Antibody profiling in patients with mild and severe leptospirosis: a genome-wide protein microarray approach

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Leptospirosis is zoonotic disease of global importance, with over a million cases and nearly 60,000 deaths annually. Symptomatic disease presentation ranges from a mild febrile disease with non-specific symptoms to severe forms, characterized by multi-organ failure, lung hemorrhage, and death. Factors governing severe outcomes remain unclear, but the host immune response likely plays an important role. In the present study, we used protein microarray chip to identify the antibody profiles of patients with severe and mild leptospirosis against the complete *Leptospira interrogans* serovar Copenhageni predicted ORFeome. We discovered a limited number of immunodominant antigens, with 36 antigens specific to patients. Of these, 11 were identified during acute phase, which are therefore potential serodiagnostic antigens while 33 were detected after recovery and are potential subunit vaccine targets. Surprisingly, we found the antibody repertoire varies in patients with different clinical outcomes: in the severe group, overall IgM responses do not change and IgG responses increase over time, while both IgM and IgG responses remain relatively the same in the mild patient group. By analyzing antibody responses by individual patient, we observed that over 74% of patients with severe symptoms compared to 29% of patients with mild leptospirosis had significant IgG increases over time. Additionally, 90.0% of IgM responses did not change over time in the mild group, compared to 51.6% in the severe group. Thus, we hypothesized that patients with mild symptoms were protected from severe disease due to pre-existing antibodies, while the profile of patients with severe outcomes was representative of a first exposure. These findings represent a substantial step forward in the knowledge of the humoral immune response to *Leptospira* infection, and we have identified new targets for vaccine and diagnostic test development.

Palavras chave: leptospirosis, antibody profile, protein microarray