STIMULATION OF EPITHELIOID CELL RESPONSE IN EXPERIMENTAL GUINEA PIG TUBERCULOSIS

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In the course of experiments on the effects of anti-spleen tissue serum on the rate of wound healing in experimental animals (Maltz et al. 1948a, b), the local histological response observed led us to consider the effect of such sera on pathological processes. Miale (1947) reported that such antisera elicited a mononuclear cell response in the peripheral blood of dogs. This finding supported our observations and therefore the following trials on experimental tuberculosis in guinea pigs were undertaken.

EXPERIMENTAL METHOD

A. Animal distribution. Normal guinea pigs weighing between 350 to 450 g were controlled for enteric infection, tuberculin tested, separated into comparable groups on the basis of sex and weight, and treated as indicated:

(1) Antiserum-treated animals:—37 guinea pigs injected and treated with anti-splenic tissue serum starting on the 10th day postinfection as given below.

(2) Control animals:—(a) 12 guinea pigs infected and injected with normal rabbit serum starting on the 10th day postinfection, and (b) 25 guinea pigs infected and receiving no injections.

B. Infecting organism and dose. A suspension of virulent human tubercle bacilli H37RV cultured routinely on Petragiani's medium was prepared by grinding a weighed inoculum with a mortar and pestle under aseptic conditions. The final emulsion was prepared to contain approximately 0.5 mg of original inoculum per ml (moist weight). Each guinea pig was inoculated subcutaneously with 1 ml of this suspension in the inguinal region, using a 2½ in by 20 gauge hypodermic needle to avoid leakage of infecting dose.

C. Anti-splenic tissue serum: preparation and dosage. Fresh spleens from sacrificed normal guinea pigs were cut into small strips, washed several times in saline solution to eliminate as many erythrocytes as possible. The tissue was then emulsified in saline solution in a Waring Blender (1 part spleen to 5 parts saline solution, w/v), distributed into 1 ml portions and stored at −20 C. Rabbits were immunized with this antigen and the serum thus obtained was adsorbed with guinea pig erythrocytes to remove anti-erythrocyte factors and titrated by the standard Kolmer complement fixation techniques (Kolmer and Boerner, 1945). The titer of the antiserum obtained was taken to represent the antibody units per ml of undiluted serum, i.e. a serum with a titer of 1:160 was taken to contain 160 units per ml. On the basis of this unitage assumption, the animals were treated with anti-splenic tissue serum by intramuscular injection. The first dose was 0.8 units per kg and each subsequent injection twice the previous dose given at 4-day intervals for a total of 5 injections. The 12 control guinea pigs were injected with equivalent concentrations of normal complement inactivated rabbit serum.

D. Duration of experiment and data gathered. All animals were sacrificed at the end of the 6th week after infection. Gross autopsies were performed at sacrifice and sections of the spleen prepared for pathological evaluation (formalin fixation; H. & E. stain). Histologic evaluation was made on 3 separate occasions from coded slides to control subjective factors in evaluation.

RESULTS

The objective of this study was primarily to determine whether the anti-splenic tissue serum influenced the epithelioid cell response to the tubercle bacillus. For this reason longitudinal sections were taken through several comparable areas of each spleen and histo-pathological evaluation made on the basis of area of epithelioid cells, infiltration, size, and distribution of tubercles and the degree of caseation necrosis.

On this basis no differences were found among the untreated controls and those controls receiving normal rabbit serum. Therefore these 2
groups are considered as 1 group of controls for comparison with the anti-splenic tissue serum treated group.

The anti-splenic tissue serum treated group, as a whole, exhibited a much greater epithelioid cell reaction; the tubercles, consisting almost wholly of epithelioid cells, were considerably larger and showed markedly less caseation necrosis than the control animals. In about 50 per cent of the anti-splenic tissue serum treated guinea pigs almost the entire splenic pulp was replaced by epithelioid cells, while in the control guinea pigs this did not occur in a single instance.

SUMMARY

The effect of anti-splenic tissue serum on the histologic response in experimental tuberculosis in guinea pigs was studied.

The antiserum treated animals exhibited a much greater epithelioid cell reaction and a lesser degree of caseation necrosis as compared with the controls.

REFERENCES


