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

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Key Words
Stratum corneum
Alternative complement pathway
C5a anaphylatoxin

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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 Clq deposition. Immuno-electrophoretically 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+-chilation. Enzyme immunoassay showed that factor B split product, Bb, was generated by the SC homogenate in the Ca2+-chilated 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+-chilated 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