Genetic Factor(s) Influence Scar Formation in Experimental Pyelonephritis

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Key Words

Pyelonephritis
Chronic pyelonephritis

Abstract

Two inbred strains of rat have been identified that show markedly different responses to experimentally induced renal infection. Experiments involving these two strains and their F1 progeny have shown that a genetic factor either protects the host from a **tissue-destructive** inflammatory response (autosomal dominant gene) or potentiates lesion formation (autosomal recessive gene). The data are the first indication that genetic factors may determine the degree of renal damage in pyelonephritis.

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Introduction

Chronic renal infection and the associated parenchymal damage is still considered to be a major cause of renal failure [1] and much effort has been directed at identifying factors associated with the pathogenetic mechanisms. The dominant thesis has been that either chronic infection or persistence of bacterial antigen, stimulates an immune response against the immunogenic material leading to progressive parenchymal damage. In the light of recent studies [2], this thesis is no longer tenable and it is now clear that the acute inflammatory response to bacterial invasion of the kidney is the dominant event in the genesis of the lesions of chronic pyelonephritis. Factors such as the severity of infection and the response to antimicrobial therapy are thought to influence the outcome of individual episodes of pyelonephritis. Additionally, we believe a genetic factor associated with the inflammatory response may influence the degree of scar formation. Our thesis is based on observations made using two inbred rat strains that differ markedly in their response to experimentally induced renal infection.

(HO), and their F1 progeny by the direct inoculation of 10⁸ Escherichia coli 075 into the kidney [4]. 42 days later at necropsy, the infected kidneys were excised and assessed for the degree of scarring. Scarring was measured using a kidney profile stamp divided into ten equal areas. Scarred or infected areas were shaded and expressed as a percentage of the total surface area of the kidney. For bacterial counting kidneys were homogenized, serially diluted and cultured in nutrient agar pour plates. Significance was tested by Wilcoxon's rank sum test.

Results

The degree of infection was found to be similar in the three groups of animals ($p > 0.2$). However, we found a considerable difference in the degree of renal scar formation between the DA and HO strains ($p < 0.001$). The F1 progeny of a cross between the two strains showed the same reduction in scarring. Similar results were obtained with inocula of 10⁴ E. coli showing that the effect was not dependent on the challenge size (data not presented).

Comment

Methods

Experimental pyelonephritis was induced in male and female inbred rats from the strains Dark Agouti (DA) and Hooded Oxford

This study demonstrates that genetic factor(s) either protect the host from a tissue-destructive inflammatory response (autosomal dominant gene) or potentiate lesion formation (autosomal recessive gene). Harris et al. [3]

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375

30 -i

p= 0.0003

·p= 0.0001-

p = 0.2-

A A

A A A

◆

20

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Fig. 1. Degree of infection (left) and degree of scarring (right), 42 days after the induction of experimental pyelonephritis using 108 E. coli per kidney in Dark Agouti (DA) and Hooded Oxford (HO) rats and the F₁ progeny of their cross (DA × HO).

2 0

DA

■NS-

HO

■NS·

DAxHO

0j

DA

A A A A AAA

A A A

A A

HO

DA x HO

reported a related phenomenon involving an anaphylac-toid reaction. The present data are the first indication that a genetic factor controlling inflammation, rather than pathogen-associated virulence factors, determines the degree of renal damage in acute pyelonephritis. As mentioned, the acute inflammatory response is now believed to be the dominant event in the genesis of the lesion of chronic pyelonephritis and we will be seeking a correlation in the two strains between

their responsiveness to inflammatory stimuli and the differences in lesion size. Our findings may explain some aspects of the variable outcome to renal infection observed in man.

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