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Absence of Brain Antibodies in Senile Dementia

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In recent years the recognition of auto-immune processes has led to important advances in our understanding of certain diseases of hitherto uncertain causation (Mackay and Burnet, 1963). In psychiatry, schizophrenia has been the main focus of studies of auto-immunity, with Heath and Krupp (1967) reporting positive results of tests for antibodies to brain cell nuclei and Whittingham *et al.* (1968) reporting negative results. Studies have been described (McAlpine *et al.*, 1965) in which antibodies were detected to whole brain homogenates, mostly by complement-fixation, in various disease states that included multiple sclerosis. Wilkinson and Zeromski (1965) found, by immunofluorescence, serum antibodies to cytoplasm of neurones in four of eight patients with carcinomatous neuropathy.

Autoimmune processes in relation to ageing have also received attention (Burnet, 1968).

This paper describes an unsuccessful attempt to demonstrate antibodies to components of brain in the serum of patients with senile dementia.

Subjects

Blood samples were obtained from 18 patients, 8 men and 10 women, with senile dementia. Their ages ranged from 72 to 89 years (mean 78 years) and their length of stay in hospital was 18 months.

The diagnosis was a clinical one, agreed upon by two psychiatrists after study of all the clinical details and special investigations. There was a gradually progressive chronic brain syndrome with no focal neurological signs. No aetiology other than primary degeneration of cortical cells was apparent, though cortical biopsies were not done.

Methods

Immunofluorescence

Sera were tested for antibodies to components of human cerebral cortex obtained from the frontal lobe at operation from a 50-year-old female patient undergoing craniotomy for removal of a cerebral tumour. A 4 u section of frozen brain cut in a cryostat at −20 °C and air-dried was layered with 0·02 mls. of serum for 30 minutes at room temperature, washed in phosphate buffered saline pH 7·3 (PBS), layered with 0·02 mls. of fluorescein-conjugated anti-human IgG for 30 minutes, again washed, mounted in 10 per cent PBS in glycerol, covered by a cover-slip and examined microscopically under ultra-violet light. The sera (see results) were subsequently tested for anti-nuclear antibodies by immunofluorescence, using unfixed air-dried frozen sections of rat liver and a fixed smear of human peripheral blood (Whittingham and Mackay, 1969).

Radio-immunoassay for antibody to myelin protein

Sera were tested for antibodies to the basic protein of myelin of human brain by means of radio-immunoassay, using gel filtration and a fully automated sampling and counting device (McPherson and Carnegie, 1968). One hundred nanograms of basic protein of myelin iodinated with ^{125}I to give 2,000 counts per second was mixed with various dilutions of the test serum in a diluent containing 0·2 M Tris acetate buffer, pH 7·3, and sufficient rabbit serum, so that all samples for radio-immunoassay had the same concentration of protein and a final volume of 1 ml. Each test was allowed to react for 24 hours at 4 °C before being applied to a column (10 × 2·4 cm.) of sephadex G 100. Sera from a non-immunized rabbit and a rabbit immunized with myelin protein were used as controls.

Results

Immunofluorescence

No serum reacted specifically with brain tissue. Two sera which reacted with nuclei of brain cells were tested for antibodies to nuclei of other cells, including leucocyte nuclei in blood smears and liver cell nuclei: both sera gave a positive result, indicating that the reaction with brain cell nuclei represented non-specific anti-nuclear activity in these sera.

Radio-immunoassay

None of the sera showed binding with the iodinated basic protein of myelin in the radio-immunoassay.

Discussion

Two techniques were used to detect auto-antibodies to define constituents of cerebral tissue in patients with senile dementia. The immunofluorescence procedure was selected as being likely to demonstrate antibody if such was present to cortical neurones. The radio-immunoassay was selected to detect antibody to basic protein of myelin. This antibody is demonstrable in animals which develop, after injection of myelin protein, an acute encephalo-myelitis—though this is not in any way a close model of senile dementia. In fact, no antibody specific to brain antigens was detected by either method.

Summary

Sera from 18 patients, 8 men and 10 women, with senile dementia were tested by immuno-fluorescence for antibodies to human brain cortex and by a radio-immunoassay for anti-bodies to myelin protein. No antibody specific to brain antigens was detected by either method.

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