



# Morphologic and Clinical Features of Acute on Chronic Valproate Toxicity

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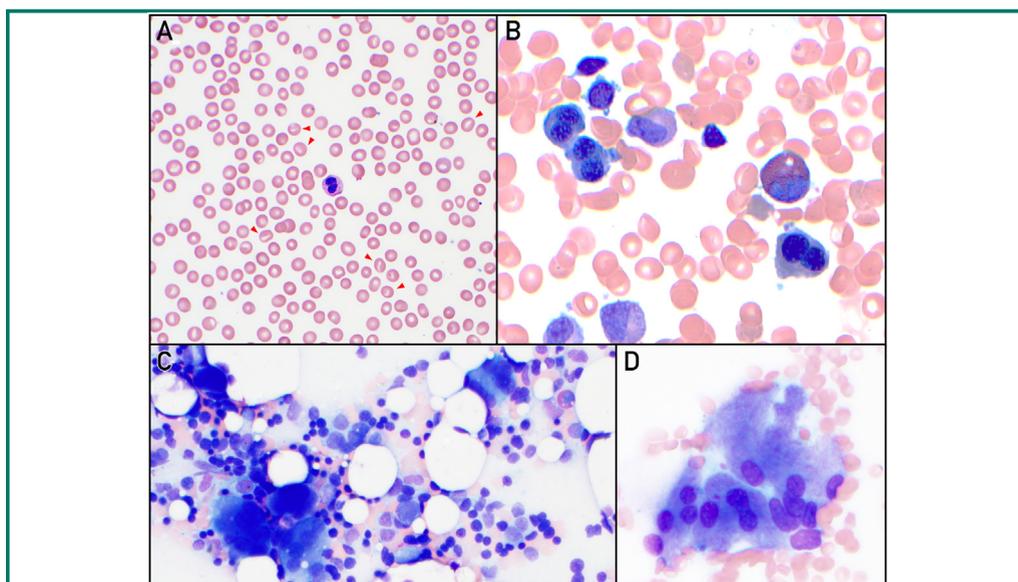
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An individual with Lennox-Gastaut syndrome developed pancytopenia. Peripheral smear showed red cell macrocytosis with stomatocytes and well-granulated pseudo Pelger-Huet neutrophils (Figure A).

Bone marrow biopsy was moderately hypocellular. There was erythroid (bi- and multinucleate forms) (Figure B) and granulocytic atypia (hypolobated neutrophils) and marked dysmegakaryopoiesis (many osteoclast-like and small hypolobated megakaryocytes) (Figures C and D). Cytogenetic studies were normal. Clinical evaluation revealed suprathreshold total and free serum valproate levels.

Hematologic toxicity of sodium valproate can manifest with trilineage dysplasia and cytopenias.<sup>1</sup> Reversible stomatocytes have been reported with neurotropic medications. The bone marrow morphology highlights the chronic changes,<sup>2</sup> whereas the cytopenias reflect superimposed acute toxicity.<sup>3</sup> Morphologic and clinical sequelae may be reversed with drug reduction, although they may progress to a myeloid neoplasm upon chronic exposure.<sup>4</sup> The blood counts improved within 5 days of valproate discontinuation.

This case highlights a therapy-induced dyspoiesis that mimics myelodysplastic syndrome. Clues supporting drug toxicity



**FIGURE.** Blood and bone marrow changes with chronic valproate therapy. A, Well-granulated pseudo Pelger-Huet neutrophils and red cell macrocytosis with stomatocytes (red arrows) (Peripheral smear, Wright Giemsa, original magnification  $\times 600$ ). B, Binucleate erythroid precursors. C, Many osteoclast-like and (D) small hypolobated megakaryocytes (Bone marrow aspirate, Wright Giemsa, original magnification  $\times 600$ ).

include well-granulated pseudo–Pelger-Huet neutrophils and predominance of osteoclast-like megakaryocytes.

#### POTENTIAL COMPETING INTERESTS

The authors report no potential competing interests.

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