WP014

SLAVIC FOUNDER MUTATION IN UNC13D GENE IN PATIENTS WITH HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS FROM BELARUS AND UKRAINE

WORKING PARTY 06: PID CARE IN DEVELOPMENT

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Background and Aims: Hemophagocytic lymphohistiocytosis (HLH) is polygenetic disease caused by mutations in genes associated with granule-dependent lymphocyte-mediated cytotoxicity (PRF1, UNC13D, STX11, STXBP2, LYST, AP3B1, AP3D1 RAB27A, XIAP, SH2D1A).

Methods: We describe the clinical and immunological manifestations and mutation spectrum in HLH cohort (n=19) diagnosed in Belarus (n=15) and Ukraine (n=4) since 1991-2022.

Results: Enrolled patients were residents of Belarus (n=14), Ukraine (n=4) and Kazakhstan (n=1). Genetic diagnose of HLH was established in 12/19 patients, NK activity was checked in 5/19. UNC13D gene variants were revealed in 10 patients (4 patients from 2 families from Ukraine; 6-from 4 families, Belarus); 3 unrelated Belarusian and Ukrainian families had c.2346_2349delCTCC(p.R782fs in homozygous state, 4pts out of 2 families (Belarus)-in heterozygous compound. Also variants in XIAP(n=2) were detected. One patient is alive after HSCT, one patient waiting for HSCT, 17 children died, 3 after HSCT, 8 were genetically diagnosed postmortem. 3/19pts had an "atypical" presentation, age of manifestation and death was 9m/2.5yr; 1.5yr/2.5yr, and 2yr/19yr (genetic diagnosis was established post-mortem in 3/3). "Atypical" manifestation was-lymphoproliferation (n=3), neurological presentation (brain cysts/epilepsy (n=1), disseminated encephalitis (n=1). Hemophagocytosis was not manifested biochemically during all period of observation; a small number of phagocytic macrophages were detected once in one patient's bone marrow.

Conclusions: Our cohort of patients demonstrated a repeated mutation in the UNC13D gene-c.2346_2349delCTCC(p.R782fs), which may be associated with the "founder effect" in Slavic countries. Atypical manifestation causes difficulties in rapid diagnosis, fast sequencing of all PID genes are necessary for establishing correct diagnosis and start appropriate treatment.

Disclosure: No.

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