CHANGES IN HEMOPOIESIS IN CONGESTIVE SPLENOMEGALY WITH OR WITHOUT DENERVATION OF THE SPLEEN

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The problem of the mechanism of the changes in the composition of the blood in clinical and experimental congestive splenomegaly still continues to be a topic of discussion. Certain authors have suggested a possible reflex influence of the pathologically changed spleen on the hemopoietic system [4].

Of great interest are the reports of histologists [1] of the development of degenerative changes in the nerve cells of the solar plexus in splenomagaly, which in itself may be of importance in the development of the disorders of hemopoiesis. Experimental researches of Soviet authors [2,3] have given evidence of the possible development of anemia after denervation of the spleen.

We have been unable to find in the literature any mention of the study of the role of the nervous system in the production of the disorders of hemopoiesis in the splenomegalies.

The aim of the present research was to study the effect of ligation of the splenic vein (congestive splenomegaly) on hemopoiesis in digs and to ascertain the importance of denervation of the spleen in the mechanism of development of these changes.

METHOD

The investigations were carried out on 5 male dogs over a period of 7-11 months.

Ligation of the splenic vein was performed in two dogs, and in two more, ligation of the vein was combined with denervation of the spleen; in one dog denervation of the spleen alone was performed.

Congestive splenomegaly was produced by ligation of the main venous trunk and all the small veins composing the hilum. In denervation of the spleen, all the visible nerves leading to the spleen were divided. The adventitia was removed from the walls of the arteries for a distance of 2 cm, and the walls were then painted with a 10% solution of carbolic acid. In the course of the experiment we determined the red cell count, the hemoglobin concentration, the white cell count and formula, the platelet count, the osmotic resistance of the red cells to a hypotonic solution of NaCl and the serum bilirubin (Jendrassik's method), and we examined the bone marrow from puncture specimens.

In the present communication we give the results of observations over a period of 6 months.

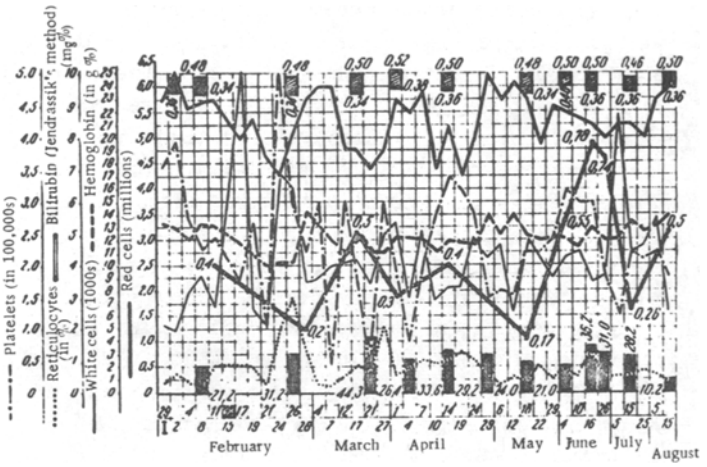

Fig. 1. Changes in the indices of hemopoiesis after ligation of the splenic vein (the dog Zhuk). February 15, 1958 — ligation of the splenic vein. Legend: ■ — number of erythroblasts in the bone marrow, in %; ▨ — osmotic resistance of the red cells to hypotonic saline.

RESULTS

In Fig. 1 are shown details of the changes in the peripheral blood picture and in the bone marrow after ligation of the splenic vein in the dog Zhuk. Immediately after operation a normochromic anemia developed, with a chronic remittent subsequent course. The periods of anemia were accompanied by an increase in the reticulocyte count, increased growth of cells of the erythroid series in the bone marrow, and a relative increase in the serum bilirubin concentration. In individual investigations a fall occurred in the osmotic resistance of the red cell. The development anemia was accompanied by a leukocytosis with an increase in the

number of segmented neutrophils, a slight eosinophilia during the first month, and a transient rise in number of monocytes and cells of the reticulo-endothelial system, and also by variations in the platelet count, which showed a tendency to fall.

In the next dog (Okhotnik), the hemoglobin concentration before operation was 90-92%, the red cell count 5,6000,000-6,200,000, the color index 0.73-0.86, the reticulocytes 0.1-0.5%, the osmotic resistance of the red cells 0.46-0.34, the serum bilirubin 0.5mg%, the white cell count 7400-11,500, the platelet count 120,000-230,000, and of the bone marrow cells, 11.8% were erythroblasts.

Immediately after ligation of the splenic vein a progressive anemia began to develop and on the 6th day the red cell count was 3,000,000. In the course of 2 months a remittent anemia was maintained, with a gradual restoration of the normal red cell count at the beginning of the 3rd month.

The development of anemia was accompanied by reticulocytosis (6.8%) and by an increase to 50.2% in the number of erythroblasts in the bone marrow.

Starting with the 3rd month, in spite of the restoration of the normal red cell count, intermittent increases took place in the reticulocyte count of the peripheral blood to 2.1%, accompained by similar intermittent fluctuations in the number of erythroblasts in the bone marrow. In respect to leukopoiesis, an intermittent leukocytosis was observed, with an increase in the segmented neutrophils; lymphocytosis with a slight eosinophilia, and an increase in the monocytes and cells of the reticuloendothelial system in the course of the first month after operation. Throughout the whole period of the observations there were intermittent increases in the platelet count to 310,000-470,000.

When ligation of the splenic vein was combined with denervation of the spleed (the dog Sever), as can be seen from Fig. 2, for 2 months there was a normochromic anemia with a slight reticulocytosis and an increase in the number of erythroblasts in the bone marrow. Starting with the 3rd month, a progressive fall took place in the red cell count, with a tendency towards hyperchromia (color index 1.1-1.2), with a marked reticulocytosis (75%), sharp stimulation of the erythroid series in the bone marrow (80% of erythroblasts), and an increase in the serum bilirubin concentration to 0.95 mg%.

In view of the unremitting increase in the anemia, splenectomy was performed (August 5, 1958, see Fig.2), after which a rapid rise took place immediately in the red cell count, with a simultaneous decrease to normal figures in the reticulocyte count and the serum bilirubin concentration. Signs of stimulation of the erythroid series in the bone marrow disappeared.

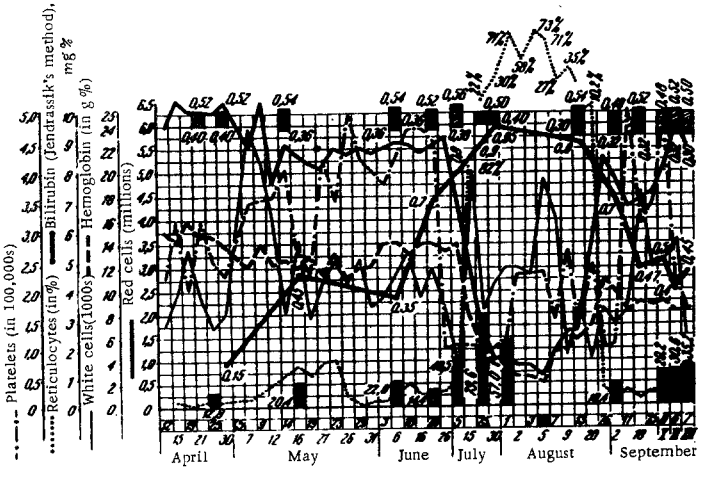

Fig. 2. Changes in the indices of hemopoiesis after ligation of the splenic vein, combined with denervation of the spleen (the dog Sever). May 15, 1958 — ligation of the splenic vein combined with denervation. August 5, 1958 — splenectomy. Legend as in Fig. 1.

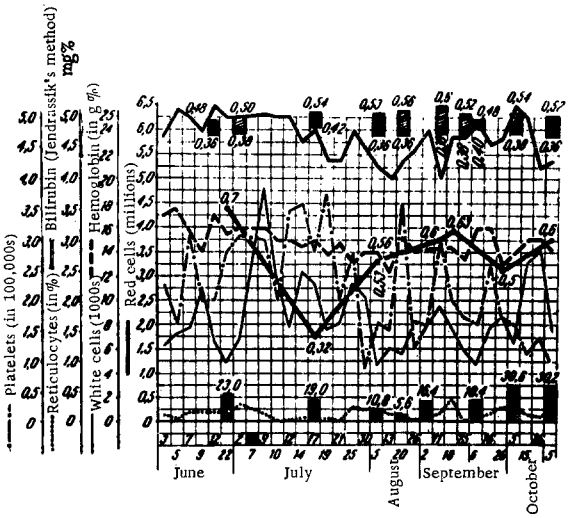

Fig. 3. Changes in the indices of hemopoiesis after denervation of the spleen (the dog Ryzhii). July 7, 1958 — denervation of the spleen. Legend as in Fig. 1.

Subsequently, as is apparent from Fig. 2, besides a slight fall in the red cell count, a considerable lowering of the hemoglobin concentration was observed (color index 0.5-0.4). In the bone marrow at this stage there was an increase in the number of erythroblasts with a relative increase in the proportion of basophilic forms.

These changes provide evidence in favor of inhibition of the maturation of erythroblasts and a diminution of the hemoglobinization of the red cells, evidently on account of a disturbance of the iron metabolism. Several authors have pointed out the possible development of such changes affecting hemopoiesis after splenectomy. At the height of development of the anemia, leukocytosis was observed with eosinopenia, lymphocytopenia and a considerable increase in the number of monocytes and cells of the reticulo-endothelial system. Thrombocytopenia was also observed. After splenectomy the normal indices of leuko- and thrombopoiesis were restored.

In another dog (Seryi), on which a similar operation was performed, the preoperative findings were: hemoglobin 74.4-90%, red cells 5,700,000-6,300,000, reticu-

locytes 0.1-0.8%, osmotic resistance of the red cells 0.50-0.36, bilirubin 0.7 mg%, white cells 7860-12,000; the bone marrow contained 21.4% of erythroblasts. After operation the development of a normochromic anemia was observed, with maximum decrease in the red cell count on the 13th day to 4,000,000. A moderate degree of anemia was maintained during the next two months. Starting with the middle of the second month, simultaneously with an increase in the red cell count, there was a reticulocytosis (1.9%) and stimulation of erythroblastic maturation in the bone marrow. This was not observed in the period of development of the anemia. After restoration of the normal red cell and reticulocyte counts, the number of erythroblasts in the bone marrow fell to normal figures.

A slight fall and rist in the maximum and minimum red cell resistance was observed. The bilirubin concentration was unchanged. For 2 months an increased white cell count to 46,000 was observed, which in the next months was around 14,000. The platelet count remained unchanged.

In the dog in which denervation of the spleen alone was performed (Ryzhii), from the 10th day after operation the animal developed a moderate normochromic anemia with a tendency towards intermittent fluctuations in the red cell count (Fig. 3). The development of anemia was accompanied by reticulocytopenia and by a fall in the number of erythroblasts in the bone marrow. A fall in the osmotic resistance of the red cells occurred in individual experiments. The bilirubin concentration was unchanged. For a period of 1/2-1 month the platelet count showed a tendency to rise and fall, and starting with the 3rd month a tendency towards thrombocytopenia was apparent.

The changes in the hematological indices in the experiments in which the splenic vein was ligated testify to the hemolytic character of the developing anemia (the rise in the reticulocyte count, the increased bilirubin concentration and the stimulation of erythropoiesis in the bone marrow in the absence of signs of disturbance of maturation of erythroblasts). In the experiments in which ligation of the vein was combined with denervationof the spleen, one dog (Sever) also developed a hemolytic anemia, but it was much less pronounced than in the dogs in which the vein was ligated only. In the other dog (Seryi) the development of anemia was not associated with intensification of hemolysis. It should be mentioned, however, that in this dog a small vein was left unligated.

During denervation of the spleen only, the development of anemia was due to depression of erythropoiesis (reticulocytopenia, decreased number of erythroblasts in the bone marrow), which agrees with the findings of other authors, working with dogs.

We consider that in congestive splenomegaly, when increased hemolysis of red cells takes place, denervation of the spleen may evidently increase this process still further.

It also follows from our observations that the presence of splenomegaly in its turn alters the character of the hematological changes usually observed in dogs after denervation of the spleen only.

SUMMARY

Following ligation of the splenic vein in two dogs, they showed development of wave-like hemolytic anemia. In one of the two dogs in which the vein was ligated in combination with splenic denervation, the hemolytic anemia manifested itself to a considerably greater degree than was the case in the experiment with the vein ligation alone. A rapid rise in the red cell count occured after splenectomy had been performed in connection with the progressive anemia. In dogs with splenic denervation alone, the development of anemia is connected with the depression of erythropoesis.

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