Ferrokinetics of the patients with Hypoplastic Anemia, Especially Regarding Splenectomy

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There are many reports on ferrokinetics of the patients with hypoplastic anemia. The data of these reports are elevated serum iron level, decreased unsaturated iron-binding capacity of the serum, decreased uptake of $^{59}\text{Fe}$ into the bone marrow, and decreased red blood cell $^{59}\text{Fe}$ utilization rate.

On the other hand, there are splenectomy as the treatment of the patients with hypoplastic anemia as well as blood transfusion, ACTH and adrenocorticosteroid hormone. The clinical entity for indications of splenectomy is not established yet. This presentation is made to discuss the indications of splenectomy for the patients with hypoplastic anemia.

Ferrokinetics of the six patients with hypoplastic anemia were studied with Hoff and Polycove's method. The splenectomy was done two patients out of six. Two patients out of four patients without splenectomy showed characteristic pattern of hypoplastic bone marrow failure; relatively lower uptake of $^{59}\text{Fe}$ into the bone marrow, prolonged disappearance of radioactivity from bone marrow, lower level of red blood cell $^{59}\text{Fe}$ utilization, and elevated uptake of liver and spleen.

One of the splenectomized case who did not take a improved clinical course after splenectomy showed little change of red blood cell utilization rate, of plasma iron disappearance time and of $^{59}\text{Fe}$ uptake of bone marrow. This case had an aplastic bone marrow.

The other case of the splenectomized hypoplastic anemia, whose clinical course was obviously improved after splenectomy, was observed normal range life span of $^{51}\text{Cr}$ labelled red blood cell, improved red blood cell $^{59}\text{Fe}$ utilization rate and plasma iron disappearance time as well as improved bone marrow picture, bleeding tendency and no necessity of blood transfusion after splenectomy. From these data, hypoplastic anemia could classify into two groups from ferrokinetics. The first group had a relatively higher uptake of $^{59}\text{Fe}$ into bone marrow, prolonged disappearance of radioactivity from bone marrow, decreased red blood cell $^{59}\text{Fe}$ utilization rate, and hypererythroblastic maturation arrest form bone marrow. The second group had a lower uptake of $^{59}\text{Fe}$ into bone marrow. The second group had a lower uptake of $^{59}\text{Fe}$ into bone marrow, higher uptake of $^{59}\text{Fe}$ into liver and spleen, extremely decreased red blood cell $^{59}\text{Fe}$ utilization rate, and hypo- aplastic bone marrow. The indication of splenectomy for the patients with hypoplastic anemia was considered to be on the first group.

The $^{59}\text{Fe}$ Ferrokinetics in the Mice Developed Experimental Hematological Disorders

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It is known that the chloramphenicol (CP) induces the hematological disorders such as hypoplastic anemia, however, the etiology of this mechanism is not clear. The ferrokinetics in the mice received massive chloramphenicol, were studied in this paper.

Female ICR mice, weighing 20 to 24 gm, were used for all experiments. Five mg of chloramphenicol was administered intraperitoneally twice a day for three days (CP three
days group), and five mg of chloramphenical was administered intraperitoneally once a day for thirty days. (CP thirty days group). The ferrokinetics was studied at twelve hour after last CP administration. For the studies of ferrokinetics, 1.6 μCi of $^{59}$Fe-ferrous citrate in a volume of 0.25 ml of sterilized physiological saline was administered into mouse tail vein intravenously. Peripheral red blood cell count, reticulocyte count, the serum iron level, plasma iron disappearance time, and $^{59}$Fe uptake of bone marrow, liver and spleen were determined in such mouse.

The results were as follow.

1) In normal mice, serum iron level was 242 γ/dl, red blood cell count was $1051 \pm 85 \times 10^4$, reticulocyte count was $28 \pm 15\%$, P.I.D.T. was 70±10 minutes and $^{59}$Fe reappearance rate was $83\%$ at 24 hours: 97±12% at 48 hours. The uptake of $^{59}$Fe in the bone marrow and spleen showed a peak at six hours after $^{59}$Fe administration. The uptake of $^{59}$Fe in the liver increased until six hour after $^{59}$Fe injection, and then made a plateau line.

2) In CP three days group, serum iron level was 298 γ/dl, P.I.D.T. was $100 \pm 30$ minutes, $^{59}$Fe reappearance time was $33 \pm 13\%$ at 24 hours; $55 \pm 20\%$ at 48 hours, red blood cell count was $1053 \pm 119 \times 10^4$ and reticulocyte count was $16 \pm 11\%$. The uptake of $^{59}$Fe in the spleen was extremely decreased, and slightly increased the uptake of liver and bone marrow.

3) In CP thirty days group, serum iron level was 360 γ/dl, P.I.D.T. was $100 \pm 20$ minutes, $^{59}$Fe reappearance time was $67 \pm 6\%$ at 24 hours: $82 \pm 3\%$ at 48 hours, red blood cell count was $757 \pm 72 \times 10^4$, and reticulocyte count was $54 \pm 23\%$. The uptake of $^{59}$Fe in the bone marrow, spleen and liver were decreased.

4) From these data, it was concluded that CP damaged the erythroblast colonies in the spleen at first, and then bone marrow failure was followed.

Erythrokinetic Studies in Patients with Ineffective Erythropoiesis

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Erythrokinetic studies were performed in twenty-eight cases, including patients with hereditary spherocytosis (7), pernicious anemia (2), paroxysmal nocturnal hemoglobinuria (3), erythroleukemia (4), refractory anemia (5), myelofibrosis (6, primary one 5 and secondary one 1) and thalassemia (a case of β-thalassemia minor). (Figures in brackets show the number of cases.)

Simultaneous $^{59}$Fe and $^{51}$Cr measurements as well as morphologic examinations were studied on these patients. Plasma iron turnover and bone marrow index were used as total erythropoiesis indices and as effective erythropoiesis indices were used reticulocyte, red cell iron turnover and red cell survival ($^{51}$Cr) index. The erythropoiesis indices (total and effective) and bone marrow efficiency were calculated according to the formulas presented by Haurani and associates. High degree of ineffective erythropoiesis was observed in all cases of erythroleukemia and pernicious anemia and some cases of paroxysmal nocturnal hemoglobinuria, myelofibrosis, refractory anemia and thalassemia. Mean values of bone marrow efficiency in blood disorders studied were as follows: hereditary spherocytosis 82.0%, pernicious anemia 40.4%, paroxysmal nocturnal hemoglobinuria 46.4%, erythroleukemia 8.8%, refractory anemia 49.8%, myelofibrosis 73.3% and thalassemia minor 56.2%.

In this paper, the meanings and limitations of each erythropoiesis index, especially ferrokinetics indices, in various blood disorders were discussed on the basis of presented data. Moreover, it has been clarified in patients with ineffective erythropoiesis that significant cor-