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Association between Agglutination, Severe Malaria, and Host Age in Young Individuals

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Abstract

The diversity of antigens on the surface of Plasmodium falciparum-infected red blood cells is likely a crucial target for naturally acquired immunity against malaria. In response to natural infections, antibodies that cause agglutination are triggered specifically by the variant surface antigen (VSA) expressions of the infecting parasites. Previous examinations involving diverse parasite isolates exposed to heterologous plasma from Kenyan children revealed a highly variable proportion of plasma inducing agglutination, indicating the presence of both rare and common variants. In this context, the agglutination factor (AF) of 115 isolates from Kenyan children was assessed. The findings demonstrated a notable elevation in AF for isolates causing severe malaria compared to those causing mild malaria. Additionally, AF substantially decreased as the age of the infected child increased. We propose that parasites responsible for severe illness tend to express a specific subset of VSA variants that are particularly associated with infections in children with limited immunity.

Introduction

The natural development of resistance to malaria in children within the first five years of life lends support to the feasibility of developing an effective malaria vaccine [1]. While acquiring natural immunity to malaria typically requires several years of exposure, epidemiological data indicates a reduced risk of severe disease manifestations after only a few clinical episodes. The identification of targets for this immunity is a top priority.

Plasmodium falciparum variation surface antigens meet several criteria as potential immune targets. Firstly, through coordinated gene expression in parasites, variant surface antigen (VSA) undergoes clonal antigenic variation similar to surface antigens expressed by trypanosomes, Borrelia, and Neisseria species. Until recently, VSA was believed to be exclusively composed of P [2]. Falciparum erythrocyte surface protein-1, denoting a large family of parasite adhesion molecules expressed by the var genes, is one aspect. A recently characterized large family of clonally variable surface molecules called rifins, however, has an unknown role in the agglutination of field isolates.

Secondly, individual VSAs can bind to various combinations of microvasculature endothelial receptors, including thrombospondin, CD36, intercellular adhesion molecule 1, vascular cellular adhesion molecule, E-selectin, CD31, P-selectin, chondroitin sulfate A, and αvβ3 integrin [3]. These interactions are believed to play a crucial role in the distinct pathology of falciparum malaria, particularly the sequestration of infected red blood cells in the microvasculature of the brain. Lastly, VSAs are highly immunogenic, as demonstrated by our previous findings that naturally occurring anti-VSA antibodies provide variation-specific protection against malaria.

Despite the prominence and immunogenicity of VSAs, their high diversity, observed through the analysis of expressed var genes from field isolates and comparisons of the specificities of naturally occurring anti-VSA antibodies, may be considered a limiting factor in vaccine development. However, some level of antibody cross-reactivity is detectable toward the epitopes expressed by different parasite isolates [4]. Additionally, children's immune systems learn to recognize most local isolates during the period of naturally acquired immunity development, and adults' immune systems can generate responses recognizing infected erythrocytes from different continents, suggesting that the global diversity of VSA is finite.

We have previously proposed that the cytoadherence function of VSA may restrict the range of distinct antigenic phenotypes that parasites can present to the host immune system. Consistent with this idea, in vitro studies show that the affinity selection of parasites on purified endothelial receptors leads to the purification of limited subsets of variants [5]. The extent to which in vivo affinity selection on endothelial receptors could limit the overall range of epitopes discovered within the parasite population remains unknown. However, recent evidence indicates that the VSAs of parasites sequestered in the placenta during pregnancy are distinct in both their adhesive and antigenic properties, suggesting close associations between the epitope regions and cytoadherence ligands of at least some VSA subsets.

Results

Between January 1997 and February 1999, a total of 213 parasite isolates were collected and cultivated. These isolates were sourced from individuals, with 37 cases classified as having mild effects, 96 cases as moderately infected, and 80 cases as seriously afflicted patients [6]. Exclusion criteria were applied to instances of failure to grow, parasitemia below 1% after culture, high auto-agglutination, giant resetting, and parasites bursting from erythrocytes. Following the exclusion of these isolates, the presence of agglutination factor (AF) was identified in 70 isolates—49 from moderate cases and 21 from severe cases—among pediatric malaria patients admitted to the hospital for the initial phase of the investigation. In the study's second phase, 45 isolates—24 from mild cases and 21 from severe cases—underwent determination of their AFs.

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The agglutination profiles displayed significant variation, with AF differing markedly among isolates. To investigate their connection with AF, various parasite parameters were scrutinized. No correlation was discerned between AF and the percentage of isolates forming early gametocytes or experiencing death in culture. Likewise, there was no correlation between AF and the parasitemia of the culture or the proportion of isolates forming early gametocytes. An analysis of this data indicated that agglutination factor heterogeneity (AFH) was not exclusively a consequence of cell stress during cultivation [7]. Nevertheless, the formation of agglutinates in homologous acute-phase plasma was strongly correlated with AFH, whereas auto-agglutination and resetting demonstrated only a weak association with AF. Correspondingly, a robust correlation was identified between AF and the titers of agglutinating antibodies in the pool of immune adult plasma and Kenyan children's plasma. The antibody titer consistently exhibited higher levels in immune adult plasma than in the children's plasma pool, supporting the idea that the immune adult donor had encountered the infection on multiple occasions.

Discussion

The data obtained from the use of malaria in treating neurosyphilis demonstrated that repeated exposure to the same parasite isolate often led to the swift development of immunity to that particular isolate [8]. In light of these findings, it has been frequently suggested that the prolonged duration of exposure needed for the natural acquisition of immunity to malaria reflects the diversity of essential parasite target antigens in natural populations and the necessity for encountering numerous parasite genotypes.

Despite the potentially vast diversity within the overall parasite population, recent epidemiological data analysis indicates that substantial protection against severe malaria can emerge after just one or two clinical episodes. Our analysis of information collected from Kenya and the Gambia has unveiled that antibody responses to variant surface antigens (VSAs) may play a crucial role in establishing naturally occurring immunity to malaria. Considering the diversity of these molecules, responses to VSAs could contribute to the rapid development of resistance to severe illness only if protective responses target conserved regions or if a subset of VSA variants specifically linked to infections in young children, plays a role in the development of severe malaria [9,10]. Building on the earlier observation that parasites from children with severe malaria are notably prone to agglutination by plasma from other children, this study was undertaken to investigate the latter hypothesis, namely, whether the parasites were associated with agglutination factor (AFH).

Conclusion

We discovered that severe illness and a young host age are related to high parasite AF. We have suggested that a subset of VSA variations may exist that are connected to infections in early infants and may contribute to the development of severe malaria. Such a subset of variations might be able to explain why immunity to severe malaria develops relatively quickly. Epitopes expressed by AFH isolates may be functionally and epidemiologically characterised, which may prove to be a fruitful new strategy for discovering crucial malaria immune targets. Additional research is required to determine the prevalence of these epitopes in the parasite population over time and space, test the association of AFH isolates with particular disease syndromes, link the age-specific reduction in AF to particular immune responses, and identify the involved epitopes. Particular consideration must be given to the amount of expression of the epitopes in AFH isolates in relation to molecules such the cytoadherence-linked asexual gene.

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References

1. Watanabe M, Otake R, Kozuki R, Toihata T, Takahashi K, et al. (2020) Recent progress in multidisciplinary treatment for patients with esophageal cancer. Surg Today 50: 12-20.
2. Napier KJ, Scheerer M, Misra S (2014) Esophageal cancer: A Review of epidemiology, pathogenesis, staging workup and treatment modalities. World J Gastrointest Oncol 6: 112-120.
3. Kato H, Nakajima M (2013) Treatments for esophageal cancer: a review. Gen Thorac Cardiovasc Surg 61: 330-335.
4. Green NM, Marshak-Rothstein A (2011) Toll-like receptor driven B cell activation in the induction of systemic autoimmunity. Semin Immunol 23: 106-112.
5. Shlomchik MJ (2009) Activating systemic autoimmunity: B's, T's, and tolls. Curr Opin Immunol 21: 626-633.
6. Thompson WW, Shay DK, Weintraub E, Brammer L, Cox N, et al. (2003) Mortality associated with influenza and respiratory syncytial virus in the United States. JAMA 289: 179-186.
7. Kassiotis G, Zamoyska R, Stockinger B (2003) Involvement of avidity for major histocompatibility complex in homeostasis of naive and memory T cells. J Exp Med 197: 1007-1016.
8. Kieper WC, Burghardt JT, Surh CD (2004) A role for TCR affinity in regulating naive T cell homeostasis. J Immunol 172: 40-44.
9. Goronzy JJ, Weyand CM (2001) T cell homeostasis and auto-reactivity in rheumatoid arthritis. Curr Dir Autoimmun 3: 112-132.
10. Emura T, Suzuki N, Yamaguchi M, Ohshimo H, Fukushima M (2004) A novel combination antimetabolite, TAS-102, exhibits antitumor activity in FU-resistant human cancer cells through a mechanism involving FTD incorporation in DNA. Int J Oncol 25: 571-578.