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CASE REPORT

Unrelated hematopoietic stem cell transplantation for familial platelet disorder/acute myeloid leukemia with germline *RUNX1* mutations

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Abstract

Germline mutations in *RUNX1* result in rare autosomal-dominant familial platelet disorder with predisposition to acute myeloid leukemia (FPD/AML). As genetic analysis is becoming increasingly prevalent, the diagnosis rate of FPD/AML is expected to increase. In this report, we present two pedigrees, one diagnosed molecularly and another highly suspected to be FPD/AML, whose members both received allogeneic hematopoietic stem cell transplantation (HSCT). Both pedigrees had a family history of thrombocytopenia, platelet dysfunction, and hematological malignancies. One family inherited a frameshift mutation (p.P240fs) of *RUNX1*, a known pathogenic variant. Another family inherited a point mutation (p.G168R) in the runt-homology domain, the clinical significance of which is uncertain at this point. As this mutation was completely absent from all population databases and had a relatively high REVEL score of 0.947, we thought that it would be dangerous to ignore its possible pathogenicity. Consequently, we avoided choosing HSCT donors from relatives of both families and performed HSCT from unrelated donors. In conclusion, our experience with two families of FPD/AML highlights the importance of searching for gene mutations associated with germline predisposition and indicates the necessity of developing a donor coordination system for FPD/AML patients, as well as a support system for families.

Keywords Familial platelet disorder · Myelodysplastic syndrome · Acute myeloid leukemia · *RUNX1* mutation · Germline · Genetic pedigree

Introduction

Germline mutations in runt-related transcription factor 1 (*RUNX1*) result in rare autosomal-dominant familial platelet disorder with predisposition to acute myeloid leukemia (FPD/AML) [1]. The clinical application of next-generation sequencing has revealed a higher preponderance of FPD/AML families than expected, with more than 130 independent FPD/AML families with germline *RUNX1* genetic alterations reported [2]. However, their clinical presentation and prognosis, along with the respective characteristics of genetic alterations in each pedigree, are still insufficiently understood. Furthermore, a standard donor selection procedure for these patients has also not been developed, although allogeneic hematopoietic stem cell transplantation (HSCT) is the only curative treatment. In this report, we present two pedigrees: one diagnosed molecularly and another highly suspected to be FPD/AML, both of whose members underwent allogeneic hematopoietic stem cell transplantation (HSCT) (Table 1).

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