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A Review on Concomitant Immunity in Plasmodium

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Abstract

Malaria causes great morbidity and mortality, this implies that they can incompletely escape from protective effector mechanisms of their hosts, but also that hosts can develop partial immunity to the parasite. One of this natural acquired immunity is called premonition or concomitant immunity since a low parasitemia mostly persists in the presence of circulating antibodies to the various stages and in the absence of clinical disease. In children who do not have circulating antibodies to the parasite, concomitant immunity is probably caused by antitoxic immunity. Concomitant immunity relies on the cooperation between the parasite and human antibodies, leading to the induction of antibody dependent cellular inhibition of the intra-erythrocyte growth of the parasite. The immunity, however, is not a sterilizing type in that the infection persists longer than the symptoms and individuals can exhibit relapses or become re-infected. This review considers the phenomenon of concomitant immunity to plasmodium in their hosts, examining that is available to support conclusions that have been drawn.

Introduction

Malaria is the most common of all parasitic diseases. Each year there are 2 billion exposures to the organism. Of these, approximately 500 million are symptomatic. In areas of high transmission intensity, the burden of severe malarial disease lies in the pediatric age group. But, it have evolved to maintain a well-balanced relationship with their in older human hosts. The unique characteristic of a parasite when it is in its normal host is its ability to make itself tolerated, which indicates that it has sophisticated means to ensure the neutrality of its host. As well, parasites could reduce the cost of intraspecific competition within a host by excluding entry of additional specific parasite. This may be an adaptive manipulation of the host's immune response, or simply an incidental result of normal host immune function.

In human malaria, most individuals fail to develop true sterilizing immunity and remain vulnerable to chronic carriage of low-density asymptomatic infections into adulthood [1]. Such a phenomenon is suggested to result in tolerance to malaria infection. A state of concomitant immunity or premunition is quickly acquired in young children who survive their earliest few infections. Although premunition does not protect against the development of symptomatic malaria, it does protect against its severe complications [2].

Infections may remain asymptomatic if major disruptions of physiological functions are prevented by tolerance mechanisms. Such tolerance developed by the host is likely to be multifactorial and includes the neutralization of parasite toxins and other virulence factors and immunoregulatory mechanisms that reduce the damage triggered by excessive immune responses

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of the host as well as cellular and systemic adaptive responses that limit the deleterious effects associated with stress imposed by pathogens and/or host immunity [3]. An ongoing infection is thought by many workers not only to induce, but also to be necessary for immunity to a superimposed infection of parasites with the same or different genotype [4,5]. Premunition has not been well-studied, and although it likely occurs broadly, it is mainly emphasized for its role in malaria, tuberculosis, syphilis and relapsing fever [6].

The following review will discuss concomitant immunity response against malaria infections.

Literature review concomitant immunity in plasmodium

Concomitant immunity, also known as infection-immunity, is a host response that protects against high numbers of parasite and illness without eliminating the infection [7]. It is progressive development of immunity in individuals exposed to an infective agent [8] mainly belonging to protozoa and Rickettsia, but not in viruses [9]. After the initial infection, which generally occurs in childhood, the effect in subsequent infections is diminished. Infections thereafter may exhibit little or no symptom in spite of parasitemia. The next stage is resistance to infection altogether. This type of immunity is relatively rapid, progressively acquired, short-lived, and partially effective [10]. For malaria, premunition is maintained by repeated antigen exposure from infective bites [10]. Thus, if an individual departs from an endemic area, he or she may lose premunition and become susceptible to malaria [10].

Seasonality of transmission also influences the age of presentation of patients with severe symptoms. If average annual intensity is held constant, geographical areas with marked seasonality to their transmission patterns have a higher average age of CM patients than areas with year-round transmission. This is assumed to occur because those living in areas where exposure to the parasite is restricted to only part of the year acquire partial immunity more slowly than those exposed year round. Immune response against malaria parasite could be directed at either the pre-erythrocyte or erythrocyte stages of the parasite's life cycle. However, the erythrocyte stage of the life cycle is probably the most important in terms of clearing the parasite and lessening the disease [11].

Mechanism of immunity

Among these strategies, antigenic polymorphism could be considered the most important requiring that after infection an individual will acquire immunity only to that specific isolate, but not to heterologous parasites [12,13,]. Among the many polymorphic antigens of *P.falciparum* the polymorphism in the erythrocyte membrane proteins of the EMP-1 family is very extensive and serves immune evasion tremendously. These EMPs are found in the knob structures which are involved in attachment of infected erythrocytes to vascular endothelium allowing the parasite to avoid splenic death [14]. The EMP-1 proteins are encoded by a comprehensive set of genes, known as *var* (for variation) genes, of which already 150 different genes scattered over the entire *P. falciparum* genome are known [15,5]. This down-regulation, accompanied with an increased frequency of CD8+ cells, elevated levels of free CD8 and a decreased frequency of CD4+ T cells, may also be the result of a (cytokine-mediated) defective activation of helper T cells, activation of suppressor T cells and of lymphocyte reallocation, but the underlying mechanisms are not understood.

Antibody Dependent Cellular Killing

Antibody action contributes to premunition [16]. However, premunition is probably much more complex than simple antibody and antigen interaction [10]. In the case of malaria, the sporozoite and merozoite stages of Plasmodium elicit the antibody response which leads to premunition [16]. Immunoglobulin E targets the parasites and leads to eosinophil degranulation which releases major basic protein that damages the parasites, and other factors elicit a local inflammatory response [16].

However, *Plasmodium* can change its surface antigens, so the development of an antibody repertoire that can recognize multiple surface antigens is important for premunition to be achieved [17]. The efficacy of these antibodies is however dependent on their cooperation with effector cells like monocytes, macrophages and the Polymorphonuclear (PNM) phagocytes. These phagocytes readily opsonize merozoites *in vivo*. This natural defense mechanism known as premonition or concomitant immunity relies on the cooperation between the parasite and circulating human antibodies to the various stages, leading to an Antibody Dependent Cellular Inhibition (ADCI) of the intra-erythrocyte growth of the parasite is the prevention of super-infection by novel genotypes entering an already established infection in a vertebrate host [18].

Tolerance to Plasmodium Infection

The mechanisms contributing to disease tolerance and the control of tissue damage remain poorly understood. However, several adaptive responses have been suggested to operate in the context of tolerance to malaria infections. The poor and slowly developing immune responses to malaria are partly due to immune evasion strategies of the parasite. Among these strategies, antigenic polymorphism could be considered the most important requiring that after infection an individual will acquire immunity only to that specific isolate, but not to heterologous parasites [12,13].

In each infected red blood cell only one or at most a few *var* genes are expressed and the rate of switching between the genes may be as high as 2.4% per generation [5]. This enables the parasite to evade immune attack. Similarly, many other antigens may have a high antigenic diversity which may be the product of multiple copies of genes. In addition, shedding of parts of parasite proteins may have immune evasion purposes as well. Consequently, the 310 kDa large sexual stage proteins Pfs230 could originate from a 360 kDa precursor while the 50 kDa protein that is shed contains very immunogenic amino acid repeats.

The immune response, as a result is diverted to this irrelevant epitope by a deceptive effect, thereby suppressing the formation of high-affinity anti-Pfs230 antibodies. It is thought that the many cross-reactive epitopes of antigens of different developmental stages are also a heritage of the parasite's ability to divert the immune system. Very often these cross-reactive epitopes confer immuno-dominant amino acid repeats, with the implication that the formation of antibodies to important adjacent areas is suppressed.

Conclusion and Recommendation

In humans repeated infection induce a progressive modulation of the immune response, eventually leading to an anti-parasite immunity characteristic of premunition. This progressive immune type can elucidated by partially clarified mechanism

of action. Besides immunological influences, malaria infection could also be controlled by antimalarial treatments; but inadequate antimalarial treatments may prolong the presence of malaria parasites in the host and this may serve as a prerequisite for the acquisition of protective immunity against re-infection. The mechanism of action of this type of immune system was not fully identified. So further study should be recommended to fully understand.

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