

Platelets aid in host defense during melioidosis

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Introduction

Melioidosis, caused by the Gram-negative bacterium *Burkholderiapseudomallei*, is an important cause of community-acquired pneumonia and sepsis in Southeast Asia with a mortality of up to 40%. Recently, it has been shown that thrombocytopenia is associated with mortality. However, the role of platelets in pathogenesis of melioidosis is unknown. The objective of this study was to assess the role of platelets in the host response during *B. pseudomallei* infection.

Methods

Mice treated with a low or high dose of platelet-depleting antibody (depletion to <5% or <1% of normal, respectively) or IgG control were inoculated intranasally with *B. pseudomallei* and sacrificed at 24, 48 and 72 hours. *B. pseudomallei* growth was studied in mice lacking either platelet Toll-like receptor (TLR) signaling (Platelet factor 4-Cre- Myd88-Lox mice) or Glycoprotein-Iba signalling (GPIb/IL4R mice) and in mice with impaired neutrophil extracellular trap (NET) formation (PAD4-/- mice). Ex vivo human neutrophils were inoculated with *B. pseudomallei* and assessed for internalization by electron microscopy with or without platelet supplementation.

Results

During experimental melioidosis, mice developed thrombocytopenia. Platelet depletion increased mortality and bacterial growth in both lung and liver. Platelet depletion also increased chemo and cytokine responses, but reduced pulmonary neutrophil influx. Mice with deficient NET formation had increased bacterial growth in the blood. However, in platelet-depleted mice NET formation was not impaired. Platelet TLR signaling did not influence bacterial growth but mice lacking platelet GPIba showed increased bacterial growth in the lung with decreased platelet counts. Platelet depletion also resulted in bleeding in the lung, not seen in uninfected mice. In human neutrophils, platelets increased *B. pseudomallei* internalization and altered phagosome morphology.

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Discussion and Conclusion

During experimental melioidosis, platelets play a protective role in host defence and prevention of bleeding.