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LETTER TO THE EDITORS

Kawasaki disease and hyponatremia

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Sirs,

We read with great interest the recent contribution by Watanabe et al. in Pediatric Nephrology [1]. They reported that hyponatremia in Kawasaki disease (KD) is a common finding, which suggests severe inflammation. They suggested that renal salt wasting due to renal involvement might underlie the development of hyponatremia in their patients with KD. They also cited that the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) in KD has sometimes been reported, and cerebral vasculitis is thought to be the etiology of SIADH in KD. Nakamura et al. [2] also recently reported that hyponatremia at the patient's first visit to hospital might be a predictor of giant coronary aneurysm (>8 mm), which was not mentioned in Watanabe et al.'s study. Nakamura et al. speculated that the relationship between hyponatremia and giant coronary aneurysms is based on the permeability of the endothelium, severity of the illness, dehydration, duration of period with fever, and so forth [2].

Although the exact mechanism for the development of hyponatremia in KD remains unknown, the relationship between interleukin (IL)-6 or IL-1 beta and ADH secretion has been suggested [3, 4]. Mastorakos et al. [3] 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 et al. [4] reported four cases with hyponatremia due to SIADH, which seems to be related to inflammation. The plasma Na concentration decreased when the patients had fever and increased plasma C-reactive protein (CRP) level. In such conditions, plasma ADH and IL-6 concentrations were increased and there was a significant correlation between them. Therefore, they performed animal experiments to investigate the role of IL in the development of SIADH. Intravenous administrations of IL-1 beta increased ADH, atrial natriuretic hormone (ANH), and adrenocorticotropic hormone (ACTH). The changes in ADH and ACTH were abolished by the pretreatment with an intravenous administration of indomethacin. Also, the intravenous administration of IL-1 beta increased the urinary sodium excretion. The pretreatment of HS142-1, an ANH antagonist, abolished the increase in urinary sodium excretion induced by IL-1 beta. Based on these findings, they speculated that IL-6 and IL-1 beta play an important role in the development of SIADH associated with inflammation.

These findings suggest that natriuresis in KD might be due to not only renal involvement but also cytokines, such as IL-6 or IL-1 beta. One of our authors reported that serum IL-6 was markedly elevated in the acute stage of KD and serum IL-6 positively correlated with the serum CRP level [5]. IL-1 beta is also recognized as a mediator of endothelial damage in KD [6]. Therefore, there is a possibility that these cytokines might involve the pathogenesis of hyponatremia due to SIADH rather than cerebral vasculitis in KD, although they did not measure serum and urinary osmolarity and urinary electrolytes. Further studies are necessary to elucidate the possible relationship between these cytokines and hyponatremia due to SIADH in KD.

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