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Systemic Capillary Leak Syndrome Caused by Granulocyte Colony-Stimulating Factor

Nakagawa Naoki, Hasebe Naoyuki

To Authors Reply : Systemic Capillary Leak Syndrome caused by Granulocyte Colony-Stimulating Factor

Naoki Nakagawa [1], and Naoyuki Hasebe [1]

[1]Division of Cardiology, Nephrology, Pulmonology and Neurology, Asahikawa Medical University, Asahikawa, Japan

Corresponding author: Naoki Nakagawa, M.D., Division of Cardiology, Nephrology, Pulmonology and Neurology, Department of Internal Medicine, Asahikawa Medical University, Asahikawa, Japan, Phone : +81-166-68-2442, FAX : +81-166-68-2449, E-mail : naka-nao@asahikawa-med.ac.jp

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We thank Dr. Shinohara for his interest in our paper (1). Systemic capillary leak syndrome (SCLS) is a very rare idiopathic disorder which presents with periodic episodes of hypovolemic shock, due to plasma leakage to the extra-vascular space reflected by accompanying hypoalbuminemia, hemoconcentration and edema, and in most cases, the presence of a paraproteinemia. SCLS occurs after infusions of granulocyte colony-stimulating factor (G-CSF) as Dr. Shinohara and some researchers have reported (2, 3).

In our patient, serum G-CSF levels, but not interleukin (IL)-2, IL-6 and vascular endothelial growth factor (VEGF) levels, increased parallel to disease activity and were significantly associated with the levels of blood neutrophils in response to administration of prednisolone (1). Recombinant human G-CSF increases the neutrophil count and enhances their phagocytic and cytotoxic functions as well as their expression of adhesion molecules (4). Dagdemir et al reported that a patient developed SCLS twice while receiving G-CSF, without any time relationship between the onset of symptoms and the rapid increase in white blood cell count (3). They suggested that a direct effect of G-CSF on the endothelium may have played a major role and that G-CSF is able to cause SCLS even when the white blood cell count is very low. Based on these reports, G-CSF, irrespective of whether the serum level increases idiopathically or after therapeutic administration, might have triggered neutrophil activation and the release of inflammatory mediators, resulting in tissue damage and systemic manifestations of increased capillary permeability.

Moreover, increased levels of G-CSF have been reported after infusions of IL-2, IL-4, IL-6, tumor necrosis factor, and granulocyte-macrophage colony-stimulating factor as well as after allogeneic hematopoietic stem cell transplantation (1, 2, 5). Therefore, in some SCLS, G-CSF might be useful biomarker for the severity of attacks in SCLS, but not in all cases. In the future, it is hoped that this avenue of research will clarify the pathophysiology and treatment of SCLS.

We agree that clinicians should consider the diagnosis of SCLS in patients with unexplained edema, increased hematocrit, and hypotension and be reminded of this particular adverse effect of G-CSF.

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