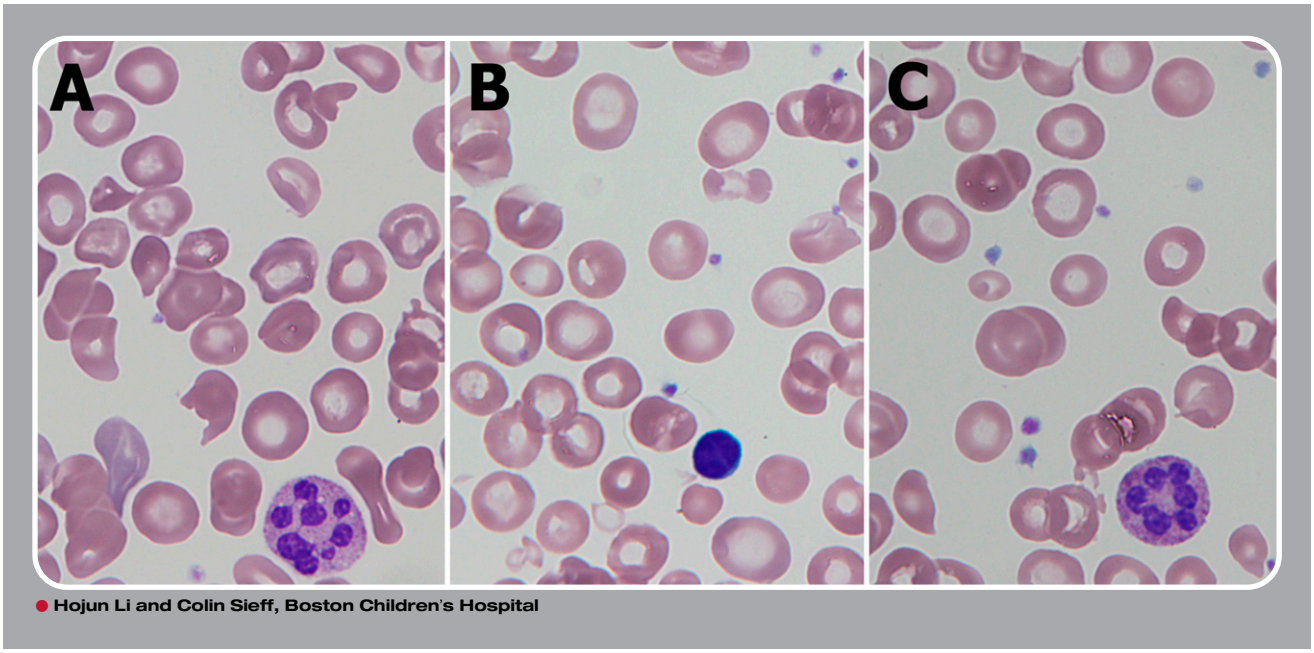
bloodwork
IMAGES IN HEMATOLOGY

Characteristic peripheral blood smear findings in disorders of cobalamin metabolism



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A 7-month-old boy with a history of necrotizing enterocolitis and developmental delay was admitted for anemia (hemoglobin 4.8 g/dL) and thrombocytopenia (platelets 91 $\times$ 10^9/L) with normal white blood cell count (5.4 $\times$ 10^9/L), mean corpuscular volume 90.2 fL, lactate dehydrogenase 757 U/L, and 3+ hemoglobinuria without microscopic hematuria. The blood smear demonstrated hypersegmented neutrophils (panels A,C), macrocytes (panel B), and red blood cell fragments (panels A,C). Serum folate and vitamin B_{12} were normal, but plasma homocysteine was elevated (>100.0 μmol/L), methionine decreased (10 μmol/L), and methylmalonic acid normal, indicating a specific homocysteine to methionine conversion defect. Fibroblast functional analysis showed reduced ^{14}C methyltetrahydrofolate incorporation, and methionine synthase (*MTR*) gene sequencing revealed a known pathogenic mutation and a previously unreported mutation affecting splicing. Thus, cobalamin (cbl)G deficiency was diagnosed.

Peripheral blood smear analysis was key in this case, linking microangiopathic hemolytic anemia to a megaloblastic process. This combination of findings is described in pernicious anemia and inborn errors of cobalamin metabolism affecting homocysteine methylation and conversion to methionine, specifically the methylcobalamin deficiencies cblC-G and cblJ. Key considerations in management are betaine and hydroxycobalamin supplementation, as well as thromboprophylaxis for intravascular coagulation attributable to markedly elevated homocysteine levels.

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