GENETICS AND GENODERMATOSES

CONGENITAL NEUTROPENIA AND CUTANEOUS MANIFESTATIONS: WHAT TO THINK ABOUT?

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Background: An homozygous missense mutation that abolish the enzymatic activity of G6PC3 (glucose-6-phosphatase, catalytic subunit 3) was first described by Boztug et al. The phenotype of patients with G6PC3 deficiency is broad and includes congenital neutropenia and recurrent thrombocytopenia. More than 75% of patients have been reported as having a congenital cardiac anomaly. Neurological features include intellectual disability, sensorineural hearing loss, and microcephaly. Other findings are urogenital anomalies, facial dysmorphism, and a prominent superficial venous pattern are described in more than 65% of patients. The prognosis is generally good. Prophylactic antibiotics, G-CSF, transfusion or bone marrow transplantation, should be recommended according to the severity of neutropenia. Untreated disease can be fatal.
The differential diagnosis includes several genetic syndromes like Ehlers-Danlos, Wiskott-Aldrich, Kabuki, Cohen, Schwachman-Diamond, Di Geoge and Fanconi anemia, among others.

Observation: An 8-year-old male patient, product of consanguineous parents, with a history of cyclic thrombocytopenia and congenital neutropenia, neonatal sepsis, recurrent aphthous ulcers, and recurring respiratory tract infections was referred to our outpatient clinic. He also had cardiac valvulopathy, cryptorchidism, chronic renal disease, neurological developmental delay and failure to thrive. On physical examination, he had facial dysmorphism, aphthous stomatitis, and a prominent venous circulation on his trunk and extremities.
The karyotype was 46 XY. No mutations were found for ELANE, HAX1 and WAS genes. Bone marrow aspiration revealed delayed granulocyte maturation. Test of the G6PC3 gene revealed an homozygous 1bp deletion in the exon 2. The same heterozygotic mutation was detected in his parents and brother. Our patient persisted with mild neutropenia, and prophylactic antibiotic treatment has been administered.

Key message: Although cutaneous findings of G6PC3 deficiency are sparingly described in

the literature, they could help to establish an early diagnosis of this condition. Echocardiogram, kidney and pelvic ultrasound should be performed in all cases to rule out malformations.