CHANGES IN LYMPH NODE MORPHOLOGY AND FUNCTION DURING THE FEBRILE REACTION

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UDC 616.428-092:612.57]-076-092.9

KEY WORDS: febrile reaction; lymph nodes

Lymph nodes (LN) are important organs of homeostasis, "unique cleansing structures, freeing the lymph from toxic waste products" [2]. Consequently, the mechanisms and degree of adaptive processes taking place in a particular kind of pathology can be largely judged by the character of changes in lymph node morphology and function.

This paper describes pathomorphological and morphometric studies of LN of different functional groups — somatic (popliteal and cervical) and visceral (mesenteric) — in rabbits during a febrile reaction (FR) of varied duration.

EXPERIMENTAL METHOD

Experiments were carried out on 28 Chinchilla rabbits weighing 2.5-4.2 kg. FR was produced by intravenous injection of pyrogenal [3]. Animals receiving an injection of pyrogen-free physiological saline served as the control group. To obtain LN the rabbits were killed by exsanguination under intravenous 3% thiopental anesthesia (15 mg/kg), on the 4th, 6th, and 11th days respectively after 3, 5, and 10 daily injections of pyrogenal. Pieces of LN were fixed in Carnoy's fluid, dehydrated in alcohols of increasing concentration, cleared in xylol, and embedded in paraffin wax. Paraffin sections (5-6 μ thick) were stained with hematoxylin and eosin, with methyl green and pyronine by Brachet's method, and with Schiff's reagent (after McManus). Besides qualitative evaluation of the morphology of the lymphoid tissue a quantitative study was made of the cells (lymphocytes, pyroninophilic blast cells, and PAS-positive cells) in the follicles, paracortical zone, medullary cords, and sinuses. The width of the paracortical (T-dependent) zone and the diameter of the follicles (B-dependent zone) also were measured. The results of the measurements were expressed in microns. The results were subjected to statistical analysis [4].

EXPERIMENTAL RESULTS

The response of LN in different parts of the body and with different functional specialization to fever was systemic and nonspecific in character.

After three injections of pyrogenal the pattern of the follicular structure of the popliteal and cervical LN had become indistinct, and the lymphoid follicles were small, with no clear boundaries or germinative centers. By contrast, in the mesenteric LN there was an increase in the number of follicles and in their diameter (Table 1), accompanied by widening of the germinative centers of the follicles. The latter contained chiefly blast cells, small and medium-sized lymphocytes, and solitary mitotic figures. The medullary cords of all LN showed moderate hyperplasia and were infiltrated by small and medium-sized lymphocytes. The medullary cords were thickened and infiltrated by cells of the plasma-cell series (this was particularly marked in the cervical LN). The structure of the paracortical zone of LN was indistinguishable from normal. Peripheral sinuses in some parts were dilated, and in others compressed by the hyperplastic lymphoid tissue.

Department of Pathology and Pharmacotherapy, S. V. Kurashov Kazan' Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR A. D. Ado.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 112, No. 8, pp. 210-213, August, 1991. Original article submitted October 30, 1990.

0007-4888/91/0008-1197$12.50

TABLE 1. Diameter of Follicles (DF) and Width of Paracortical Zone (WPCZ) of Rabbit LN during FR (μ; M ± m)

LN	Control	Injections of pyrogenal		
		after 3, 4th day	after 5, 6th day	after 10, 11th day
Cervical WPCZ	497,00±30,46	470,14±53,38	599,14±52,02	573,02±47,25
p		>0,5	<0,01	<0,02
DF	356,71±35,52	281,86±25,21	204,29±28,17	202,57±24,47
p		<0,05	<0,01	<0,01
Mesenteric WPCZ	732,43±10,32	760,86±20,88	795,86±38,71	679,57±30,13
p		>0,2	>0,1	>0,1
DF	575,43±50,65	672,37±47,11	424,14±36,23	486,57±25,52
p		<0,05	<0,01	<0,01
Popliteal WPCZ	586,86±43,27	556,00±21,52	657,33±39,17	670,22±25,05
p		>0,5	<0,05	<0,01
DF	563,71±34,06	525,57±30,40	305,71±23,55	265,14±17,69
p		>0,5	<0,001	<0,001

Legend. In each group n = 7.

Where dilatation was present, evidence of "desquamative catarrh" could be seen. The medullary sinuses were dilated, with evidence of lymphostasis in some of them, whereas others contained many desquamated cells as well as a protein eosinophilic substance. Moderate lymphostasis and signs of "desquamative catarrh" also were observed in the intermediate sinuses. In the lumen of the sinuses were many small and medium-sized lymphocytes, together with solitary macrophages. In the region of the hilum of the mesenteric LN increased destruction of lymphocytes could be seen, the trabecular apparatus of LN was edematous, and its fibers were separated in places. At sites of loosening of the connective-tissue basis of the trabeculae activation of fibroblasts was observed. Vessels of the microcirculatory bed were dilated and congested: signs of mucoid and fibrinoid swelling were present in the wall of the arterioles, venules, and capillaries, evidence of increased vascular permeability. The endothelium of the postcapillary venules showed moderate proliferation.

After five injections of the lipopolysaccharide marked hyperplasia of the lymphoid tissue of LN was observed. However, the pattern of the follicular structure was indistinct and the diameter of the follicles of all LN was smaller than initially (Table 1). An increase in the number of macrophages was observed in the germinative centers of the follicles, and a large number of fragments of nuclei of disintegrating cells could be seen in their cytoplasm (Fig. 1a). The paracortical zone was widened, except in the mesenteric LN (Table 1), but the arrangement of the lymphoid cells in it was irregular: places with a dense distribution alternated with areas of rarefaction. In the hilar region of the mesenteric LN increased destruction of lymphoid cells was present with accumulation of nuclear chromatin. Many plasma cells could be seen in the medullary cords. The medullary sinuses were considerably widened, and evidence of desquamative catarrh and desquamation of the littoral cells were observed (Fig. 1b). In some of them there was a marked increase in the number of sinus macrophages. By contrast with 3-day fever, lymphocytosis of sinuses was observed, the density of distribution of the lymphocytes in them being much higher than in the nonfollicular cortex of the gland, evidence of increased recirculation of these cells (Fig. 2). The walls of the arterioles, venules, and capillaries showed evidence of mucoid and fibrinoid swelling. In some places foci of fibrosis appeared in them as a result of plasma seepage through the vessel walls.

Pathomorphological changes in LN after 10 injections of pyrogenal were similar to those at the previous time of investigation.

The number of PAS-positive cells was increased in the structures of all LN during FR, and this can perhaps be interpreted as destruction of the connective-tissue component of LN with accumulation of aminoglycans.

Analysis of this material indicates the diversity of morphological and functional changes in LN arising during FR. This is particularly the case with the response of the sinuses of LN. We know that enlargement of the lumen of the sinuses is evidence of the increased transport capacity of LN, and it is interpreted as a reaction accompanied an increase in the flow of lymph through them. These changes point to enhancement of the tissue drainage, which is essential for ridding the tissues of breakdown products of cells and noncellular structures [6]. Meanwhile the increase in the intensity of lymph transport through LN can be associated not only with an increase in the inflow of peripheral lymph into the organ, but also increased permeability of the walls of the exchange microvessels of the lymph nodes themselves. This conclusion is confirmed by the changes which we found in the walls of arterioles, venules, and capillaries of LN during FR.

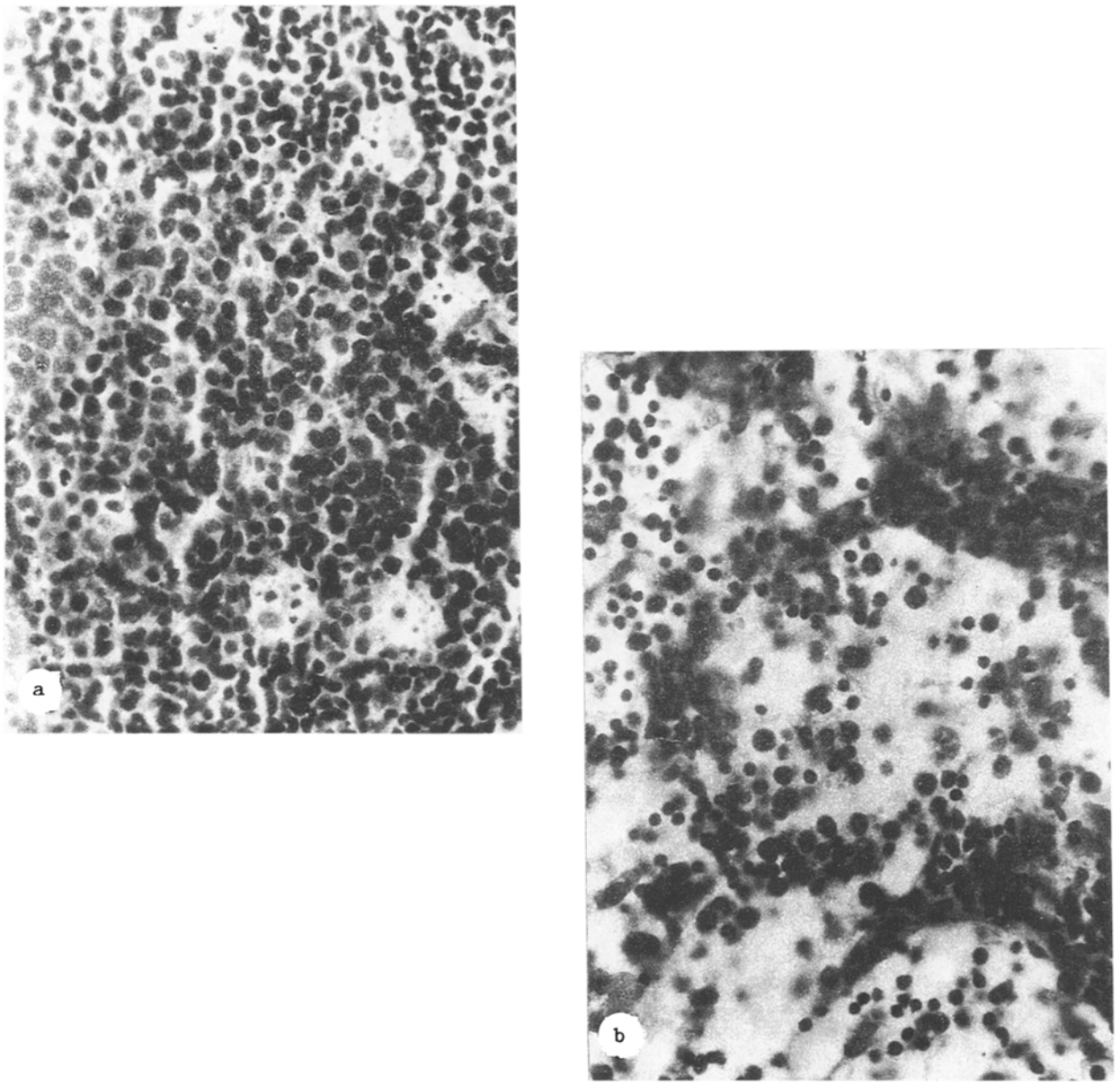

Fig. 1. Mesenteric LN on 6th day after five injections of pyrogenal: a) macrophages loaded with nuclear fragments of disintegrating cells in germinative centers of follicles; b) "desquamative catarrh" of sinuses: macrophages, plasma cells, blast cells, and histiocytes in lumen of sinuses. Hematoxylin and eosin, 240×.

During the development of FR, signs of dynamic stereotypy of LN were observed in response to the action of destabilizing factors, as described by Borodin on the basis of a study of the response of LN in other types of pathology [1]: hyperplasia of the lymphatic substance with an increase in the number of lymphocytes and of undifferentiated lymphoid cells in the follicles and paracortical zone, hyperplasia of the medullary cords, and signs of a macrophagal response. Reduction of the diameter of the follicles in LN during FR cannot be interpreted as atrophy of the nodules, for the number of cells in them is increased. Moreover, during prolonged fever there is an increase in the width of the paracortical zone of LN and in the number of blast cells and lymphocytes in it. An important and highly specific component of the paracortical zone of LN is the postcapillary venules, through which lymphocytes migrate from the blood into LN [8]. The latter can evidently explain the increase in the number of lymphocytes in the paracortical zone of LN in the present experiments. It is also claimed that glycoproteins produced by the reticular cells of the paracortical zone act as a humoral factor for stimulating lymphocytes and bringing about their recirculation [7, 9]. The increase in the number of lymphocytes

Fig. 2. Popliteal LN on 6th day after five injections of pyrogenal. Lymphocytosis of sinus. Stained with hematoxyl in and eosin, 240×.

in the medullary cords and medullary sinuses during FR is evidence of migration of the lymphocytes within the lymph node and their enhanced release into the lymph flow.

On the whole, therefore, the morphological and functional changes discovered in LN during FR can be characterized as manifestation of their mainly enhanced functional activity, which is adaptive in character and aimed at increasing cellular and humoral immunity. Meanwhile, during a longer FR marked signs of destruction of the cells of LN also appear.

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