reaction [2]. It is surprising to know that common ailments like atherosclerosis and gastrointestinal disturbances are also connected with an autoimmune component, which could be a warning for acquiring an autoimmune disease [3].

Fundamentals of the Immune System

The immune system is an intricate accumulation of immune cells programmed to protect the body from harmful pathogens only and not to react against the body itself. The hematopoietic stem cells synthesize immune cells that transform into lymphoid and myeloid cells formed of B & T-

lymphocytes, polymorphonuclear leukocytes, monocytes, mast cells, macrophages, natural killer cells (NKs), and dendritic cells. These immune cells are in continuous task to protect the body and attack a pathogenic substance. This action solely depends on the receptors present in T and B-cells, which are capable of recognizing non-self-molecules from the self. Anomalous levels of cytokines have a strong impact on triggering and the advancement of autoimmune diseases. Moreover, the medications used for therapy interfere with exogenous cytokines and have a link in disease progress. This implies that medical interventions play a key role in disease progression [4].

Immune Tolerance

Immune tolerance is a state where the immune cells show no response to specific antigens to prevent the immune system from being destructive due to over-reactivity. It prevents an immune response to antigens synthesized by the body itself or prior encounter recognition. Immune tolerance is of two types: self-tolerance and induced tolerance. Self-tolerance refers to the nature of the immune system to identify and therefore not react against self-produced antigens. An immune system devoid of this ability could mislead the body to attack its cells, initiating an autoimmune disease. Induced tolerance happens when the immune system stops responding to an external antigen. This tolerance is instigated by previous confrontations with that antigen. One example of such tolerance is an intentional manipulation of the immune system to prevent the rejection of transplanted organs or to give protection from untoward allergic reactions.

Central Tolerance vs. Peripheral Tolerance: An Insight

Immune tolerance mechanisms are of two categories: central tolerance and peripheral tolerance. These pathways occur at different stages of the lifecycle of lymphocytes, and a defect in either pathway can result in dangerous consequences for the body. Central tolerance processes occur in the lymphocyte development phase, either in the bone marrow for B cells or in the thymus for T cells. Immune cells having T cell receptors (TCRs) or B cell receptors (BCRs) through this process can identify and bind to self-antigens, which are eliminated. Peripheral tolerance processes occur when mature lymphocytes enter the lymph nodes or other tissues. These mechanisms are supposed to stop autoreactive immune cells of central tolerance from causing damage to the periphery. This event prevents the immune system from acting irrationally towards self-antigens or non-harmful substances [5].

Autoimmune Triggers

A suggestive sign of an AI condition is symptoms that are unpredictable. When there is a sudden and severe onset of symptoms, it is called an AI flare, a characteristic of every AI patient. A flare is characterized by a measurable increase in disease activity. There are increased levels of AI markers during a flare. Every AI disease may exhibit different symptoms during a flare. In Crohn's disease, a flare is characterized by mouth sores, diarrhea, abdominal pain; nevertheless, each AI disease is identified by a set of symptoms. There are some common general symptoms: Heightened pain, Poor comprehension, Depression, Forgetfulness, Poor sleep, Exhaustion, Sadness, Anxiety, frustration, Foggy thinking.

During an AI flare, the regulatory T cells that control immune responses do not function properly to stop this immune system attack. This results in a lot of inflammation. Often, the triggers initiating AI disease are the triggers that bring about a flare. Considering that AI conditions persist forever, the initial treatment goal is to place the disease into remission. This is established by finding the root cause of AI conditions and providing personalized immune support to enhance T regulatory function. If a flare is seen, the aim is remission once again. Flares can last between weeks to months, unless the approach is modified to address them.

Triggers for Autoimmune Flares

People involved in functional medicine are aware that there is a reason behind any reaction that happens in the body. If one suffers from AI conditions, it is very important to have an idea of what can cause a flare. This will differ from person to person. A close review with the medical practitioner and a close observation of the change in circumstances the body faced just before a flare will solve the doubts about the disease progress

and its maintenance. Some possible triggers that can influence AI are listed below.

Stress: Stress is a basic trigger for many AI flares. A debate is still ongoing as to how it works, a common opinion is that it triggers neuroendocrine hormones, leading to immune dysregulation.

Seasonal changes: One of the contributors to AI flares. For instance, vitamin D deficiency in winter is related to an increase in disease activity in lupus, rheumatoid arthritis, multiple psoriasis, and sclerosis. Infectious diseases like Epstein-Barr virus are prevalent in winter, which can be correlated with lupus and multiple sclerosis flares [6]. An increase in leaf mold in the fall and pollen in the spring also triggers flares.

Diet: For every individual, food triggers are different. A variety of foods including legumes, corn, dairy, gluten grains, soy, nightshades, coffee, and/or eggs can be a trigger for a particular person. A close monitoring with the medical practitioner is required to assess what diet is apt for an individual.

Environmental toxins: Many environmental toxins and molds can induce AI disease and trigger AI flares. Hence it is crucial to be in close monitoring of the environment where we live and work, making possible changes to prevent these toxins.

Infections: Infectious diseases prevalent during seasonal changes can also cause flares in AI conditions. An underlying infection like mononucleosis, Lyme disease, flu pneumonia can act as a flare in neuropsychiatric syndrome in children. Many AI patients experience flares when they are unwell. If symptoms of a disease are not prominent, it is crucial to check for underlying infections like Epstein-Barr virus or Lyme.

Medications: Some medications also act as triggers for AI flares. A predominant medication that is expected to trigger flares is antibiotics since they can alter the microbiome in the body. It is a known fact that poor gut health is one of the causes of AI disease. Other medications include procainamide (anti-arrhythmic), methyldopa (anti-hypertensive), hydralazine (anti-hypertensive) [7].

Around ten percent of the worldwide population is affected by autoimmune diseases, among which the most common is systemic lupus erythematosus (SLE). In 1945, Drug-induced lupus erythematosus (DILE) was first reported with sulfadiazine as the causative agent [8]. From this period, around 90 medications belonging to 10 drug categories are reported to play a major role in causing lupus. DILE affects around 15,000 to 20,000 people each year and contributes to 10% of SLE cases [9][10].

Drug-induced autoimmunity (DIA) is an autoimmune condition, in which medication appears to be the environmental trigger. This relationship may act as a guide for investigators to understand the pathway that is responsible for specific immune dysregulation and cause awareness of autoimmunity [11]. Similarly, around 10% of cutaneous vasculitis is proclaimed to be drug-induced among which purpuric and maculopapular are considered most common [12].

Prevalence of autoimmune disease

Autoimmune diseases are generally considered uncommon, but their impact on morbidity and mortality are of consequence. The overall occurrence of autoimmunity is around 3–5% in the general population. Age is no bar for autoimmune diseases, but each disease has its own specific age of onset. In most patients, the occurrence is increased in first-degree relatives even highest in monozygotic twins. The frequency of autoimmune disease is more in women with a female-to-male ratio being 10: 1 to 1: 1 [Crohn's disease is an exception with a ratio of 1: 1.2].

Inheritable basis of autoimmune disease

The behavior of the immune system is affected by genes. Immunodeficiency disorders considered primary which are present at birth are sure to be inherited. This implies that they are linked to genes and are passed from one generation to another. There are few immune disorders which are diagnosed during or immediately after birth. Most of the immune disorders initially may not have symptoms and they may not be found until later in childhood or in adulthood. For example, one defective gene may stop certain cells which defend the body. Another such defect can block the toxic chemicals being removed from the body [13].

The perception of the genetic basis of human autoimmune disease has been explored widely in the last 15 years. Highly penetrant mutations are responsible for uncommon monogenic autoimmune disease syndromes that disrupt

essential mechanisms of central and peripheral immune tolerance. Genome-wide association studies (GWAS) give knowledge of immune dysregulation which is caused by common genetic variants that can cause a greater risk of autoimmunity [14].

Impact of habitat on autoimmunity: There are specific environmental factors that have a crucial role to play in an individual's susceptibility to autoimmune disease. These environmental factors include infectious processes and xenobiotics nutrition, the microbiota, ultraviolet light, such as tobacco smoke, silica solvents, pharmaceutical agents, hormones, heavy metals, vaccines, and collagen/silicone implants.

Exposure to harmful chemicals is also linked to autoimmune diseases according to research in the past. A range of factors including microbiome alterations due to chemical induction in the intestine could be linked with the etiology of autoimmune disorders. Previous research on this topic gives data that accounts for up to 70% of autoimmune disorders influenced by environmental factors. Solid evidence suggests the link between environmental agents like mercury solvents, pesticides, crystalline silica, pristine, and cigarette smoking for the occurrence ADs. Though the mechanisms in these links are not clear, evidence is strong enough suggesting a detailed evaluation of their role to determine the autoimmune pathogenicity [15].

The perils of nescience of autoimmune disorders

The lack of proper knowledge about autoimmune diseases can have several significant impacts, both on individuals who may be affected by these conditions and on society as a whole:

Delayed Diagnosis: One of the primary consequences of a lack of knowledge about autoimmune diseases is delayed or misdiagnosis. Many autoimmune diseases share symptoms with other conditions, and healthcare providers may not immediately recognize the underlying autoimmune cause. This delay can lead to a progression of the disease and potentially more severe complications.

Poor Self-Management: Understanding one's autoimmune disease is crucial for effective self-management. Patients may struggle to manage their condition properly, including adhering to medications and lifestyle changes, if they do not have a good grasp of the disease and its triggers.

Quality of Life Impact: Autoimmune diseases can significantly impact a person's quality of life. Lack of knowledge can lead to unnecessary suffering and reduced overall well-being for individuals with these conditions.

Mental Health Impact: Autoimmune diseases can be chronic and require ongoing management. A lack of knowledge about the disease can lead to frustration, anxiety, and depression in individuals who may feel overwhelmed by their condition.

Economic Burden: Autoimmune diseases often result in substantial healthcare costs. Misdiagnoses, unnecessary tests, and ineffective treatments due to a lack of knowledge can add to the economic burden on healthcare systems and individuals.

Novel therapies for autoimmune disorders

The new perspective in the therapy of autoimmune diseases is the utilization of biological agents that change the specific inflammatory and/or effector pathways. The goal for treating autoimmune patients is therapy with a specific agent that can completely reverse the disease. Currently, such treatment does not exist. Rather, it is believed that it might be possible to alter the host immune system to restore tolerance. Such an alteration is considered possible in chosen mouse models of autoimmunity, the efficacy is not proven in humans despite many attempts considering immune-therapy and stem cell therapies. Recently a better understanding of this disease has thrown knowledge on the possible changes that occur in individual patients when there is a violation of tolerance. Autoimmunity is a chronic disease with poor prognosis. The treatment scenario of these diseases has remarkably improved in the recent past and has a promising outcome that shall benefit the patients in the future [15].

CONCLUSION

To mitigate the impact of unawareness of these complex disorders, it is essential to raise awareness about autoimmune diseases, educating healthcare professionals, patients, and the general public in particular. Diligent and planned research is needed to improve our understanding of this disease condition. Enhanced knowledge can lead to

earlier diagnosis, optimal management, reduced suffering, and more effective treatments, ultimately improving the lifestyle of the population affected by autoimmune diseases.

Conflict of Interest

The authors declare no conflict of interest, financial or otherwise.

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