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Mercury induces inflammatory mediator release from human mast cells

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Abstract

Background: Mercury is known to be neurotoxic, but its effects on the immune system are less well known. Mast cells are involved in allergic reactions, but also in innate and acquired immunity, as well as in inflammation. Many patients with Autism Spectrum Disorders (ASD) have “allergic” symptoms; moreover, the prevalence of ASD in patients with mastocytosis, characterized by numerous hyperactive mast cells in most tissues, is 10-fold higher than the general population suggesting mast cell involvement. We, therefore, investigated the effect of mercuric chloride (HgCl₂) on human mast cell activation.

Methods: Human leukemic cultured LAD2 mast cells and normal human umbilical cord blood-derived cultured mast cells (hCBMCs) were stimulated by HgCl₂ (0.1-10 μM) for either 10 min for beta-hexosaminidase release or 24 hr for measuring vascular endothelial growth factor (VEGF) and IL-6 release by ELISA.

Results: HgCl₂ induced a 2-fold increase in β-hexosaminidase release, and also significant VEGF release at 0.1 and 1 μM (311 ± 32 pg/10⁶ cells and 443 ± 143 pg/10⁶ cells, respectively) from LAD2 mast cells compared to control cells (227 ± 17 pg/10⁶ cells, n = 5, p < 0.05). Addition of HgCl₂ (0.1 μM) to the proinflammatory neuropeptide substance P (SP, 0.1 μM) had synergistic action in inducing VEGF from LAD2 mast cells. HgCl₂ also stimulated significant VEGF release (360 ± 100 pg/10⁶ cells at 1 μM, n = 5, p < 0.05) from hCBMCs compared to control cells (182 ± 57 pg/10⁶ cells), and IL-6 release (466 ± 57 pg/10⁶ cells at 0.1 μM) compared to untreated cells (13 ± 25 pg/10⁶ cells, n = 5, p < 0.05). Addition of HgCl₂ (0.1 μM) to SP (5 μM) further increased IL-6 release.

Conclusions: HgCl₂ stimulates VEGF and IL-6 release from human mast cells. This phenomenon could disrupt the blood-brain-barrier and permit brain inflammation. As a result, the findings of the present study provide a biological mechanism for how low levels of mercury may contribute to ASD pathogenesis.

Background

Heavy metals such as mercury result in neurological injury that may lead to developmental defects, peripheral neuropathies, and enhanced neurodegenerative changes [1]. Mercurials may be found in various drugs, in bleaching creams, antiseptics, disinfectants, as preservatives in cosmetics, tooth pastes, lens solutions, vaccines, contraceptives and immunotherapy solutions, fungicides, herbicides and in dental fillings, as well as in fish such as tuna due to water pollution [2]. Mercury can cause immune, sensory, neurological, motor, and

behavioral dysfunction similar to those associated with Autism Spectrum Disorders (ASD) [2]. The possible role of mercury used as preservative in vaccines [2] has been debated extensively, but most epidemiological studies do not support a causal association between vaccines and autism [3-7]. However, 87% of children included in the US Vaccine Adverse Event Reporting System (VAERS) had ASD [8]. Moreover, a paper based on computerized medical records in the Vaccine Safety Data-link concluded there was “significantly increased rate ratios for ASD with mercury exposure from thiomerosal-containing vaccines” [9]. Mercury has been shown to induce proliferation and cytokine production from T lymphocytes [10]. Mercuric chloride (HgCl₂) in nontoxic doses induces the release of histamine and cytokines, such as IL-4 and tumor necrosis factor-alpha (TNF-α), from a

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