Complement Activation by Stratum corneum Through the Antibody-Independent Alternative Pathway

T.		Terui
T.		Kato
H.		Tagami

Department of Dermatology, Tohoku University School of Medicine, Sendai, Japan

Key Words

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Tadashi Terui, MD, Department of Dermatology, Tohoku University School of Medicine, Seiryō-machi 1-1, Sendai 980 (Japan)

We provide evidence that stratum corneum (SC) activates complement through the alternative pathway to generate C5a anaphylatoxin. By immunofluorescence studies it was shown that in addition to circulating IgG autoantibodies, there were anti-SC antibodies of IgM and IgA classes in the sera from normal individuals. However, all the titers were significantly lower than the level of C3 deposition between corneocytes. By contrast, there occurred no C1q deposition. Immunoelectrophoretically the orthokeratotic SC homogenates were found to induce the conversion of C3 from native C3 to C3b in fresh human serum even when the classic pathway was blocked by Ca²⁺-chelation. Enzyme immunoassay showed that factor B split product, Bb, was generated by the SC homogenate in the Ca²⁺-chelated serum. Radioimmunoassay for C5a also demonstrated that the SC homogenates could generate C5a anaphylatoxin in serum to an extent similar to that in non-treated serum when restricted to the alternative pathway activation; neutrophil chemotactic activity was generated in Ca²⁺-chelated serum at levels comparable to that generated in nontreated fresh serum. We separated the SC samples into a cornified envelope, and soluble and keratin fractions. The cornified envelope was more effective in activating complement. This activity resided in heat-stable and nonlipid substances of erythrocytes. Our hypothesis is that, when the SC comes in contact with serum, it activates complement mainly through the alternative pathway to induce chemotactic C5a anaphylatoxin. Hence, inflammation in normal individuals after a traumatic injury to the skin or rupture of acne comedones or epidermal cysts and possibly the formation of subcorneal sterile pustules noted in several dermatoses are explainable through this mechanism.

Reference

Terui T. Kato T. Tagami H: Stratum corneum activation of complement through the antibody-independent alternative pathway. J Invest Dermatol. in press.