MICROBIOLOGY AND IMMUNOLOGY

Time Course of Serum Nuclease Activity in Mice Infected with *Plasmodium Malariae*

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Time course of DNase and RNase activities in the sera of random-bred mice infected with *Plasmodium malariae* (chloroquine-sensitive strain H) was studied. Similarly to viral infection, infection with a protozoa eukaryotic parasite was accompanied by increased DNAse and RNAse activities, though *Plasmodium malariae* biologically differes from viruses.

Key Words: *DNase; RNase; induction; Plasmodium malariae; nonspecific humoral defense*

Infections caused by different agents are characterized by inflammation, a universal feature of many pathological processes. Inflammation can run an uncomplicated course and eventuate in recovery or be severe in case of impaired immunity and low level of nonspecific humoral defense. We investigated natural antiinfection defense mechanisms, in particular the mechanisms of nonspecific humoral defense determining the infection resistance.

Induction of acute phase protein synthesis in response to various homeostasis disorders, e. g. disorders caused by viral and bacterial infections, is a factor of organism resistance [10]. Acute phase reaction is considered to be useful for recovery of physiological homeostasis [9]. Nucleases (enzymes hydrolyzing nucleic acids) are also interesting as the factors of infection resistance of the organism. Serum nuclease activity (NA) increases during viral infection, this parameter inversely correlates with the severity of clinical process. In some viral neuroinfections (meningitis, meningoencephalitis, *etc.*) high NA and serum level of immunoreactive trypsin (acute phase protein) determines mild abortive course of the disease [2,6,9].

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We previously showed that infection of highly resistant Standard minks with Aleutian disease virus induced a high DNase activity [11]. Measurements of NA in some viral infections confirmed the assumption [3,8] that nucleases are an important biochemical barrier preventing virus reproduction in the organism.

The purpose of this study was to elucidate whether the mechanism of NA induction in animals is specific of viral infections or universal and protects also from other viral infections. NA induction was tested in infection with *Plasmodium malariae* (PM), an eukaryotic parasite differing from viruses by its biological characteristics.

MATERIALS AND METHODS

Adult random-bred albino mice (30-40 g) were infected with MP (chloraquine-sensitive strain N). The animals with pronounced parasitemia were decapitated, blood was stabilized with 3.8% sodium citrate and diluted with normal saline to a concentration, of 10 parasites/0.1 ml. To determine the parasite concentration erythrocytes were counted in a Goryaev chamber and the percentage of damaged erythrocytes in blood smears was estimated under an electron microscope. Infected blood was injected intraperitoneally to intact animals. Controls were injected with normal saline.

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For microscopic control of erythrocyte damage and blood count, thin smears were prepared from a drop of blood collected from the caudal vein, fixed in methanol, and stained after Romanowskii. Damaged erythrocytes, leukocytes, and reticulocytes were counted under a light microscope. NA was measured 48, 57, 72, 78, and 94 h after infection (12-14 mice per point).

Serum NA was evaluated by an increase in absorption (at 260 nm) of acid-soluble fraction obtained after incubation (37°C) of substrate DNA or tRNA with the serum in the presence of Mg ions. DNase and RNase activities were measured at pH 7.4 and expressed in optical density units [7]. The results were statistically processed as described previously [4]. The significance of differences between the mean values was assessed using Student's *t* test.

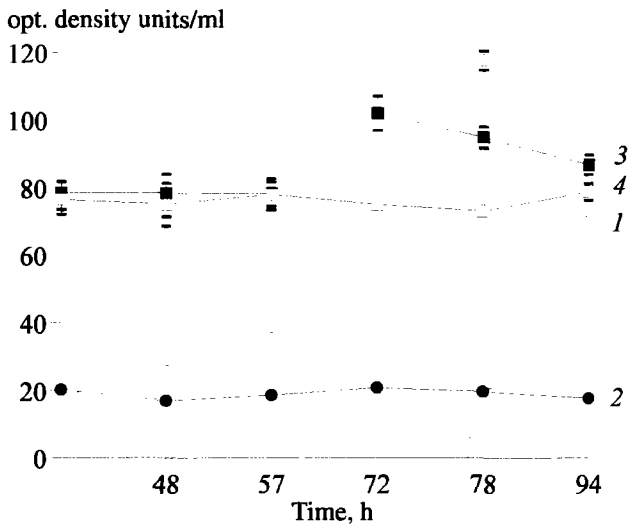

Fig. 1. Time course of DNAse (*1, 2*) and RNAse (*3, 4*) activities in the control (*2, 4*) and after infection with *Plasmodium malariae* (*1, 3*).

RESULTS

Serum DNase activity (Fig. 1, curve *1*) in mice infected with PM started to rise 48 h postinfection and reached the maximum after 78 h (6-fold increase in comparison with the initial level). After 94 h DNase activity started to decrease. RNase activity 78 h postinfection (Fig. 1, curve *3*) increased only by 30%. According to published reports, infection of cell culture with herpes simplex virus led to an increase in DNase and RNase activities (as in MP infection). We believe that RNase is involved in degradation of infective mRNA molecule covalently bound to newly produced viral DNA chains [12].

The first solitary PM appeared in blood erythrocytes of infected animals 120 h postinfection. Maximal infection of blood erythrocytes at our infective dose was observed 144 h postinfection, while NA peaked 78 h postinfection, and therefore the mechanism of nuclease production was triggered during the first stages of PM cycle (tissue schizogony and tissue merozoites). It seems that NA induction occurs in inflammatory processes caused by any infectious agent (virus, bacterium, *etc.*), because turpentine-induced aseptic inflammation characterized by cell death (macrophages, *etc.*) was not associated with NA induction [1]. Analysis of published reports and our findings suggest universal mechanisms of NA induction in humans and animals. Serum nucleases are apparently responsible for protection from viral [2,6,11] and streptococcal [1] infection. Induction of NA was observed after introduction of foreign genetic information of non-infectious nature (foreign high-polymeric DNA) [5,13].

Hence, serum nucleases are responsible for liquidation of homeostasis disorders in infection caused by PM. Like immune reaction to an antigen, NA induction is a characteristic response of the organism to various infections. It is however possible that the mechanism of nonspecific humoral defense activates the production of nucleases with different substrate specificity. More detailed studies of this mechanism hold good promise for the development of new effective means of controlling infections of different nature.

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