Preleukemic States
—Its Current Progress in Diagnosis and Treatment

The presence of preleukemic state as a syndrome preceding cancer or a precancerous phase has been known for many years. With the establishment of diagnostic criteria and treatment for hematological diseases, particularly for leukemia as well as anemia, and with the development of the concept of other types of hematologic abnormalities for standardizing such criteria and treatment, the preleukemic state has drawn much attention as a syndrome preceding these diseases. Clinically, we occasionally encounter cases suspected to be preleukemic. General interests in preleukemic states are also increasing with the progress in medicine enabling early detection and treatment of such conditions and justifying aggressive approach toward preventable diseases.

In Japan, aplastic anemia cases have been noticed as one of preleukemic states. On the other hand, the term of refractory anemia has been used in foreign countries as a syndrome preceding leukemia. The term “refractory anemia” is thought to have appeared for the first time around 1938, and it has become more commonly used since the refractory anemia with excess of blasts (RAEB) was reported by Dreyfuss and Sultan in 1970. However, the interests have been focused on such conditions as the preleukemic states and hemopoietic dysplasia, and French-American-British (FAB) group proposed such states as “myelodysplastic syndrome (MDS)” in 1982. Since then, many hematologists paid attention to such myelodysplastic states. So far, the diagnostic criteria and principle for treatment should be established in three types of MDS, that is, refractory anemia (RA), RA with ringed sideroblast (RARS) and RAEB in MDS group. We could investigate approximately 500 cases of these three types in Japan, retrospectively, and obtained the results of symptoms, hematological characteristics, diagnostic criteria, prognosis and so on. Furthermore, the interrelationship among the terminology of refractory anemia, myelodysplastic syndrome and hemopoietic dysplasia was considered and analysed.

Primary acquired refractory anemia (PARA) -RA in MDS-, primary acquired sideroblastic anemia (PASA) -RARS in MDS-, and paroxysmal nocturnal hemoglobinuria (PNH) are grouped from the view-point of bone marrow cellularity, as being different from aplastic anemia and pure red cell aplasia. Hemopoietic dysplasia is a general term for preleukemic states and some cases of PARA, PASA, PNH and aplastic anemia can be placed in this categories. Leukemic transformation rates are, however, confirmed to be 20% in PARA, 8.0% in PASA, 3% in PNH and 0.3 to 2.0% in aplastic anemia, while the rate in RAEB was 69 to 71%. These findings mean that the prognostic factors do not depend necessarily upon the leukemic transformation, namely, preleukemic states, but also upon the infection and bleeding due to leukopenia and thrombocytopenia. Therapy must be carried out according to the types of these three diseases, and also, to clinical and hematological findings in individual case. Therefore, the supportive care such as blood transfusion as well as antibiotics administration should be generally carried out, and the allogeneic bone marrow transplantation will be, if possible, beneficial. Further efforts should be made to establish the treatment protocol using Vitamin D₃ and retinoic acid derivatives and low dose Ara-c which are thought to urge the cell differentiation. There still remains many problems in refractory anemia researches, and the follow-up studies for long periods, sometimes beyond one decade, are urgently needed.

According to our preleukemia research over 20 years, the importance of the follow-up studies and of the preservations of specimens, which will be analyzed by newly developed technique, are emphasized in perspectives of the future medical studies.