EFFECT OF SPECIFIC SENSITIZATION AND CORTICOSTEROID HORMONES ON THE COURSE OF EXPERIMENTAL ACTINOMYCOSIS

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Infection of mice and rats with actinomycetes after preliminary administration of hydrocortisone leads to acute actinomycetic septicemia with a high mortality. Preliminary specific sensitization of the animals with actinomycetes or with the extracellular metabolic products of these microorganisms favors the transformation of the acute infectious process into a chronic one with the formation of actinomyotic granules in the organs. Chronic actinomycosis is accompanied by reduced phagocytic activity of the host cells, but also by the presence of circulating antibodies directed mainly against exogenous metabolic products of the actinomycetes.

KEY WORDS: hydrocortisone; specific sensitization; experimental actinomycosis.

The development of actinomycosis is accompanied by marked changes in the immunologic reactivity of the organism [1] although the role of specific sensitization in the onset and pathogenesis of the disease has been inadequately studied.

The object of this investigation was to study the role of specific sensitization and the state of immunologic reactivity of the organism in the development of chronic actinomycosis.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred and inbred (BALB/c) mice and Wistar rats. The animals were infected with a 10-day culture of the aerobic actinomycete Actinomyces albus strain 229 LIA. Mycelial cells were injected intraperitoneally into the animals in 0.5 ml of an oil–water emulsion (a mixture of equal volumes of physiological saline and mineral oil) in a dose of 2 billion cells per injection into mice and 5 billion into rats. Control experiments were carried out on animals infected with cells of the actinomycete without mineral oil or sensitized by injection of exocellular metabolic products of the actinomycetes secreted into the nutrient medium, or of a culture of the actinomycete killed by heating to 70°C for 120 min. To depress their immunologic reactivity, the animals received subcutaneous injections of hydrocortisone in a dose of 2.5 mg per mouse and 20 mg per rat daily for 5 days. The effectivenss of infection was judged by the dynamics of death of the experimental animals and also by the results of microbiological (seeding and microscopic examination of squash preparations of the lungs, liver, spleen, and kidneys and films of peritoneal exudate and blood) and morphological (hematoxylin–eosin staining and counterstaining by Gram's method to detect the granules) examination of the animals. The dynamics of the increase in titer of circulating antibodies against actinomycetes (complement fixation test) and the phagocytic activity of the blood cells also were studied in the experimental animals.

EXPERIMENTAL RESULTS

A single, double, or triple intraperitoneal injection of actinomycetes suspended in physiological saline

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TABLE 1. Characteristics of Experimental Actinomycosis in Mice Following Different Types of Infection

Number of mice	Conditions of administration of agent							Number of mice dying (I) and surviving (II) during 1st week after final injection		Characteristics of infectious process in surviving animals		
	first injection of agent (17 days before final injection		second injection of agent (12 days before final injection)		administration of hydrocortisone	final injection of agent				Actinomycetic septicemia without morphological changes in organs	Actinomycetic septicemia with morphological changes in organs (abscesses, nodules)	Morphological changes present in organs (abscesses, nodules)
	with mineral oil	without mineral oil	with mineral oil	without mineral oil		with mineral oil	without mineral oil	I	II			
4				+	+	+	+	—	4	—	—	—
4				+	+	+	+	—	4	—	—	—
4		+		+	+	+	+	—	4	—	—	—
4			+		+	+		—	4	—	—	—
4			+		+	+		—	4	—	—	—
4	+		+		+	+		—	4	—	—	4
8				+	+		+	7	1	1 (M)	—	—
8				+	+		+	6	2	2 (M)	—	—
4		+		+	+		+	4	—	—	—	—
4	+				+		+	3	1	—	1 (M)	—
4					+	+		3	1	—	—	1 (M)
4			+		+	+		4	—	—	—	—
4	K		K		+	+		3	1	—	1 (M)	—
4	K		K		+	+	+	1	3	2 (M)	1 (M)	—
4	O		O		+	+		3	1	1 (M)	—	—
4	+		+		+	+	+	2	2	—	1 (M)	1 (M)
14	+		+		+	+		3	11	—	—	11 (M)
4	E		E		+	+		—	4	—	—	4 (M)

Legend: +) injection of agent or hydrocortisone; K) injection of agent killed by heat; O) mineral oil only injected; E) injection of exocellular metabolic products of agent; M) diagnosis confirmed microbiologically.

or a single injection of actinomycetes with mineral oil into the animals did not cause the development of experimental actinomycosis and did not cause death of the animals (Table 1). However, repeated injection of actinomycetes with mineral oil was followed by the appearance of small white miliary tubercles on the peritoneum and omentum in some of the animals 2 weeks after the last injection. Actinomycetes could not be cultured from seedings or squash preparations from the organs and from these tubercles. After preliminary injection of hydrocortisone a single injection of cells of the actinomycete with mineral oil or as a suspension in physiological saline into the animals regularly led to the development of an acute infectious process in the mice, terminating in death of 75-85% of the experimental animals during the first week after infection. Cultures of the organs and blood of the dying and killed mice were regularly positive for the actinomycete.

Administration of hydrocortisone and infection of the mice and rats after preliminary single or double sensitization of the animals with a living culture of the actinomycete or with the exocellular metabolic products of the agent mixed with mineral oil reduced the severity of the actinomycosis and favored its transformation into a chronic infectious process characterized by abscesses at the sites of injection of the culture and by multiple white miliary turbercles scattered over the surface of the viscera. Cultures from these granules were always positive for the actinomycete. Other variants of preliminary sensitization of the animals were less effective (Table 1).

The scheme as developed above for the reproduction of chronic actinomycosis in mice was equally effective in rats also. Repeated sensitization of rats with actinomycetes in mineral oil was accompanied by the accumulation of complement-fixing antibodies against actinomycetes in their blood (titers of antibodies 1:1230 ± 320) and by an increase in the phagocytic activity of the peripheral blood cells (the phagocytic number of the control and experimental groups of animals were 7 ± 2 and 38 ± 5, respectively, and their phagocytic indices were 2.3 ± 0.2 and 3.5 ± 0.6). Administration of hydrocortisone to preliminarily immunized rats sharply reduced their titer of circulating antibodies and phagocytes (antibody titers 1:10 ± 5, phagocytic number 15 ± 1, phagocytic index 1.7 ± 0.2). Administration of hydrocortisone before infection of the animals also depressed the immune response (during the first week after infection the antibody titers did not exceed 1:80 ± 20, the phagocytic number 17 ± 2, and the phagocytic index 1.7 ± 0.1). However, after preliminary infection (sensitization), administration of hydrocortisone affected chiefly the rate of restora-

tion of phagocytic activity. The circulating antibody level after the corresponding injection of actinomycetes, even after preliminary injection of hydrocortisone, recovered by the third day to a titer of 1 : 1280 ± 320, but the phagocytic activity did not recover until the 12th day (phagocytic number 34 ± 4, phagocytic index 2.6 ± 0.2). Chronic actinomycosis developed against the background of these immunological changes in the animals.

The acute infectious process (actinomycetic septicemia) developed in the animals when phagocytic activity and humoral immunity were depressed by hydrocortisone. Chronic actinomycosis in previously sensitized animals appeared when their phagocytic activity was depressed, coupled with a transient decrease in the level of circulating antibodies. Under these circumstances antibodies against exocellular metabolic products of the actinomycete, secreted into the surrounding medium, plays a dominant role. These antibodies evidently also promote the formation of the typical granules around the elements of the actinomycete, and after inhibition of the phagocytic activity of the cells and of cellular immunity by hydrocortisone [2], they promote the development of typical chronic actinomycosis in the animals. Evidence of the important role of metabolic products of the microorganism in the development of chronic actinomycosis is also given by the unsuccessful results of preliminary sensitization of the animals with killed actinomycetes.

LITERATURE CITED

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