CHANGES IN THE PERIPHERAL BLOOD AND BONE MARROW OF RABBITS IN EXPERIMENTAL EPILEPSY

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During an investigation of the blood of patients with epilepsy we found [3] that a true leucocytosis and an increase in the platelet count took place under the influence of epileptic fits. The functional state of the bone marrow was characterized by the presence of a myeloid reaction with an increase in the content of myeloblasts, promyelocytes, neutrophilic myelocytes and metamyelocytes, and also an increase in the number of megakaryocytes. We regarded the changes in the bone marrow as the result of changes accumulating gradually in connection with the epileptic fits.

In order to ascertain the truth of this hypothesis, we studied the peripheral blood and the bone marrow during experimental epilepsy in rabbits.

Several authors have studied the effect of experimentally induced epilepsy on the composition of the peripheral blood. I. N. Davydov [1], who produced epileptic fits in rabbits and cats by electrical stimulation of the brain, observed an obvious leukocytosis in the peripheral blood. The increase in the white cell count took place on account of an increase in the absolute and relative number of lymphocytes, a relative decrease and an absolute increase in the number of neutrophils, and an increase in the number of monocytes. This author considers that the postparoxysmal leukocytosis is redistributive in nature, and that contraction of the spleen plays an essential role in its formation. In more prolonged investigations on rabbits, N. M. Eremeeva [2], who used electrical stimulation of the brain, observed an obvious leukocytosis within a few minutes of the action of the current, reaching its maximum after 1-2 or, occasionally, 3 hours. The leukocytosis developed on account of neutrophils, lymphocytes, and monocytes. Young forms of neutrophils sometimes appeared in the peripheral blood. Swensson [4] described the development of leukocytosis in rats 2-3 minutes after receiving injections of convulsive doses of cardiazol. We do not know of any reports on the state of hemopoiesis in the bone marrow during experimental epilepsy.

METHOD

Experiments were carried out on 16 rabbits of both sexes, weighing 1.2-2.2 kg. In order to produce fits, a 10% solution of cardiazol was injected intravenously in a dose of 0.3 ml/kg body weight. Fits were caused repeatedly at intervals of 1-3 days. Blood for examination was taken from the veins of the ear before the fit, immediately after the fit, and 15 minutes, 1 hour, 2 hours, 3 hours, and, in some experiments, 12 hours after the fit. Determinations were made of the hemoglobin concentration; the red cell, platelet, and white cell counts; and the white cell formula. Bone marrow was extracted by puncture of the ischial tuberosity before and after 8-33 fits.

RESULTS

Immediately after injection of cardiazol a fit began. Three periods could be distinguished in its development: A very short (2-12 seconds) period of major clonic convulsions, a period of tonic convulsions (12-25 seconds), and a period of medium and minor clonic convulsions, lasting from 29 seconds to 79 minutes.

In the course of the fit, all the experimental rabbits showed slight changes in the hemoglobin concentration and red cell count, which lay within the limits of error of the method. With regard to the numbers and composition of the white cells, regular changes were observed in all 16 rabbits. As a rule, after a fit, the white cell count was increased. The maximum rise in the white cell count took place in 8 rabbits immediately after the fit, in 5 rabbits 15 minutes after, and in 3 rabbits 1 hour after the fit. At the moment of maximum rise, the white cell count amounted to 150-244% of its initial value. The white cell count then gradually fell, after varying intervals of time (after 1 hour in 6 rabbits, after 3 hours in 6 rabbits, and after 12 hours in 3 rabbits). Typical changes in the number and composition of the white cells as a result of a cardiazol convulsion are shown in Table 1.

The level of the white cell count depended on the duration and severity of the convulsions. The maximum elevation of the white cell count over the original level (225-244%) was observed 4 times after long fits with severe convulsions.

Along with the changes in the white cell count, regular changes were observed in the white cell formula.

TABLE 1. Changes in the Number and Composition of White Cells in Rabbit No. 4 under the Influence of a Fit

Name of cells	Before fit	Immediately after fit	At an interval after the fit of			
			15 min	1 hr	2 hr	3 hr
White cells	6750	9800	15,000	9850	8300	7100
Basophils, in %	—	3.0	1.0	4.0	—	1.5
Eosinophils, in %	1.0	—	—	—	1.0	0.5
Pseudoeosinophils, juvenile, in %	—	—	1.0	1.5	1.5	—
Pseudoeosinophils (stab cells), in %	1.0	2.5	4.5	4.5	8.5	2.0
Pseudoeosinophils, segmented, in %	35.0	18.5	26.5	57.5	68.5	63.5
Lymphocytes, in %	57.5	61.0	64.5	28.5	18.5	25.5
Monocytes, in %	5.0	5.0	2.5	4.0	2.0	7.0

TABLE 2. Changes in the Bone Marrow in Rabbit No. 12 Under the Influence of Cardiazol Convulsions

Name of cells	Before experiment	After 21 fits	Name of cells	Before experiment	After 21 fits
	in %			in %	
Hemocytoblasts	—	0.4	Monocytes	—	—
Myeloblasts	1.4	2.2	Reticuloendothelial cells	1.6	1.8
Promyelocytes	1.8	3.4	Ferrat cells	0.2	1.0
Pseudoeosinophilic myelocytes	7.4	8.6	Plasma cells	0.2	1.0
Eosinophilic myelocytes	0.4	0.4	Botkin-Gumprecht cells	0.8	1.6
Basophilic myelocytes	—	0.2	Megakaryocytes	0.2	0.4
Pseudoeosinophilic metamyelocytes	8.2	9.4	Proerythroblasts	1.8	2.2
Eosinophilic metamyelocytes	—	0.2	Basophilic erythroblasts	5.0	5.6
Pseudoeosinophilic stab cells	7.4	10.0	Polychromatophilic erythroblasts	22.2	20.2
Eosinophilic stab cells	0.2	—	Oxyphilic erythroblasts	19.0	14.2
Pseudoeosinophilic segmented cells	13.8	17.4	Bare nuclei of erythroblasts	1.8	1.8
Eosinophilic segmented cells	0.2	0.4	Destroyed cells	0.8	1.4
Adult basophils	1.2	2.0	Dividing cells	0.8	1.4
Lymphocytes	3.2	2.3	Index of maturation of pseudoeosinophils	0.8	1.8
			Ratio between leukopoietic and erythropoietic cells	0.8	1.2

The degree of the shift also depended on the duration and, still more, the severity, of the fit.

In the first few minutes after the fit, the absolute number of lymphocytes was increased, but it then began to diminish. After 15 minutes to 1 hour pseudoeosinophils were predominant in the formula, varying in number from 39% to 82.5%. As the white cell count fell, the number of pseudoeosinophils did not diminish but, on the contrary, showed a tendency to increase. The absolute number of pseudoeosinophils remained at a high value when the total white cell count had returned to its original level.

In every case an increase in the pseudoeosinophilic stab cells (4-12.5%) was observed after injection of cardiazol, and in 11 animals 0.5-2.5% of juvenile pseudoeosinophils appeared at the height of the changes in the white cell formula. Eosinophils disappeared from the blood and the number of basophils and monocytes increased.

In 14 rabbits the platelet count was raised after the fits. The highest rise took place in the first 15 minutes after the fit, and amounted to 123-232% by comparison with the original value. Immediately after the rise in the platelet count it began to fall gradually, but in 9

cases the platelet count was still above its initial level 2-3 hours after the end of the fit.

In order to exclude any toxic action of cardiazol on the composition of the blood, in 6 experiments the drug was injected in doses too small to cause convulsions, but very close to the convulsive dose. Blood was taken at the same times as after the epileptiform attack. Under these circumstances no detectable changes took place in the number and composition of the white cells and in the platelet count.

In order to ascertain the cause of the changes in the peripheral blood, in 11 rabbits the effect of repeated convulsive fits on the functional state of the bone marrow was studied. Repeated epileptiform attacks gave rise to a myeloid reaction, which affected the granulopoietic and megakaryocytic series. As an example we describe the myelogram of rabbit No. 12 (Table 2).

The ratio between leukopoietic and erythropoietic cells was increased on account of an increase in the number of leukopoietic cells. An increase was observed in the number of myeloblasts, promyelocytes, pseudoeosinophilic myelocytes, and metamyelocytes. Whereas before the fits, their numbers varied between 3.4 and 31%, after the fits they increased to 15.3-38.8%. An increase also took place in platelet-forming megakaryocytes. We found no regular changes in erythropoiesis.

As a result of a fit, considerable changes thus took place in the morphological composition of the peripheral blood, mainly affecting the number and composition of the white cells and the platelet count. The leukocytic reaction in the first few minutes evidently arose from a redistribution of the blood. This was shown by the increase in the number of lymphocytes observed in the first minutes after the fit. The further increase in the white cell count resulted from the higher rate of liberation of adult pseudoeosinophils from the bone marrow. This was demonstrated by the shift of the pseudoeosinophils to the left, with the appearance of even juvenile forms in the peripheral blood. The true character of the resulting leukocytosis was confirmed by the onset of changes in the functional composition of the bone marrow, in the form of stimulation of granulopoiesis. The increased number of platelets in the peripheral blood after the epileptiform fit was explained by a study of the bone marrow in which an increase in the platelet-forming megakaryocytes was found.

From a comparison of the results of the investigation of hemopoiesis in experimental cardiazol epilepsy and clinical epilepsy in man, it may be concluded that the changes in hemopoiesis in both cases are closely similar.

From our findings we have reason to consider that the changes in hemopoiesis in epilepsy are connected with the fits. These changes may last much longer than the fits themselves, and may gradually become intensified.

SUMMARY

The effect of experimentally induced cardiazol epilepsy on the peripheral blood and bone marrow was studied in 16 rabbits. The epileptiform attacks provoked leukocytosis and a rise of the red cell count. The leukocytic reaction appeared during the first few minutes of an increased number of lymphocytes, and later on of pseudoeosinophils. Following several attacks, an intensified granulopoiesis and an increased number of platelet producing forms of megakaryocytes were observed in the bone marrow.

There were no modifications in the red blood picture.

The author concludes that the changes occuring in the blood are connected with the intensified bone marrow function, under the effect of epilepitform fits.

LITERATURE CITED

[1] I. N. Davydov, Byull. Éksptl. Biol. i Med. 11, 6, 557 (1941).

[2] N. M. Eremeeva, Collected Transactions of the Kursk Medical Institute 2, 15 (1955) [In Russian].

[3] B. M. Karlinskii, Trudy Karagandinskogo Med. Inst. 1, 396 (1957).

[4] A. Swensson, Ztschr. ges. exper. Med. 122, 14 (1953).