

## Aplastic Anemia in Korea

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The annual incidence rate of aplastic anemia (AA) in Asian countries is higher than that in Western countries. There is no clear explanation for this geographic difference in AA. The pathogenesis in AA has been understood through many investigations in hematopoiesis and immunology. Recently, the survival rate and the quality of life of the patients with AA have been steadily improved by the development of a variety of treatments such as the immunosuppressive therapy with anti-thymocyte globulin (ATG) or anti-lymphocyte globulin (ALG), and hematopoietic stem cell (HSC) transplantation, in case the patients have HLA matched donor. *The Korean Society of Pediatric Hemato-oncology* investigated retrospectively the incidence, treatment strategies, survival rate, and time to become independent from transfusion in patients with AA, who were diagnosed from January 1<sup>st</sup>, 1991 to December 31<sup>st</sup>, 2000 in Korea.

**Method:** All the questionnaires were sent to a group of training hospitals, and we collected about 600 questionnaire forms from 27 hospitals. However, 493 reports were available for data analysis.

**Results:** The male and female ratio in AA is 1.1 (259 males vs. 234 female). The median age at diagnosis is 9 years old (range: 0.8 ~ 16 years old). The annual incidence of children with AA in Korea is 4.5 per million on the basis of Korean pediatric population. In etiology, there are 20 cases (4.1%) in congenital and others in acquired AA. In case of acquired AA, the cause of illness was not identifiable for most of the patients, but 1 patient had hepatitis-associated AA, and 3 patients developed the illness after medication. According to the initial laboratory data at diagnosis, the peripheral blood findings

showed that hemoglobin is  $7.1 \pm 2.4$  g/dL, white blood cell  $3,200/\mu\text{L}$  (200 ~ 16,550), absolute neutrophil counts  $670/\mu\text{L}$  (0 ~ 12,487), platelets  $19,000/\mu\text{L}$  (1,000 ~ 500,000), and corrected reticulocytes 0.18% (0.0 ~ 4.7) in complete blood cell counts. The bone marrow examination revealed that cellularity was below 25 % in 348 patients, and over 25 % in 105 patients. In the available data, 269 patients (54.6%) were diagnosed of severe aplastic anemia (SAA) and 224 patients of non-SAA.

HSC transplantations were done for 96 patients (19.5%) and others received other treatments such as the immunosuppressive therapy. The ATG or ALG treatment was done for 263 patients, corticosteroids in 259 cases, cyclosporine A in 215 children with AA, and anabolic steroids in 138 patients. The combination immunosuppressive therapy including ATG or ALG plus corticosteroid plus cyclosporin A (CSA) were applied to 154 children with AA, and transfusion only in 37 cases, as conservative care. Several combination therapies were performed in 75 patients with ATG or ALG plus corticosteroid plus anabolic steroids, in 18 cases with ATG or ALG plus CSA plus anabolic steroids. In case of those patients transplanted with hematopoietic stem cells, the time from diagnosis to transplantation was 12 months (1 ~ 144 months) and the sources of HSC were bone marrow in 82 cases, growth factor mobilized peripheral blood in five, and cord blood in six. There were 57 patients transfused below 40 units of blood products before HSC transplantation. Graft rejection was identified from 16 patients and booster transplantations were done for 12 patients among them. In case of complications of HSC transplantation, the graft versus host disease was developed

in 20 patients and viral diseases in 12 cases including the CMV and herpetic infection. Three patients were shown severe hepatitis including hepatitis C virus infection and toxic manifestations after HSC transplantation. Also, one patient suffered from veno-occlusive disease.

The overall survival rate in children with AA is 64.0%. The survival rate in HSC transplantation is better than that in immunosuppressive therapy (76.9% vs. 62.6%,  $P = 0.0398$ ). There was no significant difference in terms of the sex and disease severity variables. In HSC transplantation, transfusion was not related to the survival rate. There was no significant difference in the probability of transfusion independence according to treatment strategies, even though it was 71.0% in HSC transplantation and 12.8% in immunosuppressive therapy on the end point of survey ( $P = 0.47$ ).

The response pattern was as follows. There were 155 cases of complete response, 110 patients of partial response and 120 cases of no response in spite of various treatments. The relapse after treatment was found in 11 patients after immunosuppressive therapy, of which 6 patients experienced more than 2nd relapse. The median time between the end of treatment and relapse was 16 months (6 ~ 84 months). Only three cases developed into other diseases (1 case into acute myeloid leukemia and 2 cases into myelodysplastic syndrome). The median time from diagnosis to the end of treatment was 62 months (0.5 ~ 174 months). In fatal cases, the median time between diagnosis and death was 29 months (0 ~ 144 months) despite several therapeutic strategies.

**Conclusion:** In Korea, the annual incidence of children with AA is 4.5 per million. This result is similar to the ones reported in other Asian countries, but higher than those in Western countries. Although a lot of children with AA received various therapies including immunosuppressive therapy or HSC transplantation, new treatment strategies have to be developed to improve the survival rate and the quality of life of children with AA.