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Development of a murine model of Neisseria gonorrhoeae conjunctivitis and evaluation of immunity targeting the conserved surface polysaccharide, poly-N-acetyl glucosamine (PNAG)

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Background

Neisseria gonorrhoeae (GC) is a significant cause of conjunctivitis in adults as well as in babies born to women with untreated gonorrhea (ophthalmia neonatorum). We have developed a murine model of GC conjunctivitis in both adult and neonatal mice to study virulence and immunity to this pathogen in a readily accessible laboratory animal model. We have also tested the protective efficacy of vaccines and monoclonal antibodies to the PNAG surface polysaccharide in this model.

Aim/Methods

We assessed whether significant conjunctival infection associated with microbial growth giving rise to measurable pathology and increases in CFU counts over 32-48 hours occurs in 8-9 day old neonatal or adult Balb/C mice. We tested whether active immunization with a PNAG-targeting conjugate vaccine or passive immunity with a monoclonal antibody to PNAG induced protective immunity against conjunctivitis due to GC. To induce conjunctival infection, N. gonorrhoeae (1-5 X 107 cfu in 5 µl) was injected directly into the conjunctiva of the Balb/c mice. Twenty four to 48 h post-infection eyes were scored for pathology, using a scale of 0 to 4, evaluating the palpebral and bulbar conjunctivae for erythema, edema, and exudation. Animals were euthanized at 36-48 hr and CFU/conjunctiva determined.

Results

Both active and passive vaccination against PNAG markedly reduced bacterial levels in the conjunctivae and related pathology for 3 GC strains tested in adults and FA1090 in passively vaccinated neonates, including sterile immunity in many samples. Immunized adult mice depleted of either PMN by antibody to the Ly6 antigen, or complement via local and systemic cobra venom factor treatment, were no longer protected against gonococcal conjunctivitis. There was spread of gonococci to the brains of PMN and complement-depleted mice and to the spleens of PMN-depleted mice. Antibody to PNAG mediated in vitro bactericidal killing of N. gonorrhoeae at complement concentrations above 5% and PMN-dependent opsonic killing at a lower complement concentration.

Conclusions

Immunization against PNAG demonstrated PMN- and complement-dependent protective efficacy in a mouse model of N. gonorrhoeae conjunctivitis, indicative of a potential for use of this reagent for prevention of GC disease.

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