J Korean Med Sci 2000; 15: 103-4
ISSN 1011-8934

Successful Allogeneic Bone Marrow Transplantation for Childhood-Onset Refractory Anemia with Ringed Sideroblasts

Refractory anemia with ringed sideroblasts (RARS) is an extremely rare type of myelodysplastic syndrome in children. We describe a 10-year-old boy with RARS presented with pancytopenia. He remained relatively stable with only a few transfusions until age of 20 years, when he underwent an allogeneic bone marrow transplantation (BMT) because of increased transfusion requirements. He remains in complete chimeric state at 20 months posttransplant with normal hematologic parameters. To our knowledge, this is the first description of successful BMT in a patient with childhood-onset RARS. The indication of BMT for this rare disorder in children is discussed.

Key Words: *Anemia Sideroblastic; Myelodysplastic Syndromes; Child; Bone Marrow Transplantation; Transplantation, Homologous*

Hoon Kook, Chan Jong Kim, Won Sang Yoon, Dong Wook Ryang*, Tai Ju Hwang

Departments of Pediatrics and Clinical Pathology*, Hematopoietic Stem Cell Transplant Program, Chonnam National University Medical School, Kwangju, Korea

Received: 31 May 1999
Accepted: 23 July 1999

Address for correspondence
Hoon Kook, M.D.
Department of Pediatrics, Chonnam National University Medical School, 8 Hak-dong, Dong-gu, Kwangju 501-757, Korea
Tel: +82.62-220-6645, Fax: +82.62-222-6103
E-mail: hoonkook@chonnam.ac.kr

INTRODUCTION

Myelodysplastic syndrome (MDS) is very rare in children, representing 3% or less of all hematopoietic malignancies. Refractory anemia with ringed sideroblasts (RARS) is an extremely rare subtype of MDS in children with only a few cases being reported, while the subtype constitutes about 25% of all adult cases (1). A pooled analysis of eight larger series representing 110 children with de novo MDS and a recent study of the largest 167 pediatric patients did not find any case of RARS (2, 3).

Although allogeneic bone marrow transplantation (BMT) is considered as a potential curative option for pediatric MDS patients with a survival rate of 40-60%, this is the first description of successful allogeneic BMT, to our knowledge, in a patient with childhood-onset RARS.

CASE REPORT

The child was first seen at the age of 10 years with dizziness and intermittent epistaxis for a year. Complete blood cell count revealed hemoglobin of 5.0 g/dL, white blood cell (WBC) count of 3.0×10^9/L and platelets of 43×10^9/L. He received a couple of transfusions and was discharged. He remained stable and did not seek medical attention. Four years later, he was readmitted because of epistaxis and weakness. The hemogram showed WBC count of 2.5×10^9/L, hemoglobin of 4.1 g/dL and platelets of 9×10^9/L. Bone marrow aspiration and biopsy showed a cellularity of about 50% with evidence of dyserythropoiesis and dysmegakaryopoiesis with 16% ringed sideroblasts on iron staining, rendering the diagnosis of RARS. Clonal cytogenetic abnormalities were not identified. The marrow precursor cells were not vacuolated with no evidence of mitochondrial cytopathy.

Several therapies, such as low-dose cytosine arabinoside, high-dose vitamin C, low-dose prednisolone, and granulocyte, macrophage-colony stimulating factor resulted in only slight, transient improvements in his hemogram. He remained relatively stable without transfusions, though cytopenic, until age of 20 years, when his transfusion requirements abruptly increased due to alloimmunization right after several transfusions following an accidental leg fracture. He remained in INT-1-risk group categorized by the International Prognostic Scoring System (IPSS) (4) despite transfusion dependence as his bone marrow blasts remained less than 5% with normal karyotype.

He underwent an allogeneic BMT from his HLA-identical sister. Busulfan and cyclophosphamide were used as a preparative regimen with standard cyclosporin A plus short course of methotrexate as a graft versus host disease

prophylaxis. His posttransplant course was uneventful with rapid engraftment. He remains in complete chimeric state at 20 months posttransplant with normal hematologic parameters.

DISCUSSION

In addition to the rarity of RARS in children, more than half of the reported cases in children had systemic disorders such as mitochondrial cytopathy, w/wo Pearson's disease or platelet storage pool disorder (5, 6). Bader-Meunier et al. reported seven patients with RARS, the largest cluster of childhood RARS, in a French multicenter study. However, all seven patients were associated with mitochondrial cytopathy, a polyvisceral disorder with characteristic vacuolization of marrow precursors (5).

Only a few cases of BMT experiences in childhood and adolescent RARS were reported in the literature. Castaneda et al. (7) first described a 9-year-old child with RARS who died of complications two months following an unrelated transplant. The patient had shown rapid progression to severe bone marrow aplasia which was unusual for adult RARS cases. Two adolescents with RARS were included among 27 MDS patients who were transplanted with busulfan-based conditioning regimen (8). The first patient had a secondary RARS after radiation and chemotherapy for Hodgkin's disease. The second patient was an 18-year-old female, alive 4.7+ months posttransplant, who had been diagnosed as a primary RARS at the age of 16.5 years. The indication of transplant for those patients was not specified (8). One RARS patient with familial platelet storage pool disorder died soon after matched unrelated BMT (6).

Because of the variable natural history of MDS, the patient selection for an aggressive therapy such as BMT, especially those with RA or RARS, becomes a major issue. The IPSS risk group may not be useful as seen in this case. The main indication for those patients might be progressive marrow failure, resulting in pancytopenia and/or platelet-transfusion dependence.

REFERENCES

1. Fourcar K, Langdon RM, Armitage JO, Olson DB, Carroll TJ. *Myelodysplastic syndromes. A clinical and pathologic analysis of 109 cases. Cancer 1985; 56: 553-61.*
2. Hasle H. *Myelodysplastic syndrome in childhood - classification, epidemiology, and treatment. Leuk Lymphoma 1994; 13: 11-26.*
3. Luna-Fineman S, Shannon KM, Atwater SK, Davis J, Masterson M, Ortega J, Sanders J, Steinherz P, Weinberg V, Lange BJ. *Myelodysplastic and myeloproliferative disorders of childhood: a study of 167 patients. Blood 1999; 93: 459-66.*
4. Greenberg P, Cox C, LeBeau MM, Fenaux P, Morel P, Sanz G, Sanz M, Vallespi T, Hamblin T, Oscier D, Ohyashiki K, Toyoma K, Aul C, Mufti G, Bennett J. *International scoring system for evaluating prognosis in myelodysplastic syndromes. Blood 1997; 89: 2079-88.*
5. Bader-Meunier B, Mielot F, Tchernia G, Buisine J, Delsol G, Duchayne E, Lemerle S, Leverger G, De Lumley L, Manel A-M, Nathanson M, Plantaz D, Robert A, Schaison G, Sommelet D, Vilmer E. *Myelodysplastic syndrome in childhood: report of 49 patients from a French multicenter study. Br J Haematol 1996; 92: 344-50.*
6. Jackson GH, Carey PJ, Cant AJ, Bown NP, Reid MM. *Myelodysplastic syndrome in children. Br J Haematol 1993; 84: 185-6.*
7. Castaneda VL, Williams TE, Harper JL, Graham-Pole J, Parmley RT. *Severe refractory anemia with ringed sideroblasts and bone marrow aplasia in a child. Am J Pediatr Hematol Oncol 1992; 14: 70-6.*
8. Ratanatharathorn V, Kananes C, Uberti J, Lum LG, de Planque MM, Schultz KR, Cronin S, Dan ME, Mohamed A, Hussein M, Sensenbrenner LL. *Busulfan-based regimens and allogeneic bone marrow transplantation in patients with myelodysplastic syndromes. Blood 1993; 81: 2194-9.*