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ALLERGY OF NERVOUS SYSTEM AND VASCULAR REACTIONS

By

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INTRODUCTION

Allergy and the nervous system have some very important connections, which have been evidenced mainly by experimental and clinical investigations. The anaphylactic reactions of the central nervous system, obtained by treatment with allergens, produce several brain alterations, with edema, small hemorrhagic areas, appearance of reactive cells (particularly of mononuclear type, also polynuclear cells, etc.), which are located mainly in a perivascular site. Those experimental alterations are quite similar to those which are found in acute encephalitis, in generalized acute encephalomyelitis, in acute myelitis following some infective disease (scarlet fever, German measles, influenza, etc.) or in smallpox, antirabies vaccination, etc., or during serum therapy. In all of said diseases, histology examination reveals the presence of lympho-monocyte infiltrations, mainly perivascular ones, with some more or less considerable demyelination (*Van Bogaert, Bouweldijk-Bastiaanse, Von Pirquet, Cazzullo, Glanzmann*).

It should be mentioned herewith that allergens of microbial

type have a special tropism for the blood vessel, particularly for the capillaries. Actually, the capillaries and the small vessels of the nervous system are most severely involved in the post-infective, post-vaccinal neurological complications. The microbial allergen, having sensitized the reactive cells of the vascular connective tissue, with antibody formation, in subsequent contacts triggers off with them the allergic reaction, with histamin discharge, cell proliferation, infiltration, etc. Histaminic stimulation is followed by: capillary dilatation, congestion, increase in vascular permeability, edema, sometimes hemorrhage, tissue damage, etc.

Blood vessels, particularly the capillaries, play an outstanding role in allergic reactions. In the capillaries, the basic exchanges between the blood and the body tissues take place. Substances dissolved in the blood come into full contact mainly with capillary cells. In the blood, various allergens may be present, such as foreign proteins, toxic, microbial matter, etc. The contact of those allergens with endothelial cells has no effect. However, the allergen contact with histiocytarian cells of the connective network which surrounds the capillary tube, does produce a transformation of those cells into elements of allergic reactivity, with histiocyte proliferation into lymphocytoid, monocytoïd, plasmacytoïd cells. Consequently, histiocytes of the capillary wall are the first reactive cells, which come into contact with blood-dissolved allergens. Pericapillary cell clusters, also lympho-plasma-monocytoïd cells are an important site for antibody formation. In that site, the clash between allergens and antibodies takes also place, with the consequences which have been listed above.

The proliferative reaction of pericapillary histiocytes also occurs when allergens reach the tissues from the outside. That is the case of allergic contact dermatitis. The allergenic substances carry out their sensitizing action upon pericapillary histiocytes, which proliferate, with consequent formation of perivascular nodules made up of lympho-mono-plasmacytoïd cells.

The latest findings upon function of the histo-capillary unit, particularly upon reactive function of histiocytes belong-

ing to the pericapillary connective network, have prompted us to investigate in detail the various patterns of vascular reaction in experimental encephalo-myelitis.

MATERIAL AND METHOD

Our test was carried out in three groups of adult cats of either sex. The first group (10 animals) was treated with the encephalitogenic emulsion; the second group (5 animals) was treated with saline and adjuvants in the same amount of the encephalitogenic emulsion; the third group (5 animals) was kept for control. The average weight of the 20 animals was 2,500 kg.

The animals were kept for 8 days into single cages for the purpose of checking their physical condition and their adjustment to the environment. They were fed milk and raw meat. Cages were kept at 20° C temperature.

The encephalitogenic emulsion was prepared at the time of employment, in accordance to the following formula:

homologous spinal cord	gm 0.8
complete Difco	cc 0.4
Mycobacterium butirycum	mg 20
Bayol	cc 0.4
Arlacel	cc 0.2

This emulsion was injected in the fingertips of the four paws in the amount of cc 0.1 for each paw. Before the injections, a sterility control of the encephalitogenic emulsion was performed by seeding the latter in agar and keeping it under observation for 48 hours. Histology slides were stained with hematoxylin-eosin.

RESULTS

By such histological study, we were able to notice various alterations of brain tissue. Those alterations were located mainly in the smaller vessels, particularly in the capillaries. The alterations found in blood vessels show a pattern which varies both as regards extension and severity. In the most severe alterations, a massive, irregular concentration of cells is found around the blood vessels, and among those cells many connectival elements are detected, belonging either to the histoid type or to the fibroblastic, monocytoïd, lymphocytoïd and rarely, plasmactoid ones. Intermingled with said

cells, several polynuclear cells can also be seen, particularly in the largest cell concentrations. Such polymorphic cell population is immersed in some amorphous matter of fibrinoid type. The less extensive alterations, particularly the ones located in a pericapillar site, are found to be the most interesting and significant ones (Fig. 1).

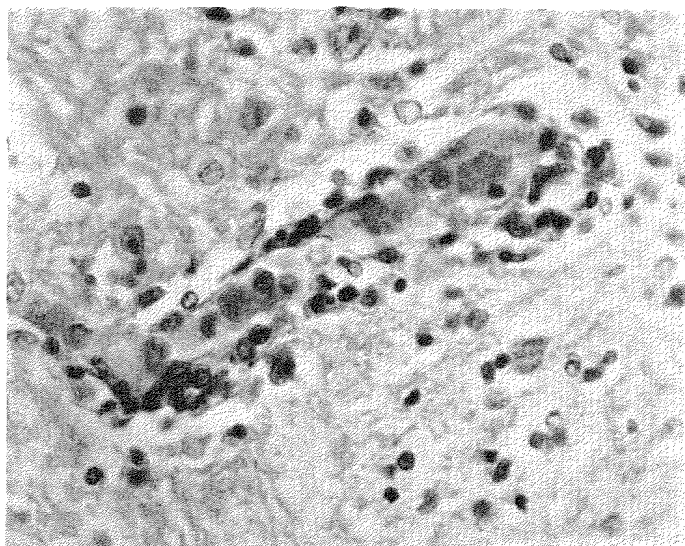


Fig. 1.

Brain tissue with a capillary, sectioned lengthwise. The capillary is ectatic and congested, surrounded by an evident stripe of edema. The capillary wall also reveals, in some areas, a thick collection of mononuclear cells of histiocyte type.

Around the vessel wall, an increase in cell number is found, including histioid cells of mononuclear type, mainly lymphocytoid, monocytoid, etc (Figs. 2 and 3). Namely, those cells are found which are typical of allergic reactivity. The presence of those cells signifies the early stage of the reactive movement produced by the allergenic stimulation within the cerebral tissue. By microscopic observation, it is possible to

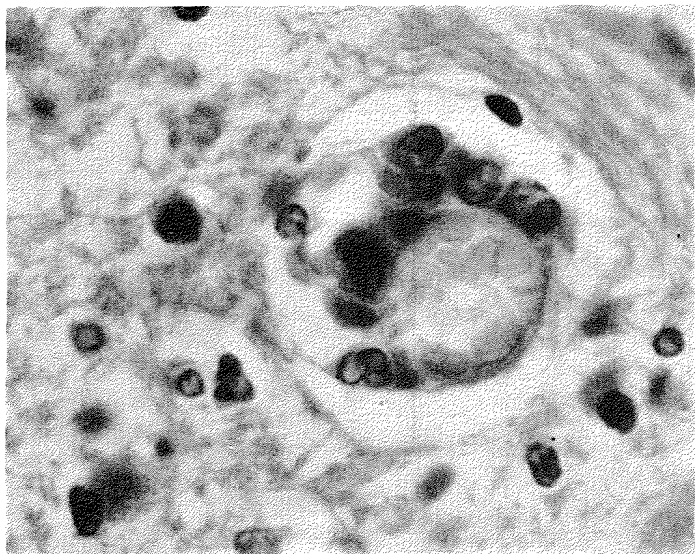


Fig. 2.

Brain tissue with a capillary being sectioned transversely (strong magnification). The vessel is markedly dilated, and its lumen is filled with erythrocytes; an extensive halo of edema can be seen all around. The capillary wall reveals a clear edematous involvement of the endothelium, with a sequence of swellings, resembling the beads of a rosary. Against the capillary wall, one can see a collection of lympho-monocytarian cells, clearly derived from local histiocytes, in the course of direct multiplying process. The surrounding tissue are also involved by the edema.

follow up the evolution of reactive proliferation which starts from pericapillary connectival cells (adventitial cells, pericytes, aristocytes, etc.). These histiocytes, following allergenic stimulation, become involved into a polymorphic proliferative reaction, changing from fixed cells into mobile cells, mainly of lymphomonocytoid, fibroblastic type, etc. (Figs 4 and 5). Only in the last stage of the reactive process one find in the histological picture polynuclear cells, fibrinoid imbibition as well as signs of degenerations within the very crowded cell population (Fig. 6).

Histology studies carried out upon the initial alterations of experimental encephalomyelitis reveal a considerable local involvement in the development of allergic reaction. The cell concentration which is found in a perivascular location, features the same cells to be found in vascular reactions observed in allergic histology. Here too, the capillary histiocyte plays a leading role in the reactive movement, which is being promptly directed towards creating the typical cells for antibody formation.

Histological changes of experimental encephalic allergy feature various alterations—mainly the finding of polynuclear cells, the considerable fibrinoid imbibition, the fibroblastic proliferation—which cannot be included within the classical

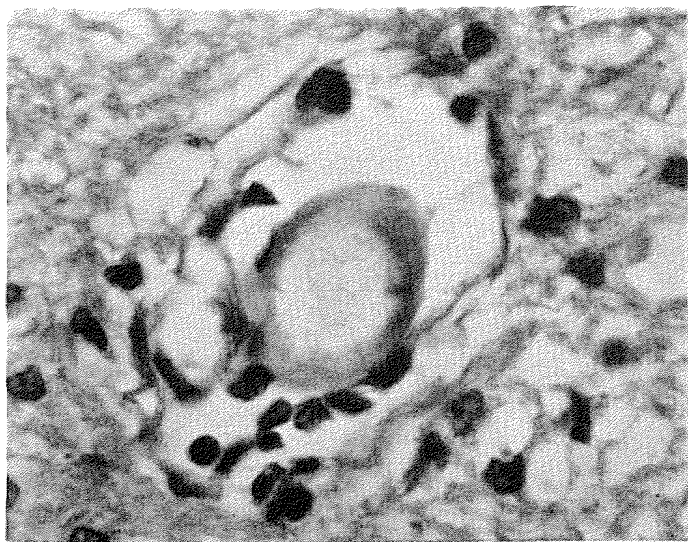


Fig. 3.

A small blood vessel, which is very congested, with edema of its wall. An extensive, perivascular halo of edema is seen. The connective tissue around the vessel wall shows an initial proliferative increase of its cells, with a tendency towards formation of monocytoïd elements, etc.

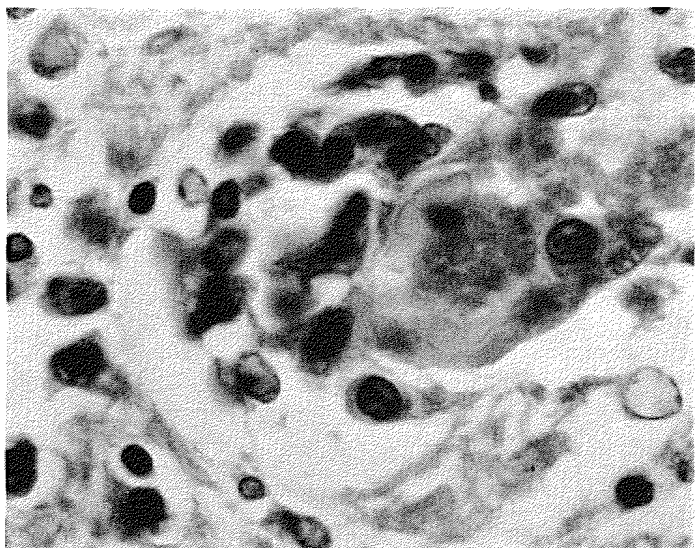


Fig. 4.

Brain tissue with a capillary in a tranverse section at a very strong magnification. The capillary appears quite congested. It is almost entirely surrounded by a wide halo of edema. A cell collection is seen around the capillary. Histiocyte-type cells of the perivascular connective tissue are seen, some of them of lymphoid type, other ones of monocytoïd, fibroblastic type etc. One histioid cell, still linked to the connectival network, is seen during plasmacytoid transformation. Altogether, the cell collection seems mainly to be the result of some complex reactive movement, started from the perivascular connective tissue.

pattern of allergic capillaritis. We believe that the presence of polynuclear cells, also the connectival reaction in a fibroblastic sense are to be ascribed mainly to a special adjuvant stimulation of the allergenic matter employed in the sensitization process. Actually, polynuclear cells, fibrinoid imbibition, fibroblastic proliferation, etc., are found in the histological picture of tuberculin-stimulated tissues.

DISCUSSION

A detailed study of vascular reactions in experimental allergy

of the nervous system reveals that the reactive process starts from histiocytes located in the wall of capillaries and of the smaller blood vessels. Allergenic stimulation elicits histiocyte proliferation, with formation of lymphocytoid, monocytoid, plasmacytoid cells, known to be charged with antibody formation. Lymphomonocytoid cells must be regarded as being the specific response to the allergenic stimulation of the heterogeneous encephalic mixture. Polynuclear cells, fibroblastic cells, fibrinoid imbibition are to be regarded as the reactive response to tuberculin stimulation.

Our histology study takes the cellular elements of vascular reaction in encephalic allergy as being mostly of local origin, not as the result of a mainly hematogenous inflammatory pro-

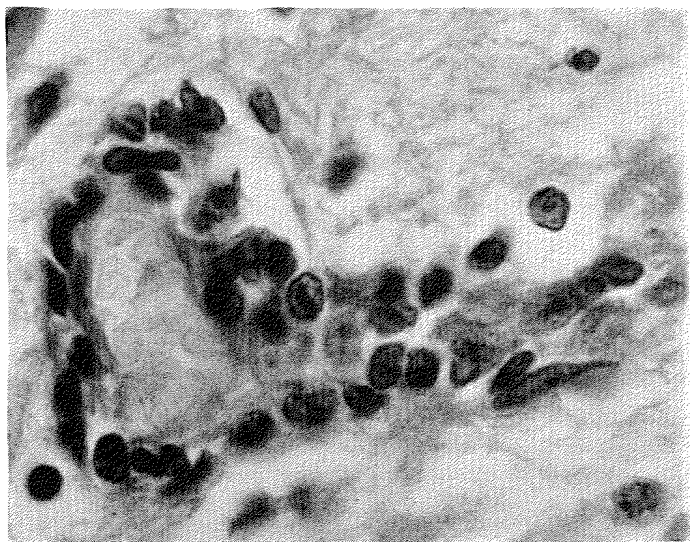


Fig. 5.

A small blood vessel, considerably congested, with halo of perivascular edema. Cells of parietal connective tissue are markedly increased in number, due to a proliferation process. Such proliferation has produced a remarkable prevalence of lympho-monocytoid cells.

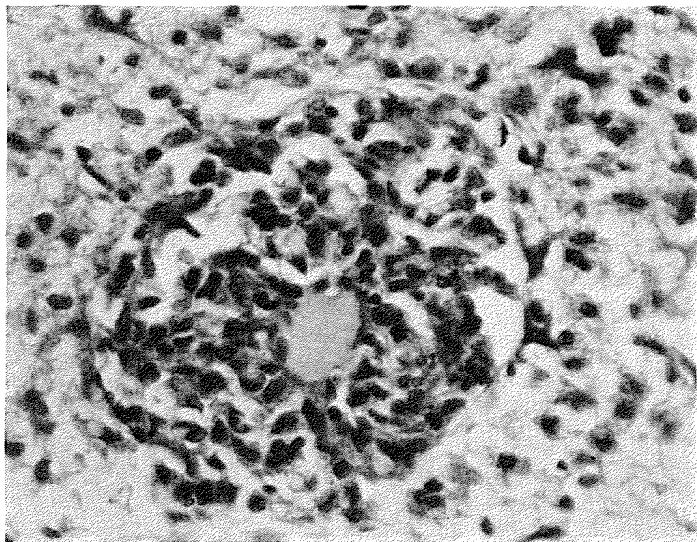


Fig. 6.

Brain tissue with a small blood vessel sectioned transversely. The vasa lumen is filled with plasma. Around the vessel, there is an extensive nodular area, with mononuclear cells of histioid, fibroid type, etc., mostly linked to a coarse network of connective tissue.

cess. Such a finding charges the encephalic vessels, particularly the papillaries, with the main responsibility, both in the sensitization process and in the development of the allergic proliferative reaction. Ascribing to blood vessels such important responsibility for the early beginning and for reactive dynamics of encephalic allergy, can provide some new elements useful both in the clinical and the therapeutic field.

SUMMARY

Injections into animals of either homologous or heterologous encephalic material produce a picture of allergic encephalomyelitis. Said picture is similar to pathology findings in human encephalomyelitis.

A histology study of experimental allergic encephalomyelitis reveals that the cells involved in vascular reaction are mostly of local origin and are produced by the proliferative movement of perivascular histiocytes, elicited by the sensitizing stimulation of the allergenic material.

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