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MORPHOLOGY UPDATE

Megakaryocyte morphology with *GATA2* germline mutation

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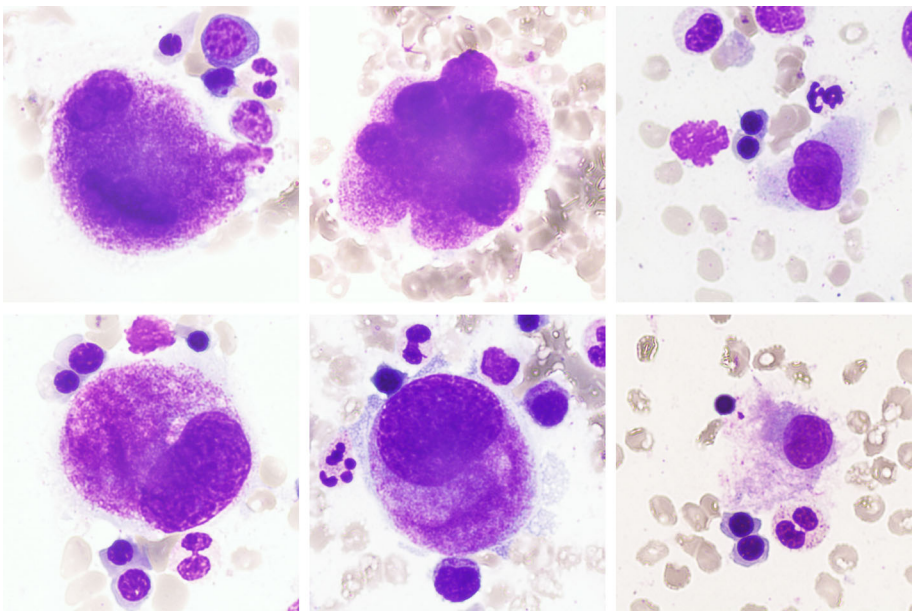

A 27-year-old man, under the care of the dermatology service with a 7-year history of extensive recurrent viral warts on his hands, eyelids, and lips, subsequently developed left-leg lymphedema with associated cellulitic episodes. An inherited immunodeficiency syndrome was considered. His full blood count showed hemoglobin concentration 134 g/L, white cell count 4.36×10^9/L, neutrophils 3.15×10^9/L, lymphocytes 1.02×10^9/L, monocytes 0.08×10^9/L, and platelets 150×10^9/L. Lymphocyte subset analysis showed reductions in CD3+CD4+ and CD3+CD8+ T cells, NK cells, and B cells. Subsequent DNA analysis revealed a heterozygous splice site mutation in intron 7 of the *GATA2* gene (c.1143+1G>C) in keeping with a pathogenic constitutional *GATA2* mutation. A baseline bone marrow aspiration biopsy showed mild dysplasia in the erythroid and myeloid lineages with more notable abnormalities in the megakaryocytes. These were highly variable in size with some showing separated and peripheralized nuclear components (top left and center) and others being non-lobated (bottom left and center). Small hypolobated megakaryocytes and micro-megakaryocytes were present (top and bottom right, all images ×100 objective). His bone marrow karyotype was normal. His subsequent yearly marrow evaluation has shown stable disease with no evidence of cytogenetic evolution.

Germline *GATA2* haploinsufficiency is associated with an immunodeficiency syndrome affecting the number and function

of dendritic cells, monocytes, and T, B, and NK lymphocytes with a predisposition to atypical mycobacterial, fungal, and viral infections. It also affects hematopoietic stem cell maturation and can lead to familial marrow hypoplasia, myelodysplastic syndromes (MDS), and acute leukemia. The megakaryocyte morphological abnormalities shown here are typical of this condition[1] and can be seen despite preservation of the platelet count. Cytogenetic abnormalities, including loss of chromosome 7 and trisomy 8, are present in some cases. This condition should always be considered in children and young adults presenting with MDS, marrow hypoplasia, or acute myeloid leukemia, even in those without a personal or family history of immunodeficiency. The associated hematological sequelae carry a poor prognosis, and as allogeneic stem cell transplantation is often considered, it is important to exclude the condition in potential sibling donors.

CONFLICT OF INTEREST STATEMENT

The authors do not have any conflicts of interest.

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