OCCURRENCE OF LYMPHOMAS AND LUPUS ERYTHEMATOSUS-LIKE SYNDROME IN THE COURSE OF EXPERIMENTAL CANDIDA ALBICANS INFECTION IN MICE

by

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Abstract

Occurrence of four lymphomas was seen following injection of $1.4 \times 10^8$ Candida albicans cells to the spleen of eighty non-inbred albino mice. These neoplastic changes occurred in three to seven months of the duration of the experiment. Extensive invasion of the subcutaneous tissue by the tumor was found in one animal. Two of the animals with lymphoma also had changes in the kidneys compatible with lupus erythematosus and presence of LE cells in the blood. In other animals most frequent and extensive pathological changes were found in the kidneys and in order of frequency were as follows: thickening of the basement membrane, fibrinoid degeneration, presence of hematoxylin bodies, wireloop formation. In total, the presence of positive LE cells in blood was found in seven instances and suggestive LE cells was observed in eight animals. Finding of perisplenitis, exudative pleuritis and pericarditis gave additional support to the resemblance of observed pathological changes with human lupus erythematosus. The fact that occurrence of lymphomas and lupus erythematosus together has been reported in humans provides additional interest to the results reported.

Results presented here and previously suggest that there may be more extensive interrelationship among variety of pathological changes observed than is accepted until now. Better understanding of host-parasite relationship of Candida albicans, and possible other fungi, could advance our knowledge of pathogenesis of these diseases.

Increased occurrence of malignancy in the course of experimental Candida albicans infection in Wistar rats has been previously reported (MANKOWSKI, 1963). In the same experiment pathological changes were seen which closely resembled some collagen diseases in humans: scleroderma, dermatomyositis, periarteritis nodosa. These pathological changes were found following injection of Candida albicans cells to the spleen. The spleen is the largest reticuloendothelial organ in the body and the injection of Candida albicans cells into this organ has been looked upon as the direct attack on this system. There is increasing awareness of the possible role of the reticuloendothelial system in human pathology and it appeared of interest to study

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pathological changes resulting from interaction of *Candida albicans* with this system. Attention to the significance of the reticuloendothelial system (RES) in neoplasia was attracted by Jaffe (1931). Stern & Wilheim (1949) reported a direct relationship between the reticuloendothelium and tumor growth. Bailiff (1956) observed that progressive loading of the reticuloendothelial system by intravenous injections of thorotrast has an influence on the growth rate of the Erlich ascites tumor. With small dosages, the cell multiplication rate became depressed to a probably significant degree. With larger dosages, the ascites tumor grew faster. It appeared to be of interest to see if one could obtain similar pathological changes in mice as had been obtained in rats in the same experimental conditions.

**MATERIALS AND METHODS**

Non inbred albino mice were obtained from Taconic Farms, Germantown, N.Y. Female mice weighing approximately 20 g were used. Animals were kept in plastic cages and maintained on a Purina Chow diet and water *ad libitum*. The temperature in the animal colony was maintained at a steady level of 72° F.

WI-1 strain of *Candida albicans* was used. The strain was isolated from a human source and maintained on glucose-peptone agar. Suspension in a sterile physiological saline (0.85 % NaCl) solution of 24—48 hour old cultures was used for injections. Mice were operated on under pentobarbitol-ether anesthesia and 1.4 × 10⁴ of *Candida albicans* cells with 0.05 volume of sterile physiological saline solution were injected into the spleen. With this dosage there was considerable mortality in the first two weeks following the operation. Additional mice were operated on to have eighty mice available for the study of chronic infection induced in this manner. Eighty control mice were operated on in the same manner as the experimental mice and the same amount of sterile solution of physiological saline was injected into the spleen. Blood from retroorbital venous plexus was used for the study for the presence of LE cells. The technique of Dubois & Freeman (1957) was used when searching for the presence of LE cells.

The organs from the dead or sacrificed animals which were prepared for histological studies were fixed in Bouin's solution, imbedded in paraffin, sectioned at 4 u, and stained with hematoxylin and eosin (H & E) and periodic acid Schiff (PAS).

For isolation of the injected organisms, pouring plate cultures, using Sabouraud's medium with addition of Kanamycin sulfate (Kantrex), were prepared from the various organs. The removed organs were homogenized with 10 % (weight per volume) of sterile physiological saline solutions in Kontes tissue grinders. After incubation at 37° C for 48 hours the number of colonies was counted with the help of a Gallenkamp electronic colonies counter.