Abstract

Spontaneous Identification of Bordetella bronchiseptica in a Baboon Colony: Potential Ramifications for Bordetella pertussis Modeling

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Objectives: While developing pertussis therapies, we performed efficacy studies in a recently described baboon infection model. Surprisingly, despite intranasal inoculation of B. pertussis, some animals failed to develop the leukocytosis and/or the high levels of pertussis antibodies in the nasopharynx that are characteristic of the disease. We isolated early time points from these efficacy studies to determine if infection with another Bordetella species could be the root cause of the disease.

Methods: Sixteen baboons were inoculated with 6 x 10^6 CFU of B. pertussis via intranasal and intrarectal routes. The infection was confirmed via ELISA for antibodies against filamentous hemagglutinin ( FHA), which is expressed on mucosal surfaces and provides a protective immune response to B. pertussis. FHA titers were measured prior to any experimental intervention, WBC counts and B. pertussis from nasal washes were also measured. Eight baboons were euthanized before the time points to determine if the titers changed were characteristic of primary or secondary immune responses.

Results: Eight baboons had undetectable anti-FHA antibodies prior to infection. At the 2\(\text{/}3\) day time point, all eight had high B. pertussis levels (>10^7 CFU/ml) in the nasal washes, and seven had elevated WBC counts. Two baboons, #10 and #13, had elevated WBC counts, but the B. pertussis levels remained low. In the other six baboons, anti-FHA titers were low or non-detectable (++) on day 2, the WBC counts remained low, and the B. pertussis levels remained low. Three of these animals were followed for 3 weeks, and their WBC and nasal wash counts never reached elevated levels. The third group, baboons #10 and #13, were overgrown with a second bacterium definitively identified as B. bronchiseptica in animals #10 and #13, and B. bronchiseptica (based on their negative FHA serology) and became unusually debilitated for this model. FHA antibody levels were followed in five animals that were FHA(-) prior to infection, and #10 and #13. The FHA(-) animals did not develop FHA titers three weeks, whereas the FHA(+) animals displayed a rapid titer increase indicating prior Bordetella exposure.

Conclusions: These data indicate that B. bronchiseptica can spread in baboon colonies and can alter the course of infection in baboons used for a pertussis model. Prior exposure to B. bronchiseptica, as suggested by high FHA titers, provided protection from infection by B. pertussis, whereas consistent initial exposure to both Bordetella species appeared to exacerbate the clinical course (M2 and M7). Thus, when using this baboon model it is important to be cognizant of B. bronchiseptica in the colony. Finally, since recent data from Merkle’s lab (1-3) indicate that B. pertussis can spread between baboons, it may be wise to investigate B. pertussis exposure in colonies used for pertussis modeling.

Pre-Treatment Screening for anti-FHA Antibodies

Serum collected from 16 baboons prior to B. pertussis infection was screened using ELISA for anti-FHA antibodies. The presence of anti-FHA antibodies indicates prior exposure to a Bordetella species.

Pre-Immune Serum Anti-FHA Antibody Titers

Eight baboons had undetectable anti-FHA titers. The other eight displayed titers that ranged from 1 to 100 (++) indicating previous exposure to a Bordetella species.

Elevated Anti-FHA Titers Preclude Infection with B. pertussis

Selected animals were infected with B. pertussis. After two or three days, prior to any therapeutic intervention, WBC counts and nasopharyngeal pertussis levels were determined. Unexpectedly, 4 of 16 nasal wash plates were overgrown with a second bacterium, confirming the prior Bordetella infection.

Baboons with No Pre-Infection Titer

Animals with no pre-infection anti-FHA titers were readily infected with B. pertussis as it displayed leukocytosis and had nasopharyngeal pertussis levels of 10^7-10^8 CFU/ml. Three of those animals were watched for 3 weeks and developed leukocytosis. Interestingly, a third category with animals 113 and 115 that had (+) or (+) titters, displayed an intermediate infection profile, with elevated white counts but normal pertussis levels. As nasal washes from animal 131 were confirmed positive for B. bronchiseptica, we postulated that both 113 and 115 had been exposed to B. bronchiseptica shortly before B. pertussis infection. Accordingly, these two animals would have a primed immune response prior to B. pertussis infection, but not one that was sufficiently developed to be completely protective.

Baboons with Pre-Infection Titer

Concurrent infection with B. pertussis and B. bronchiseptica led to a clinical picture that was more severe than that described for this model. Accordingly, animals 63, 67, and 85 were housed together. Three no detectable anti-FHA titers prior to the study, but 63 and 85 were presumed to have an active B. bronchiseptica infection at the time of B. pertussis exposure. All three became extremely sick, huddled on the floor of the cage, and had poor food intake. Animal 67 displayed a disease which is unusual for this model. Similarly, animals 89, 102, and 116 were housed together. Animal 99 was presumed to be actively infected with B. bronchiseptica concurrent with the time of B. pertussis exposure. While animals 99 and 102 were protected from infection by high anti-FHA titers, animal 116 was not. Animal 116 became critically ill and euthanized.

References