Apoptosis is essential for neutrophil functional shutdown and determines tissue damage in experimental pneumococcal meningitis.

Abstract:

During acute bacterial infections such as meningitis, neutrophils enter the tissue where they combat the infection before they undergo apoptosis and are taken up by macrophages. Neutrophils show pro-inflammatory activity and may contribute to tissue damage. In pneumococcal meningitis, neuronal damage despite adequate chemotherapy is a frequent clinical finding. This damage may be due to excessive neutrophil activity. We here show that transgenic expression of Bcl-2 in haematopoietic cells blocks the resolution of inflammation following antibiotic therapy in a mouse model of pneumococcal meningitis. The persistence of neutrophil brain infiltrates was accompanied by high levels of IL-1beta and G-CSF as well as reduced levels of anti-inflammatory TGF-beta. Significantly, Bcl-2-transgenic mice developed more severe disease that was dependent on neutrophils, characterized by pronounced vasogenic edema, vasculitis, brain haemorrhages and higher clinical scores. In vitro analysis of neutrophils demonstrated that apoptosis inhibition completely preserves neutrophil effector function and prevents internalization by macrophages. The inhibitor of cyclin-dependent kinases, roscovitine induced apoptosis in neutrophils in vitro and in vivo. In wild type mice treated with antibiotics, roscovitine significantly improved the resolution of the inflammation after pneumococcal meningitis.
infection and accelerated recovery. These results indicate that apoptosis is essential to turn off activated neutrophils and show that inflammatory activity and disease severity in a pyogenic infection can be modulated by targeting the apoptotic pathway in neutrophils.

Zeitschriftentitel / Abkürzung:
PLoS Pathog

Jahr:
2009

Band:
5

Heft / Issue:
5

Seiten:
e1000461

Sprache:
eng

Pubmed:

Print-ISSN:
1553-7366

TUM Einrichtung:
r Medizinische Mikrobiologie, Immunologie und Hygiene

Occurences:
· Einrichtungen > Fakultäten > Fakultät für Medizin > Kliniken und Institute > Institut für Medizinische Mikrobiologie, Immunologie und Hygiene > 2009

entries: