Spontaneous remission and loss of monosomy 7: a window of opportunity for young children with SAMD9L syndrome

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Abstract

Monosomy 7 is the most common cytogenetic abnormality in pediatric myelodysplastic syndrome (MDS) and associated with a high risk of disease progression. However, in young children, spontaneous loss of monosomy 7 with concomitant hematologic recovery has been described, especially in the presence of germline mutations in *SAMD9* and *SAMD9L* genes. Here, we report on our experience of close surveillance instead of upfront hematopoietic stem cell transplantation (HSCT) in seven patients diagnosed with SAMD9L syndrome and monosomy 7 at a median age of 0.6 years (range, 0.4-2.9). Within 14 months from diagnosis, three children experienced spontaneous hematological remission accompanied by a decrease in monosomy 7 clone size. Subclones with somatic *SAMD9L* mutations in *cis* were identified in five patients, three of whom attained hematological remission. Two patients acquired *RUNX1* and *EZH2* mutations during the observation period, of whom one progressed to myelodysplastic syndrome with excess of blasts (MDS-EB). Four patients underwent allogeneic HSCT at a median time of 26 months (range, 14-40) from diagnosis for MDS-EB, necrotizing granulomatous lymphadenitis, persistent monosomy 7, and severe neutropenia. At last follow-up, six patients were alive, while one passed away due to transplant-related causes. These data confirm previous observations that monosomy 7 can be transient in young children with SAMD9L syndrome. However, they also indicate that delaying HSCT poses a substantial risk of severe infection and disease progression. Finally, surveillance of patients with SAMD9L syndrome and monosomy 7 is critical to define the evolving genetic landscape and to determine the appropriate timing of HSCT (*clinicaltrials gov. Identifier: NCT00662090*).