Increased Innate T cells Frequencies In Infants And School-age Children With Neonatal Encephalopathy

Nawal Abdullah Taher¹, Alhanouf alharbi¹, Mary O'Dea^{2,3,4}, Tammy Strickland², Zunera Zareen^{2,3}, Eleanor J Molloy^{2,3,4,5}, Derek G. Doherty¹.

¹Immunology and ²Paediatrics, School of Medicine, Trinity College Dublin; TTMI, ³Paediatrics, Tallaght University Hospital, Dublin; ⁴Paediatrics, Coombe Women's and Infants' University Hospital, Dublin; ⁵Neonatology, Our Lady's Children's Hospital, Crumlin, Dublin 12, Ireland.

Introduction

Neonatal encephalopathy (NE) is the leading cause of neurodevelopmental delay, epilepsy and cerebral palsy with a prevalence of 1-3 per 1,000 live births. Epidemiological and experimental evidence suggests that pre-existing intrauterine infection and inflammation, involving neutrophils and monocytes, are implicated in brain injury and subsequent cerebral palsy (1, 2). Lymphocytes of the innate and adaptive immune systems play important roles in early immunity against infection and in inflammation (3). They can control the responses of monocytes and neutrophils and offer potential targets for therapeutic intervention. The aim of this study was to measure the frequencies of innate and adaptive lymphocytes, including subsets of T cells, B cells and natural killer (NK) cells in neonates and school-age children with NE and in age-matched controls.

Methods

Whole blood from neonates with NE (n=22) and neonatal controls (n=14) and school-age children with NE (n=19) and age-matched controls (n=23) subjects was stained with monoclonal antibodies specific for lymphocyte surface markers and analysed by flow cytometry. The frequencies of CD4⁺, CD8⁺, CD4-CD8- (double negative or DN) and CD4⁺CD8⁺ double positive (DP) T cells (CD3⁺), B cells (CD19⁺), NK cells (CD3-CD56⁺) invariant natural killer T cells (iNKT cells; CD3⁺Vα24Jα18⁺), mucosal-associated invariant T (MAIT) cells (CD3⁺CD8⁺CD161⁺Vα7.2⁺) and the Vδ1⁺, Vδ2⁺ and Vδ3⁺ subsets of gamma/delta (γδ) T cells were compared between the NE and control groups.

Results

Figure 1. Lymphocyte frequencies in neonates and school-age children with NE. Frequencies of T cells (A), CD8⁺ cells as percentages of total T cells (B), B cells (C), and NK cells (D) as percentages of total lymphocytes in neonates and school-age children with NE and age-matched control subjects. *P<0.01

References

1. Azzopardi et al. N Engl J Med 2014; 371: 140-149.
2. Jenster et al. Ped Res 2014; 76: 93-99.
3. Godfrey et al. Nat Immunol 2015; 16: 1114-1123.[-

Conclusion

Our findings suggest that CD8⁺ T cells and B cells are involved in immune responses that lead to NE and that NK cells may be depleted. Our results do not suggest a role for innate T cells, including iNKT cells, MAIT cells or γδ in the pathogenesis. These findings provide new insights into the pathogenesis of neonatal brain injury and its associated sequelae, such as cerebral palsy, and suggest that immunotherapeutic interventions may improve these neurologic disabilities in childhood.