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LETTER TO THE EDITOR

Acute myeloid leukemia in a child with dedicator of cytokinesis 8 (DOCK8) deficiency

To the Editor: Dedicator of cytokinesis 8 (DOCK8) deficiency is an immunodeficiency characterized by recurrent respiratory tract infections, elevated IgE levels, eosinophilia, severe atopic dermatitis, asthma, food allergies, increased incidence of viral cutaneous infections,[1,2] and high risk of malignancy.[3,4]

A 7-year-old male with DOCK8 deficiency was referred to our hospital for hematopoietic stem cell transplantation (HSCT). The patient had a history of eczema, recurrent sinopulmonary infection, food allergy, and molluscum contagiosum. On admission, he was found to have anemia and thrombocytopenia (Hb 8.3 g/dl, white blood cell count 5,500/mm^3, thrombocyte count 68,000/mm^3); his peripheral blood smear showed myeloblasts and a bone marrow aspirate showed 22% myeloblasts, 3% promyelocytes, 1% myleocytes, 2% metamyelocytes, 8% neutrophils, 9% eosinophils, 17% normoblasts, 33% lymphocytes, and 5% monocytes. Flow cytometric analysis showed CD13 56%, CD15 40%, CD33 61%, CD34 74%, CD45 98%, CD117 72%, HLA DR 90%, and MPO 24%. Cytogenetic analysis showed 46; XY and FISH was negative for deletion 5q, deletion 7q, monosomy 7, 11q23 abnormality, and trisomy 8. t(15;17), t(8;21), and inversion 16 were also negative on molecular analysis. He was diagnosed with acute myeloid leukemia (AML), and the AML-BFM 2004 Interim chemotherapy protocol was started. According to this protocol, the patient was placed in the high-risk group. The patient was given induction chemotherapy (cytarabine, idarubicin, etoposide, and intratechal cytarabine) of AML BFM 2004 Interim protocol. Then, the patient was given a second induction (high-dose cytarabine, mitoxantrone, and intratechal cytarabine) of the same protocol. However, remission was not achieved. The chemotherapy protocol was switched to fludarabine, cytarabine, idarubicin, and granulocyte colony-stimulating factor (FLAG-IDA); subsequently, the patient underwent HSCT from an HLA-identical sibling. Nonmyeloablative conditioning regimen included fludarabine (175 mg/m^2), melphalan (140 mg/m^2), and antithymocyte globulin (Fresenius; 30 mg/kg). Cyclosporine A and methotrexate were used for graft versus host disease (GvHD) prophylaxis. Neutrophil and thrombocyte engraftments were achieved on day +17 and +23, respectively. Chimerism analysis showed 98% donor engraftment at +1 month and 99% at +2 month. Eczema, food allergy, and disseminated molluscum contagiosum infection resolved after HSCT. No pulmonary complications or worsening of pulmonary findings, acute or chronic GvHD, nor venoocclusive disease were observed after HSCT. Immunologic findings are presented in Table 1. Eosinophilia and IgE levels normalized after HSCT. Four months after HSCT, the patient's leukemia relapsed and he died 6 months after HSCT with relapsed AML.

TABLE 1 Immunological features of the patient

	Before HSCT	After HSCT (+3 months)
Absolute eosinophil count (/mm^3)	500 (40–360)	100 (40–360)
IgA (mg/dl)	<6.67 (70–303)	41 (7–303)
IgG (mg/dl)*	1,590 (764–2,134)	803 (764–2,134)
IgM (mg/dl)	28 (69–387)	43 (69–387)
Total IgE (IU/ml)	1,047 (0-90)	29 (0–90)
CD3 (%)	60 (60–76)	86 (60–76)
(cells/mm^3)	780 (1,200–2,600)	774 (1,200–2,600)
CD4 (%)	33 (31–48)	24 (31–47)
(cells/mm^3)	429 (650–1,500)	216 (650–1,500)
CD8 (%)	24 (18–35)	66 (18–35)
(cells/mm^3)	312 (370–1,100)	594 (370–1,100)
CD19 (%)	13 (13–27)	1 (13–27)
(cells/mm^3)	169 (270–860)	9 (27–860)
CD16-56 (%)	6 (4–17)	8 (4–17)
(cells/mm^3)	78 (130–820)	72 (13–720)
DOCK8 gene defect	Homozygous deletion in exon 26 on DOCK8 gene	

HSCT, hematopoietic stem cell transplantation; DOCK8, dedicator of cytokinesis 8.

*Under intravenous immunoglobulin therapy.

DOCK8-deficient patients show a predilection to develop malignancies, most frequently squamous cell carcinoma and lymphoma. This is possibly linked to chronic viral skin infections and impaired tumor surveillance resulting from defective CD8+ T-cell function.[5,6] The development of AML in DOCK8 deficiency has not been reported in the literature before. Many patients with DOCK8 deficiency have organ damage necessitating reduced-intensity conditioning, which in turn carries a higher risk of mixed donor chimerism.[7,8] The patient had severe pulmonary disease related to DOCK8 deficiency and had received intensive chemotherapy for resistant AML. Due to the risk of toxicity and transplant-related mortality, nonmyeloablative regimen was preferred may have affected the transplant outcome.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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