Anti-inflammatory actions of maggot secretions

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Introduction

Maggot therapy is successfully used tot treat chronic, infected wounds. In chronic wounds the inflammatory phase of wound healing is prolonged, which leads to tissue damage and prevents progress of the physiological healing process. The inflammatory response results in chemotaxis of neutrophils into the tissue and can be triggered by complement activation, an essential part of the innate immune system. Earlier research showed that maggot excretions/secretions (ES) inhibit multiple neutrophil pro-inflammatory responses [1]. In this study, the effect of maggot ES on the complement system is investigated. Do maggots modulate the host's inflammatory response by interaction with complement activation and thereby stimulate healing of chronic wounds?

Methods

Maggot ES were collected following a standardized method [2]. The effect of ES on complement activation was examined in healthy sera and in pre- and postoperatively obtained sera from trauma patients who were scheduled for an surgical procedure. Different immunoassays, which are also clinically used to determine complement deficiencies in patients, were performed in absence or presence of ES.

Results

Results show that ES reduced complement activation in healthy and immune-activated sera up to 99.9% ($p<0.0001$), via all pathways of complement activation in a dose-dependent manner. ES proved to be temperature-tolerant and boiled ES showed the best complement activation reducing properties. Protease treatment of ES decreased complement-reducing effects markedly, indicating the involvement of a protein component. The underlying mechanism of the observation most probably involves breakdown of individual complement components, at least C3 and C4, in a cation-independent manner.

Discussion

This research shows the first pathway independent complement-reducing substrate, probably a boiled stable protein, that already is successfully used in clinical practice. The anti-inflammatory effect of ES may explain part of the improved wound healing caused by maggot therapy. If ES decrease the inflammatory response, the healing process can progress.

Evolutionary, maggots may indeed have developed a strategy to evade the activation of the complement system. Larvae of the *Anisakis simplex*, a parasitic worm, were previously shown to have complement inhibiting properties [3]. The larvae of *Lucilia sericata* infest the wounds for feeding purposes, however humans do not develop an inflammatory and/or immune reaction against them. This could be explained by the results of this study: the larvae are able to break down complement components.

In future research, the complement-reducing properties of ES are further investigated.

Clinical relevance

Efforts to identify the responsible ES components are ongoing and it is expected that future research on this topic will contribute to new insights into the underlying mechanism of ES-mediated complement reduction as well as the clinical success of maggot therapy. Ultimately, this finding could provide a novel treatment for diseases resulting from an (over)active complement system, e.g. infections in trauma patients, ischemic-reperfusion injury and Severe Inflammatory Response Syndrome (SIRS).

Conflict of Interest

None of the authors has a commercial association that might pose a conflict of interest.

References

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