Indian Journal of Pediatrics
https://doi.org/10.1007/s12098-024-05070-9

SCIENTIFIC LETTER

Emerging Spectrum of DOCK8 Deficiency in Children and Challenges Associated with Providing Treatment

Kavitha Ganesan[1] · Suresh Duraisamy[1] · Anupama Nair[1] · Vijayshree Muthukumar[1] · Venkateswaran Vellaichamy Swaminathan[1] · Indira Jayakumar[2] · Vidya Krishna[3] · Ramya Uppuluri[1] · Revathi Raj[1]

Received: 1 November 2023 / Accepted: 2 February 2024

To the Editor: Dedicator of cytokinesis 8 (DOCK8) is a combined immunodeficiency associated with autosomal recessive hyper IgE syndrome. The study included nine children, up to 18 y of age with genetically proven DOCK8 deficiency (Supplementary Table S1). Immunological workup included lymphocyte subset analysis, naïve and memory T cells, and immunoglobulin levels which were documented to be normal in all children. DOCK8 expression was performed in four children where it was noted to be decreased.

Median age at presentation was 5 y (range 2 mo–8 y). Infections encountered were molluscum contagiosum in two children, cytomegalovirus colitis in one child, and a combination of molluscum contagiosum and herpes simplex in another child. Repeated *Klebsiella pneumoniae* meningitis was the presentation in one child. All children were on long-term prophylaxis with cotrimoxazole and itraconazole and were continued on monthly intravenous immunoglobulin infusions.

Out of the total five children who underwent hematopoietic stem cell transplantation (HSCT), 3/5 had haploidentical HSCT, and one child each had a matched family donor HSCT and one matched unrelated donor HSCT, with brisk engraftment in all children. Early and refractory viral reactivation were noted post-HSCT, with 17,00,000 copies of cytomegalovirus in one child and 8,53,95,600 copies of adenovirus in another child. One patient who underwent a matched sibling donor transplantation had secondary graft failure, two years post-HSCT. One child who underwent a matched unrelated donor HSCT was doing well. The overall survival was 45.5% (4/9).

Literature on DOCK8 deficiency is emerging, with recent publications from India reporting diverse clinical features in these children [1]. Recent data has confirmed the role of HSCT in DOCK8 deficiency, with resolution of eczema and molluscum [2, 3]. Maintaining complete chimerism with reduced toxicity conditioning has been shown to improve outcomes [4]. Collaborative work and research are required to guide optimal treatment outcomes.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12098-024-05070-9.

Declarations

Conflict of Interest None.

References

1. Gowri V, Chougule A, Gupta M, et al. Clinical, immunological and molecular findings of patients with DOCK-8 deficiency from India. Scand J Immunol. 2023;98:e13276.
2. Aydin SE, Freeman AF, Al-Herz W, et al; Inborn Errors Working Party of the European Group for Blood and Marrow Transplantation and the European Society for Primary Immunodeficiencies. Hematopoietic stem cell transplantation as treatment for patients with DOCK8 deficiency. J Allergy Clin Immunol Pract. 2019;7:848–55.
3. Shah NN, Freeman AF, Su H, et al. Haploidentical related donor hematopoietic stem cell transplantation for dedicator-of-cytokinesis 8 deficiency using post-transplantation cyclophosphamide. Biol Blood Marrow Transplant. 2017;23:980–90. Erratum in: Biol Blood Marrow Transplant. 2019;25:e65–7.
4. Raedler J, Magg T, Rohlfs M, et al. Lineage-specific chimerism and outcome after hematopoietic stem cell transplantation for DOCK8 deficiency. J Clin Immunol. 2021;41:1536–48.

✉ Ramya Uppuluri
ramya.december@gmail.com

[1] Department of Pediatric Hematology, Oncology, Blood and Marrow Transplantation, Apollo Hospitals, 320, Padma Complex, Anna Salai, Teynampet, Chennai 600035, Tamil Nadu, India

[2] Department of Pediatric Critical Care, Apollo Hospitals, Chennai, Tamil Nadu, India

[3] Department of Infectious Diseases, Apollo Hospitals, Chennai, Tamil Nadu, India

Published online: 09 February 2024