descent may have lower TREC levels, in general, irrespective of HEU status.

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Detecting 22q11.2 Deletion Syndrome in Newborns With Low T Cell Receptor Excision Circles From Severe Combined Immunodeficiency Screening

Liao HC, Liao CH, Kao SM, Chiang CC, Chen YJ. *J Pediatr*. 2019;204:219–224.e1

PURPOSE OF THE STUDY: To evaluate the prevalence of 22q11.2 deletion syndrome within a set of newborns screening positive for low T-cell receptor excision circles (TRECs) by assessing a patient's copy number of the TBX1 and/or HIRA genes, which are located in the 22q11.2 region.

STUDY POPULATION: This population evaluated 486 newborns born in Taiwan who were diagnosed with low TRECs (<90 copies per microliter) on the severe combined immunodeficiency newborn screening from February 2012 to January 2015.

METHODS: The newborn screening dried blood spots from the 486 patients with TREC levels <90 copies per microliter were reassessed, and the spots underwent DNA extraction. The extract was then evaluated with quantitative real-time polymerase chain reaction to assess the copy number of TBX1 and/or HIRA genes. The patients with low copy number in both genes were retested 2 times to confirm the abnormal copy number. Then, those confirmed patients had their DNA re-extracted and assessed by multiplex ligation-dependent probe amplification. This series of testing confirmed 13 cases of 22q11.2 deletion syndrome.

RESULTS: The results of the study showed that ~13 cases of 22q11.2 deletion syndrome were confirmed out of the 486 patients with TREC levels <90 copies per microliter. The rate of detection was 2.7% in the entire group of patients with low TRECs. However, the positive detection rate of 22q11.2 deletion syndrome was higher at 10.7% if the patient had <30 TRECs.

CONCLUSIONS: Investigators in this study showed that in a group of nearly 500 Taiwanese newborns with TREC levels <90 copies per microliter, they were able to detect patients with 22q11.2 deletion syndrome through the assessment of copy numbers of TBX1 and/or HIRA genes rather than full chromosomal microarray in 2.7% by using the previously collected dried blood spot.

REVIEWER COMMENTS: This confirms that TREC newborn screening can be used to find a multitude of T-cell lymphopenia problems apart from severe combined immunodeficiency. Furthermore, genes of interest can be evaluated for copy number variation as a cost-effective second tier analysis of low TRECs to further delineate patients with 22q11.2 deletion syndrome.

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Inherited p40^{phox} Deficiency Differs From Classic Chronic Granulomatous Disease

van de Geer A, Nieto–Patlán A, Kuhns DB, et al. *J Clin Invest*. 2018;128(9):3957–3975

PURPOSE OF THE STUDY: To characterize clinical and laboratory aspects of p40^{phox} deficiency, a unique autosomal recessive form of chronic granulomatous disease (CGD) previously described in only 1 patient.

STUDY POPULATION: The population included 24 patients with p40^{phox} deficiency from 12 families in 8 countries. Both male and female patients are reported, with age ranging from 1 to 47 years.

METHODS: Clinical history of each case was collected, including autoinflammatory manifestations and infection history. Laboratory analysis included both gene sequencing and numerous functional studies of the immune system.

RESULTS: Mean age at diagnosis for symptomatic patients was 15 years (range: 1–46 years). Twenty patients were symptomatic. Four were asymptomatic (age 1–10 years, recognized by family history). Of the symptomatic patients, skin inflammation was present in 50%, and granulomatous gastrointestinal manifestations were present in 50%, with varied presentation from oral ulcers to severe Crohn-like inflammatory bowel disease. Cutaneous infections were reported in 42%. The phorbol myristate acetate–induced dihydrorhodamine (DHR) oxidation test gave normal or just below normal results for all patients.

CONCLUSIONS: Excessive inflammatory lesions of the skin (lupuslike) and gastrointestinal tract (Crohn-like) are common in patients with p40^{phox} deficiency. Compared with classic CGD, it is often diagnosed later in life and demonstrates a normal DHR laboratory test result (the laboratory test widely used for diagnosis of CGD). Patients experience peripheral bacterial infections, but fungal infections and invasive infections of any type are not common. Identification of 4 asymptomatic children demonstrates that there is incomplete clinical penetrance, at least until adolescence.

REVIEWER COMMENTS: It is essential for pediatricians to be aware of this disease and how it differs from classic CGD.