ADVERSE DRUG REACTIONS, INCLUDING SJS, TEN

ELEVATED SERUM OSTEOPONTIN IN DRUG-INDUCED HYPERSENSITIVITY SYNDROME/DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS

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Background: Osteopontin (OPN) is a secreted multicellular cytokine that signals through integrin and CD44 receptors and is highly upregulated in acute and chronic inflammation. OPN activity has been implicated in physiological and pathophysiologic processes.

Objective: Drug-induced hypersensitivity syndrome (DIHS), also referred to as drug reaction with eosinophilia and systemic symptoms (DRESS), is a multi-organ systemic drug reaction characterised by haematological abnormalities and reactivation of human herpesvirus-6 (HHV-6). DIHS/DRESS is triggered by a limited number of drugs, including anticonvulsants. It is potentially fatal and may cause various sequelae; therefore, proper diagnosis is critical. However, biomarkers of the severity of DIHS/DRESS are insufficient. We examined the possibility of using OPN as a biomarker for DIHS/DRESS.

Materials and Methods: We collected serum from 10 DIHS/DRESS patients and 100 elderly healthy controls from the Japanese Red Cross Society. Among the 100 controls, there were 10 men and 10 women per age group (20s, 30s, 40s, 50s, and 60s). OPN levels were assessed using an ELISA. Only cases meeting the diagnostic criteria were included in the DIHS/DRESS group. Immunohistochemical labelling of OPN was performed in biopsy specimens obtained from five DIHS/DRESS patients.

Results: No significant differences were detected in serum OPN between age groups, or between males and females in the control group. Serum OPN in DIHS/DRESS patients was significantly higher than in the control group ($p<0.01$). After DIHS/DRESS treatment, serum OPN decreased to the control level ($p<0.02$). Immunohistochemical analysis revealed that OPN was expressed by keratinocytes and a certain number of dermal inflammatory infiltrates in DIHS/DRESS.

Conclusions: These findings suggest that OPN could serve as a biomarker for the acute phase of DIHS/DRESS.