Mast cell activation and proinflammatory cytokines contribute to persisting inflammation in children with cerebral palsy

Cemalettin Demir[1], Yasemin Baranoğlu Kılınç[2], Erkan Kılınç[1]

[1]Department of Physiology, Bolu Abant Izzet Baysal University, Bolu, Turkey
[2]Department of Pediatrics, Bolu Abant Izzet Baysal University, Bolu, Turkey

Aim

Cerebral palsy is a common disabling disease characterized by non-progressive brain injury. It is well established that inflammatory processes during intrauterine life or before three years of age are related to pathophysiology of cerebral palsy but, inflammatory processes on the persisting of disease in children above two years of age are unknown. Mast cells are the multifunctional immune cells that are one of the most important sources of pro-inflammatory cytokines. There are limited experimental animal studies investigating the role of mast cell activation in the pathogenesis of cerebral palsy, however, clinical studies are needed on this subject. We aimed to investigate the association between mast cells, pro-inflammatory cytokines and the persisting of disease in children with cerebral palsy above two years of age.

Methods

Thirty patients aged 3-18 years with clinically confirmed cerebral palsy and twenty-six healthy volunteers from Western Black Sea region between November 2018 and June 2019 were included in the study. Patients were receiving rehabilitation services at the Izle Special Education and Rehabilitation Center in Duzce. In accordance with the Helsinki Declaration, all participants and their parents gave their signed consents. Inclusion criteria for cerebral palsy group were, i) being clinically diagnosed with cerebral palsy, ii) being between the ages of 3-18, iii) having stable for health status. Venous blood samples were collected from 30 cerebral palsy patients and 26 healthy volunteers. Plasma levels of pro-inflammatory cytokines including IL-1β, IL-6 and IL-9, and biomarkers of number and activation of mast cells including tryptase beta-2 and histamine were determined using ELISA. Data were analysed using Kruskall Wallis or Mann-Whitney U test.

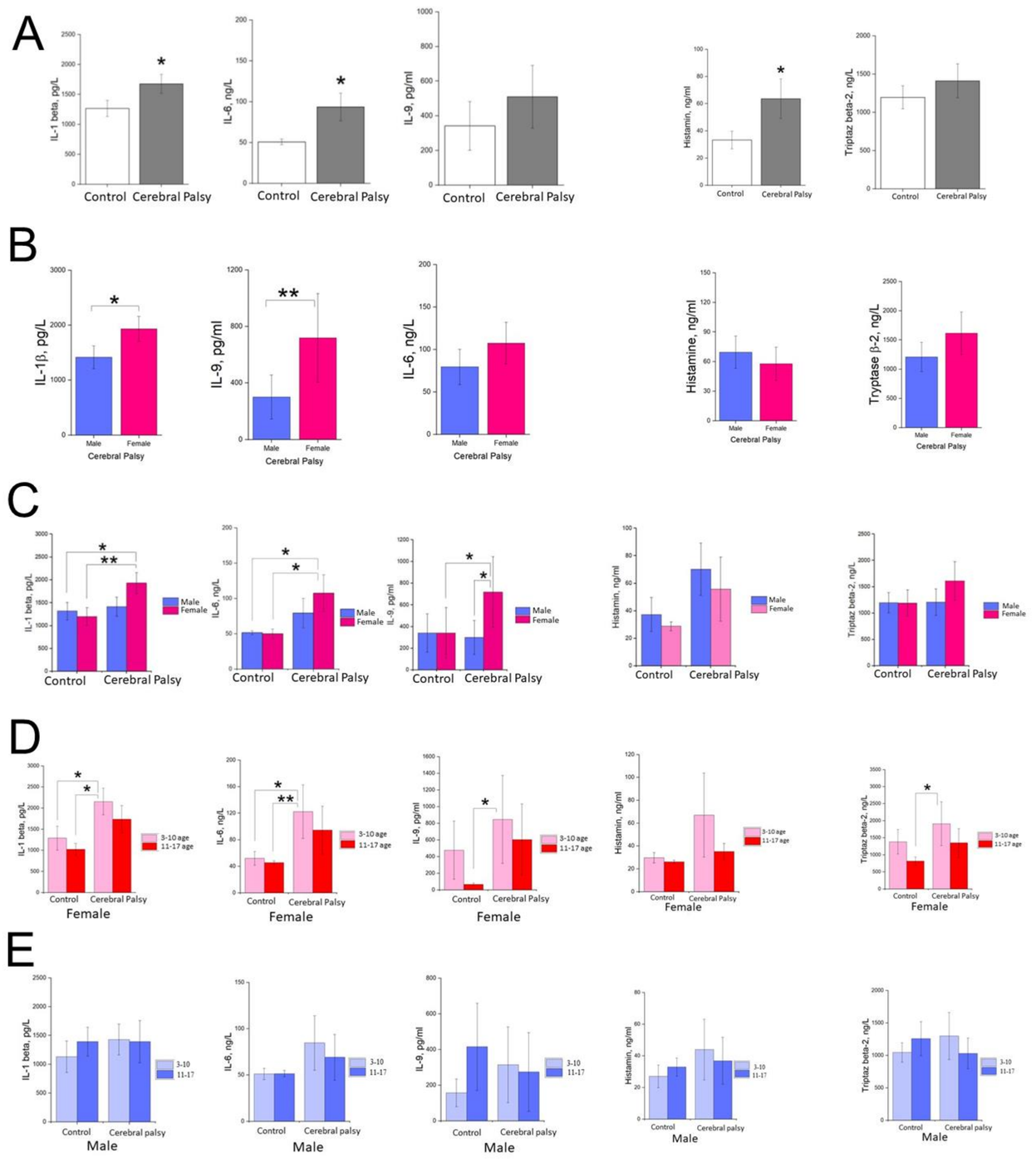

Fig 1. (A) High plasma IL-1β, IL-6 and histamine levels in patients with cerebral palsy compared to healthy controls
(B) High plasma IL-1β and IL-9 levels in females compared to males in the cerebral palsy group
(C) High plasma IL-1β, IL-6 and IL-9 levels in female subjects with cerebral palsy compared to healthy female controls
(D) High plasma IL-1β, IL-6 and IL-9 and tryptase beta-2 levels in female subjects with cerebral palsy compared to healthy female controls in preadolescence
(E) Plasma levels of pro-inflammatory cytokines and mast cell mediators in male subjects with cerebral palsy and healthy controls by age periods

Results

IL-1β, IL-6 and histamine levels were higher in the patients compared to controls ($p<0.05$, Fig 1A), but significant difference between groups was not determined for IL-9 and tryptase beta-2 levels ($p>0.05$, Fig 1A and B). IL-1β and IL-6 levels were increased in female patients compared to female and male controls ($p<0.05$, Fig 1C). IL-9 levels were elevated in female patients compared to female volunteers in control ($p<0.05$, Fig 1C). IL-1β, IL-6 and IL-9 and tryptase beta-2 levels were elevated in preadolescence female patients compared to both preadolescence and adolescence female volunteers in control ($p<0.05$, Fig 1D). There was no significant difference between male patients and controls regarding developmental periods ($p>0.05$, Fig 1E).

Conclusion

- Increased levels of proinflammatory cytokines (IL-1β, IL-6 and IL-9) and mast cell activation biomarker (histamine) indicate that inflammation contributes to the persisting of disease in children with cerebral palsy above two years of age.
- Enhanced systemic inflammatory response is more potent in female patients than male patients, however it declines during adolescent age.
- Therefore, activation of mast cells, without changing their number, contributes to aggravate systemic inflammatory response in children with cerebral palsy above two years of age

*The study was supported by Bolu Abant Izzet Baysal University Scientific Research Fund [2019.08.02.1415]