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Plasmapheresis for Spur Cell Anemia

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ABSTRACT. A 45-year-old male patient with spur cell anemia was treated by plasmapheresis. At first, a membrane plasma separator was employed six times successively to try to prevent the progressive anemia. No significant improvement was achieved with respect to hematological parameters of hemolysis. A discontinuous flow centrifuge was then used four times consecutively. The spur cell count decreased and the progression of the anemia was transiently interrupted after every plasmapheresis of this type.

Sequential measurements of the free cholesterol/phospholipid (FC/PL) molar ratio of the red cell membrane lipid revealed the importance of a plasma factor for spur cell formation. It showed that abnormal changes in FC/PL ratio of the red cell membrane were entirely dependent on a precursory change in the lipid composition of the patient's plasma.

Although, to our knowledge, plasmapheresis to treat spur cell anemia has not yet been recorded in the literature, in our experience, this therapeutic measure is recommendable for patients with spur cell anemia unresponsive to other forms of treatment.

Recently plasmapheresis has been widely used for the treatment of various diseases primarily on the basis of an immunological concept. Many reports have been published about the application of plamapheresis to the care of hematological disorders, especially of idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP) and autoimmune hemolytic anemia (AIHA).[1] However, no information has yet been obtained as to the plasmapheresis treatment of the anemias due to hemolysis of red cells with an abnormal shape, such as spur cell anemia. Spur cell anemia is characterized biochemically by an increased amount of free cholesterol (FC) and an elevated free cholesterol/phospholipid (FC/PL) molar ratio of the erythrocyte membrane.

We tried plasmapheresis in patient with spur cell anemia for the purpose of removing the plasma components which probably play an important role in spur cell formation. This communication aims to describe our experience and to evaluate the effectiveness of plasmapheresis to spur cell anemia.

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CASE PRESENTATION

A 45-year-old male with a 20-year history of alcoholism was accidentally wounded with a scissor in his right thigh, which produced a big hematoma, in 1982. Thereafter he was transferred to our hospital because of progressive anemia and bleeding tendency.[7)]

On physical examination, the blood pressure was 128/78 mmHg, and the pulse 102. Anemia, jaundice, vascular spiders and palmar erythema were noted. The abdomen showed hepatosplenomegaly and ascites. There was no peripheral edema. A big hematoma was present on his right thigh.

The hematocrit was 29.8 per cent ; the white cell count was 14,300, with 79 per cent neutrophils, 7 per cent band forms, 4 per cent lymphocytes, 10 per cent monocytes. The platelet count was 83,000/μl, and the reticulocyte count was 2.1 per cent.

The serum protein was 7.4 g per 100 ml (the albumin 2.5 g and the globulin 4.9 g). The total bilirubin 13.8 mg per 100 ml (the conjugated bilirubin 6.3 mg per 100 ml), the cholesterol 89 mg per 100 ml, the lactic dehydrogenase (LDH) 352 I.U. per litter, the SGOT was 111 I.U. per litter, the SGPT was 43 I.U. per litter, the creatinine 2.5 mg per 100 ml, the blood urea nitrogen 56 mg per 100 ml, the triglyceride 68 mg per 100 ml, β-lipoprotein 171 mg per 100 ml. The prothrombin time 15.7 seconds (10.4～11.2 seconds : normal), the activated partial thromboplastin time 36.5 seconds (23.8～28.8 seconds : normal), the antithrombin- III 10.4 mg per 100 ml (29.1±3.5 : normal).

Evidence of hyperbilirubinemia, very low levels of serum haptoglobin (less

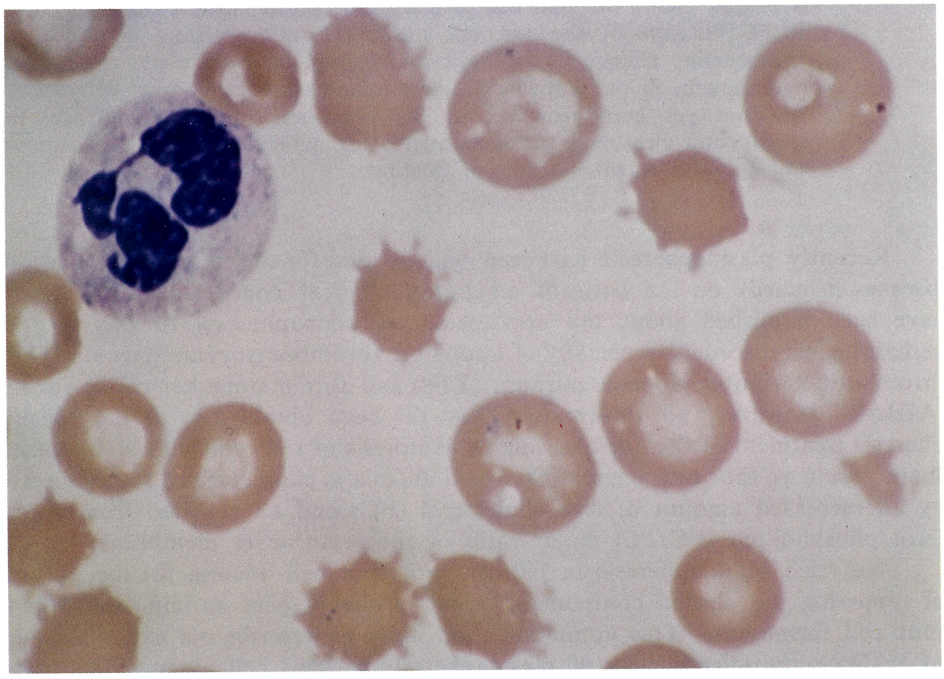

Fig. 1. Peripheral blood smears of patient with spur cell anemia. Thorny projections are seen on the surface of erythrocytes.

than 10 mg per 100 ml) and a shortened red cell life span (^{51}Cr T $\frac{1}{2}=16$ days) revealed a hemolytic anemia.

About 30 per cent of the erythrocytes were spur cells as observed on the peripheral blood smear (Fig. 1), and typical spur cells were demonstrable by scanning electron microscopy as shown in Figure 2.

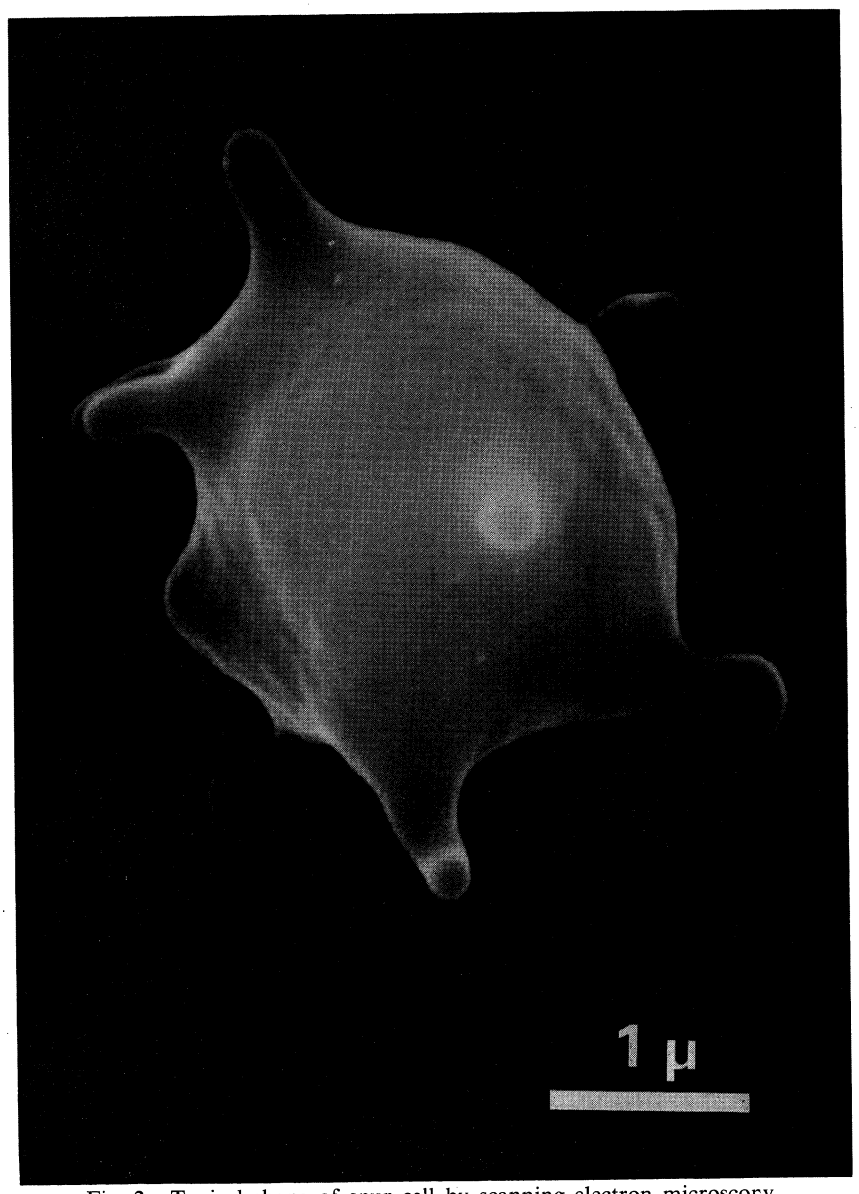

Fig. 2. Typical shape of spur cell by scanning electron microscopy.

PLASMAPHERESIS

1. *In vitro* studies (Fig. 3)

Incubation experiments were performed at 37°C for 12 hours by preparing three kinds of mixtures : the red cells from the patient with spur cell anemia mixed with normal plasma, with albumin solution (4.5 per cent), or with the spur cell anemia patient's own plasma. During the incubation experiments, the changes of the free cholesterol/phospholipid (FC/PL) molar ratio of the erythrocyte membrane lipids were pursued by means of Iatroscan.[4] As shown in Figure 3, elevated FC/PL molar ratio (normal range : 0.91±0.05) was characteristic of spur cell anemia. FC/PL ratios in the mixtures of albumin [▲] and normal plasma [●] with red cells from the patient with spur cell anemia returned to the near normal range (1.00, 1.01), respectively. No transformation from spur cells to discoid erythrocytes were observed by mixing normal plasma with the red cells of the spur cell anemia patient in spite of the fact that a marked improvement of FC/PL molar ratio was obtained.

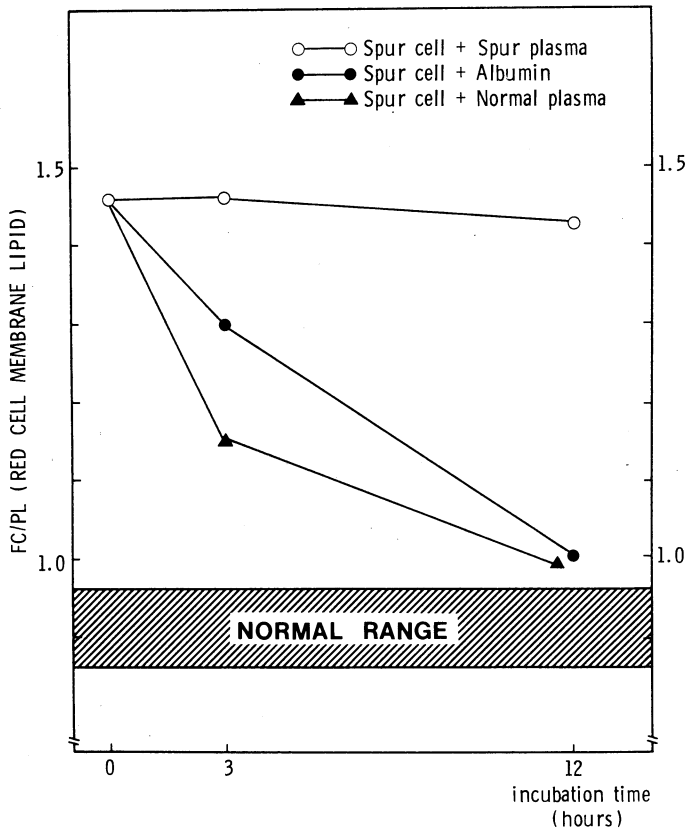

Fig. 3. Effect of incubation on FC/PL ratio of the red cells from the spur cell anemia patient mixed with normal plasma and that with albumin. FC/PL ratio was 1.46 at 0 hour. After 3 hours of incubation, the ratios shifted to the level of 1.46 [○], 1.30 [●] and 1.15 [▲], respectively. At 12 hours of incubation, these were 1.43 [○], 1.01 [●] and 1.00 [▲].

2. *In vivo* studies (Fig. 4)

A) Plasmapheresis by membrane plasma separator

We anticipated the effectiveness of plasmapheresis for spur cell anemia from the experimental data obtained in *in vitro* studies (Fig. 3). Therefore, plasmapheresis was carried out six times by means of a membrane plasma separator, replacing with albumin solution (four times) and fresh frozen plasma (2 times). After the plasmapheresis, the levels of serum LDH improved to some extent but no improvement was observed regarding the level of total bilirubin and the spur cell count in the peripheral blood smear. Serum haptoglobin was constantly below 10 mg/dl. It was felt that plasmapheresis with the membrane plasma separator did not seem to lead to elimination of the substances that cause spur cell formation, because progressive anemia was persistent in spite of six repeated plasmaphereses for thirty-three days.

B) Plasmapheresis by Haemonetics Model PEX (Fig. 4)

The disappointing results with membrane plasma separator led us to adopt the Haemonetics Model PEX which was used four times successively. By this procedure, a decreased spur cell count in the peripheral blood smear was successfully obtained and blood transfusion was unnecessary for a short while.

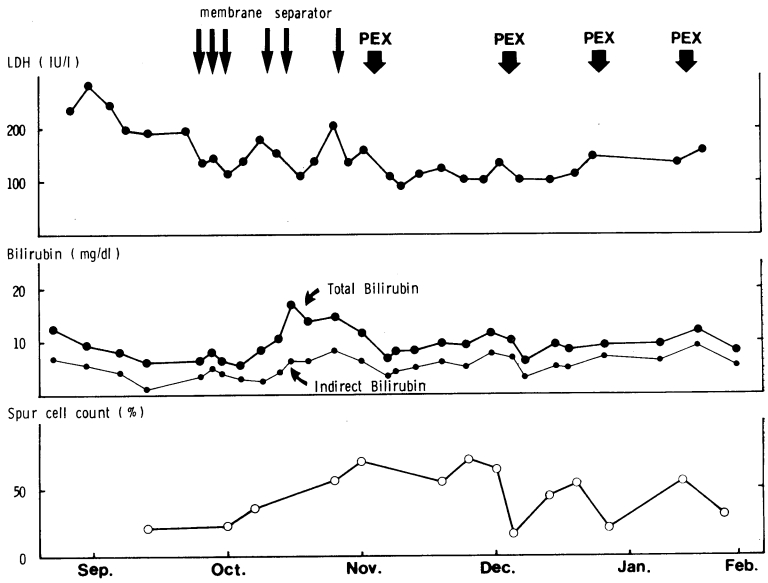

Fig. 4. Clinical course of spur cell anemia (82-5024). Membrane plasma separator was performed by use of MA-2500 (KURARE, JAPAN, pore size 0.2 μ) and discontinuous flow cell separating was by Haemonetics Model PEX.

DISCUSSION

In 1964, spur cell anemia was described as a hemolytic anemia syndrome which was characterized by the presence in the peripheral blood of red cells

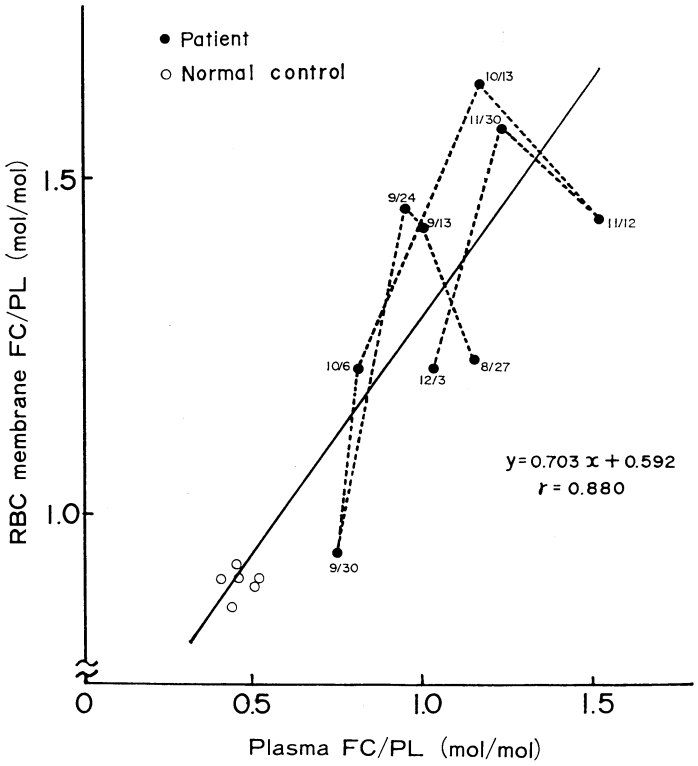

Fig. 5. Dynamic changes of FC/PL ratios in the clinical course of spur cell anemia. Dates are indicated by the figures of month/day (9/30 is September 30, as for instance).

possessing spur-like projections.[5] Later, Cooper *et al.*[2,6] proposed the characteristic features of spur cell anemia as follows: ① elevated FC and FC/PL ratio of the erythrocyte membrane, ② low lecithin cholesterol acyltransferase (LCAT) activity, ③ increased serum betalipoprotein, ④ rise in the concentration of bile salts and ⑤ positive formation of spur cells by incubating a mixture of erythrocyte from a normal subject (compatible in blood group with the spur cell anemia patient) with the patient's plasma. We, however, reported negative results in incubation experiments with a mixture of normal discocytes with patient's plasma.[3]

It is therefore conceived that the factors which promote spur cell formation must be present in some unknown plasma components. Thereafter, plasmapheresis was applied ten times consecutively to decrease the spur cell count in the patient's peripheral blood (Fig. 4).

Plasmapheresis with a membrane plasma separator was carried out successively with about five day intervals. Neither improvement of the anemia nor a decrease in the spur cell count was achieved. It is concluded that the substances responsible for spur cell formation were not eliminated by the use of a membrane plasma separator.

Subsequently, we employed a discontinuous flow cell separator (Haemonetics Model PEX, Haemonetics Inc.) and the patient underwent plasmapheresis four

times during 71 days. The intervals between plasmaphereses were about eighteen days, and after every procedure the spur cell count decreased significantly, though transiently.

However, hemolysis seemed to be persistent throughout the clinical course as judged from the low level of serum haptoglobin and hyperbilirubinemia.

After every plasmapheresis with the Haemonetics, a number of spur cells might have destroyed mechanically during the centrifugation procedure. So, relative decrease in spur ceil counts was observed soon after plasmapheresis (Fig. 4). Mechanical destruction of spur cells during plasmapheresis might be partly responsible for the hyperbilirubinemia and the decreased spur cell count. Figure 5 shows the time course, fluctuation of the FC/PL ratio of red cell membrane compared with that of plasma (dotted lines) which was observed in the *in vitro* incubation experiment. Erythrocytes from normal subjects are shown by open circles and the red cells from the spur cell anemia patient by closed circles (Fig. 5). It is conceivable from this figure that the lipid composition of red cells and that of plasma were improved to a considerable extent on the days after plasmapheresis, on September 30 and December 3 for example.

The improved FC/PL ratio of the red cell membrane and of the plasma after plasmapheresis suggest that the use of plasmapheresis will be a useful measure to inhibit the progression of anemia, although it is not sufficiently powerful to prevent hemolysis completely, because of the low level of haptoglobin during clinical course.

Acknowledgment

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