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Kawasaki Disease and Hyponatremia

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Kawasaki disease (KD) is an acute febrile vasculitis of unknown etiology that predominantly affects children younger than 5 years.^{1,2)} Because KD causes systemic vasculitis, multiple organ involvement may ensue, including coronary artery lesions (CALs), carditis, arthritis, hepatitis, central nervous system disease, kidney and urinary tract abnormalities, muscle involvement and hyponatremia.^{2,3)} Nakamura et al.⁴⁾ also recently reported that hyponatremia at the patient's first visit to hospital might be a predictor of giant coronary aneurysm (>8 mm), and speculated that the relationship between hyponatremia and giant coronary aneurysms is based on endothelial permeability, severity of the illness, dehydration, duration of febrile period. Although hyponatremia is not uncommon in patients with KD,³⁾ the clinical characteristics of KD patients with hyponatremia remain inadequately understood. Patients with hyponatremia may exhibit more severe inflammatory findings, including longer duration of fever, higher C-reactive protein (CRP) concentrations and alanine aminotransferase levels and increased incidence of CAL, than in patients without hyponatremia.⁵⁾ Lim et al.⁶⁾ also reported that serum sodium was inversely correlated with neutrophil, CRP, and N-terminal pro-B-type natriuretic peptide, and speculated that hyponatremia occurs in KD patients with more severe inflammation.

Although the pathogenesis of hyponatremia in KD remains inadequately understood, several possible mechanisms have

been postulated, including the syndrome of inappropriate antidiuretic hormone secretion (SIADH), hyponatremic dehydration and ingestion of fluid that is hypo-osmolar relative to the fluid lost.³⁾ Recently, the relationship between interleukin (IL)-6 or IL-1 beta and ADH secretion has been suggested.^{7,8)} Mastorakos et al.⁷⁾ reported that plasma ADH levels were elevated after IL-6 injection in cancer patients, suggesting that IL-6 activated the magnocellular ADH-secreting neurons, and that it might be involved in SIADH. Ohta and Ito⁸⁾ reported four cases with hyponatremia secondary to SIADH, which seems to be related to inflammation. Plasma Na⁺ concentrations decreased and plasma CRP level increased when the patients had fever. In such conditions, plasma ADH and IL-6 concentrations were increased and there was significant correlation between them. Intravenous administrations of IL-1 beta increased ADH, atrial natriuretic hormone, and adrenocorticotrophic hormone (ACTH). The changes in ADH and ACTH were abolished by pretreatment administration of intravenous indomethacin. Also, intravenous administration of IL-1 beta increased urinary sodium excretion. Based on these findings, they speculated that IL-6 and IL-1 beta play an important role in SIADH development associated with inflammation. These findings suggest that natriuresis in KD might be secondary not only to renal involvement, but also cytokines, such as IL-6 or IL-1 beta. IL-1 beta is also recognized as a mediator of endothelial damage in KD.^{6,9)} Therefore, there is a possibility that these cytokines may involve in the pathogenesis of hyponatremia due to SIADH, rather than cerebral vasculitis in KD.¹⁰⁾ Further studies are necessary to elucidate the clinical characteristics of KD patients with hyponatremia, and the pathogenesis of hyponatremia in KD.

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