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abstract

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abstract

Homozygous TET2 Mutation Presenting as Familial Hemophagocytic Lymphohistiocytosis (HLH)

Authors: Mubashir Hassan Shah, Javid Rasool

Affiliation: Sher-i-Kashmir Institute of Medical Sciences

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Introduction: HLH is a life-threatening immune deficiency, multi-organ inflammatory disorder affecting all age groups. Familial form of HLH occurs due to mutations in genes involved in NK cell and T cell function, leading to aberrant immune response to infectious or non-infectious stimuli.
TET2 (ten-eleven translocation methylcytosine dioxygenase 2) is a known epigenetic regulator of gene expression. Recently, germline mutations in the TET2 gene have been implicated in immunodeficiency, lymphoma development, and adult-onset HLH(1,2). Here, we report a case of a congenital homozygous missense mutation in the TET2 gene presenting as Familial HLH.

Case Presentation: A 6-year-old male child, born of a third-degree consanguineous marriage, presented to our department with a history of fever, splenomegaly, and pancytopenia. Further investigations showed increased ferritin and triglycerides with decreased fibrinogen levels. Bone marrow aspiration showed florid hemophagocytosis. The diagnosis of HLH was made, and the child was started on the HLH 2004 protocol.

After the initiation of steroids, the fever subsided, and the pancytopenia resolved. Whole-exome sequencing was carried out to rule out any congenital mutation, which showed a homozygous missense mutation in TET2 (c.3232A>G). This was confirmed by Sanger Sequencing in the patient and both parents, who were found to be heterozygous carriers of this mutation. Currently, the patient is on the HLH 2004 protocol and is being planned for allogenic stem cell transplant.

Conclusion: Our patient is the first reported case of familial HLH due to homozygous TET2 mutation, emphasizing the importance of yet unknown pathways for the development of this hyperinflammatory syndrome.