SUPERAFFINITY OF THE HUMAN BLOOD EOSINOPHIL FOR ENDOTOXIN

M. Yu. Yakovlev, A. A. Kubatiev,
A. N. Krupnik, V. M. Bondarenko,
and E. V. Sudzhan

UDC 616.155.35-02:616.153.915.5'458-008.6

KEY WORDS: endotoxin; lipopolysaccharides; eosinophils

Lipid A (LA), a unique lipid skeleton found in the composition of lipopolysaccharides (LPS) of all Gram-negative microorganisms [7], is a carrier of the biological activity of endotoxin [7]. It is one of the most powerful bacterial toxins with a broad spectrum of biological activity, nothing like which is possessed by any of the known natural or synthetic agents [6, 7]. The ability of LA to act on the myelocytic branch of hematopoiesis in the bone marrow and the quantitative and qualitative composition of the peripheral blood polymorphonuclear leukocytes (polymorphs) in systemic endotoxinemia (SEE) are well known and LPS-polymorph interaction has been characterized in detail [1, 8]. Investigations [2, 4] have shown that the principal human blood cells accepting LPS are polymorphs.

The aim of this investigation was to determine the ability of eosinophils to interact with LPS.

EXPERIMENTAL METHOD

The test material consisted of 500 peripheral blood films from patients with diffuse suppurative peritonitis, chronic pyelonephritis, focal and lobar pneumonia, traumatic and burn shock, and late toxemia of pregnancy with a nephrotic syndrome. LPS-positive blood cells were identified with the aid of specific adsorbed luminescent immunoglobulins to the Re-mutant of Salmonella typhimurium with elimination of the 60-megadalton host plasmid, in the structure of whose LPS only LA and ketodeoxyoctanate remained. These luminescent antibodies can detect LA-positive blood cells in a dilution of 1:64, and after exhaustion with packed leukocytes, in a dilution of 1:16. Blood films were examined in the LYUMAM I1 microscope, using SZS24-4, FS1-2, ZhS18, and ZhS19 filters and a "green" light-dividing plate. Before treatment with FITC-labeled serum the blood films were examined and sectors with an area of 0.5 cm^2 for examination were chosen so that it excluded the presence of even single cells with autofluorescence. LA-positive blood cells were verified by staining the film in situ with azure-eosin which, just as previously [2, 3, 4], showed that the principal LPS-accepting cell is the polymorph. The low level of luminescence of single polymorphs was demonstrated in virtually all cases and was accepted as the basic level and was disregarded.

In the peripheral blood of most patients polymorphs with a high intensity of luminescence were found, and as a rule this was accompanied by fever and changes in the biochemical and hematologic blood parameters. A shift of the leukocyte formula to the left to a varied degree was observed, with leukocytopenia or, more often, leukocytosis, whereas eosinophils were virtually absent in the peripheral blood films of most patients. Thrombocytopenia was observed in some patients, often with activation of the thrombocytic series (the appearance of blast forms) in the bone marrow, etc.

During examination of the peripheral blood films our attention was drawn to extremely brightly fluorescent cells, much brighter than polymorphs with affinity for LPS. These cells were found in by no means every film. They were found in blood films in which solitary eosinophils were present. Verification of these cells with superaffinity for LPS showed

Department of Pathomorphology, N. V. Sklifosovskii Emergency Aid Research Institute. Department of Pathophysiology, Central Laboratory of Genetics and Breeding of Microorganisms N. F. Gamaleya Research Institute of Epidemiology and Microbiology, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR, N. K. Permyakov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 107, No. 6, pp. 765-766, June, 1989. Original article submitted December 25, 1988.

 0007-4888/89/0006-0900$12.50

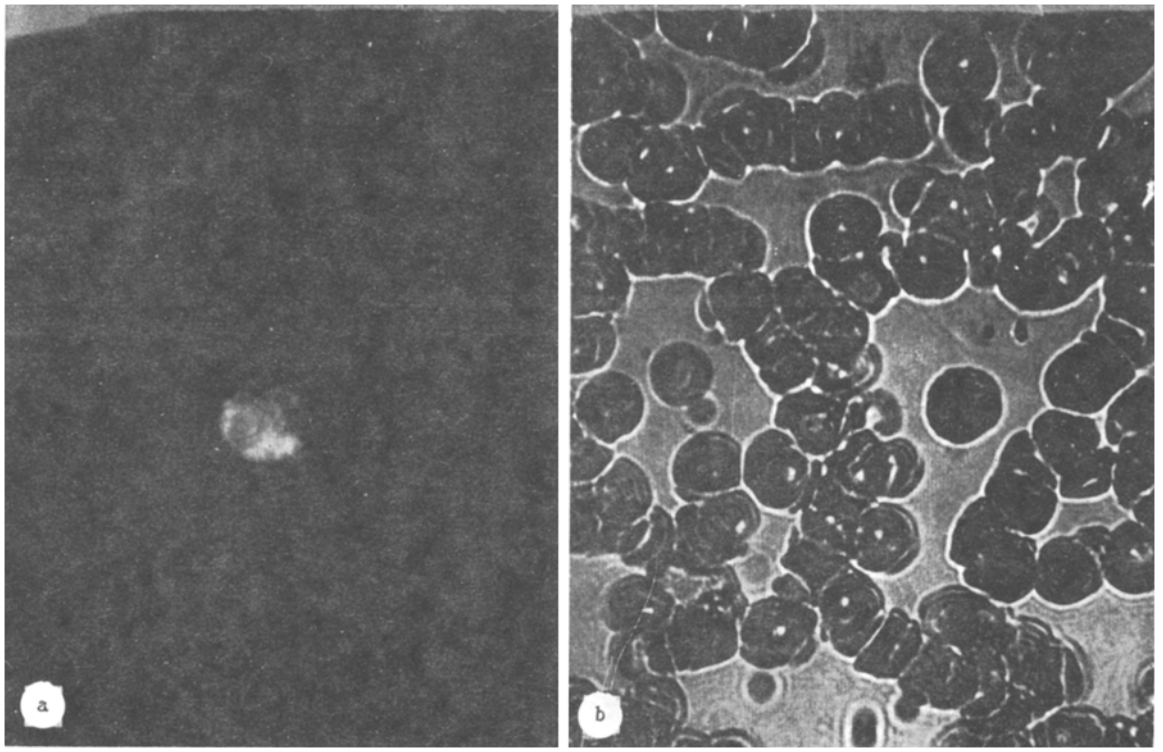

Fig. 1. Verification of human blood cells with superaffinity for endotoxin with the aid of fluorescent antibodies to lipid A. 1350 ×. a) Luminescent object is an endotoxin-positive eosinophil (note intensity of luminescence), direct Coons' method; b) the same object in transmitted light. Stained with azure and eosin.

that they were eosinophils (Fig. 1a, b). LPS are evidently among the main factors determining the development of eosinopenia, for on the one hand SEE is a very frequent clinical phenomenon [3], and on the other hand, the ability of LPS to exert a leukopenic effect [8] with deposition (sequestration) of polymorphs in the microcirculatory bed of the parenchymatous organs, especially the lungs [4], is well known. In this connection there are some very interesting clinical studies [5] which showed that a definite role in the pathogenesis of lung damage in septic shock with the development of an acute respiratory distress syndrome (ARDS) is played by eosinophils and, in particular, by the specific granular protein released by them, known as eosinophilic cationic protein. The plasma concentration of this protein rises considerably (despite the eosinopenia), and according to some workers [5] this may be an early diagnostic sign of the development of ARDS during septic shock.

The eosinophil, a blood cell with superaffinity for LPS, can thus mediate the pathogenic effect of SEE, and the fact that eosinopenia develops along with thrombocytopenia and leukocytosis or leukocytopenia, is one piece of indirect evidence in support of this development.

LITERATURE CITED

1. D. S. Sarkisov, A. A. Pal'tsyn, I. I. Kolker, et al., Arkh. Patol., No. 12, 6 (1986).
2. É. N. Sitdykov, A. N. Krupnik, M. É. Sitdykova, and M. Yu. Yakovlev, Arkh. Patol., No. 5, 31 (1988).
3. M. Yu. Yakovlev, Kazan' Med. Zh., No. 5, 353 (1988).
4. M. Yu. Yakovlev, V. N. Galankin, A. I. Ipatov, et al., Arkh. Patol., No. 11, 84 (1988).
5. R. Halgen, T. Borg, P. Venge, and J. Modig, Crit. Care Med., 12, No. 1, 14 (1984).
6. E. T. Rietschel, U. Schade, M. Jensen, et al., Scand. J. Infect. Dis., Suppl. 31, 8 (1982).
7. O. Westphal, Int. Arch. Allergy, 49, No. 1-2, 1 (1975).
8. M. E. Wilson, Rev. Infect. Dis., 7, No. 3, 404 (1985).