PSORIASIS

THE CONCEPT OF INFLAMMATORY SKIN MARCH: IL-1–MEDIATED SKIN INFLAMMATION AND CEREBROVASCULAR AND CARDIOVASCULAR EVENTS

Keiichi Yamanaka [(1)] - Yoshiaki Matsushima [(1)] - Kento Mizutani [(1)] - Karin Okada [(1)] - Ai Umaoka [(1)] - Eri Rikiishi [(1)] - Makoto Kondo [(1)] - Koji Habe [(1)]

Mie University, Graduate School Of Medicine, Dermatology, Tsu, Japan [(1)]

Background: Once the skin is activated, it produces large amounts of inflammatory cytokines including IL-1; inducing prolonged systemic inflammation. Psoriasis and atopic dermatitis(AD) are inflammatory cytokine-mediated skin disorders with high risk for cardiac and cerebrovascular comorbidities.

Objective: We investigated the association between skin-derived cytokines and cerebral and cardiovascular events using established skin inflammatory mice model. The potential roles of systemic IL-1α/β in development of organ involvements were also observed.

Materials and Methods: Keratin-14 driven caspase-1 transgenic mouse(KCASP1Tg), that releases IL-1α/β from the skin lesions was used. KCASP1Tg was also treated with anti-IL-1α/β antibodies. Histological analysis was performed for abdominal aorta specimens. Blood pressure and peripheral blood circulation were measured. To observe cerebral involvement, the India-ink angiography and 18F-FDG PET were performed.

Results: KCASP1Tg developed arteriosclerosis with impaired peripheral blood circulation. Thermographic analysis revealed hampered circulation in lower limbs. The mean diameter of brain arteries was decreased in KCASP1Tg, which was prevented by anti-IL-1α/β antibody. 18F-FDG uptake of KCASP1Tg decreased in whole brain, which was reserved in treated-KCASP1Tg.

Conclusions: We demonstrated persistent release of IL-1α/β from inflammatory skin induces abdominal aortic remodeling, including vascular stricture, and deteriorated peripheral circulation mimicking arteriosclerosis. The decreased brain glucose uptake as well as anatomical changes in vasculature were observed. These morbid conditions were ameliorated by administration of anti- IL-1α/β antibodies. Our results suggest the importance of proper control for long-lasting skin inflammation, including psoriasis and AD, and IL-1α/β may be one of critical cytokines for vascular changes. Although the pathogenesis is very different between AD and psoriasis, the inflamed keratinocyte releases

massive amount of pro-inflammatory cytokines stored in the epidermis into the systemic circulation in both diseases. This concept is not limited to skin diseases but also may be applicable to other systemic disorders such as IL-1-associated auto-inflammatory diseases.