Virchows Arch. A Path. Anat. and Histol. 374, 271–273 (1977)

Virchows Archiv A

Immunohistochemical and Electronmicroscopic Observations on the Local Immune Response in Ulcerative Colitis*

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Summary. Inflammatory cell infiltrates in ulcerative colitis have been investigated by means of the immunoperoxidase method and by electronmicroscopy. Considerable morphological and functional changes of the local plasma cell population have been found. The absolute number of plasma cells is raised with a marked increase of IgG-cells and a relative decrease of IgA-cells. In particular complement (C3) has been demonstrated at the basement membrane of the surface epithelium and between epithelial cells. The significance of these findings, as a local humoral immune response, is briefly considered, with regard to their possible pathogenetic importance in aggravating and perpetuating the disease.

Key words: Ulcerative colitis – Immunoperoxidase – Complement demonstration – Electron microscopy.

Colonoscopically obtained biopsies of a selected group of 50 young patients with ulcerative colitis (UC) were examined for the content and distribution of immunoglobulin containing cells, by the indirect immunoperoxidase method (Taylor, 1974). We have attempted to demonstrate local activity of complement (C3) by the same method. Ultracytochemical findings in the inflammatory infiltrate were also obtained from the same material.

Results: The local immune response in UC is characterized by a distinct plasma (B-)cell reaction with a general increase of their number in the lamina propria mucosae; an increase and focal predominance of IgG containing cells, and a relative decrease of IgA-cells. There are no marked quantitative changes of the IgM- and IgE-cell populations. IgA-cells are concentrated in the upper parts of the lamina propria near the surface mucosa, whereas the IgG-cells are more frequently found in the parts near the submucosa, at crypt bases and the sites of crypt abscesses and lymph follicles. Free interstitial IgG can be demonstrated in the lamine propria, in particular bound to the basement membrane of the surface epithelium (Fig. 1). At this site complement can be

* Supported by a grant of the Deutsche Forschungsgemeinschaft

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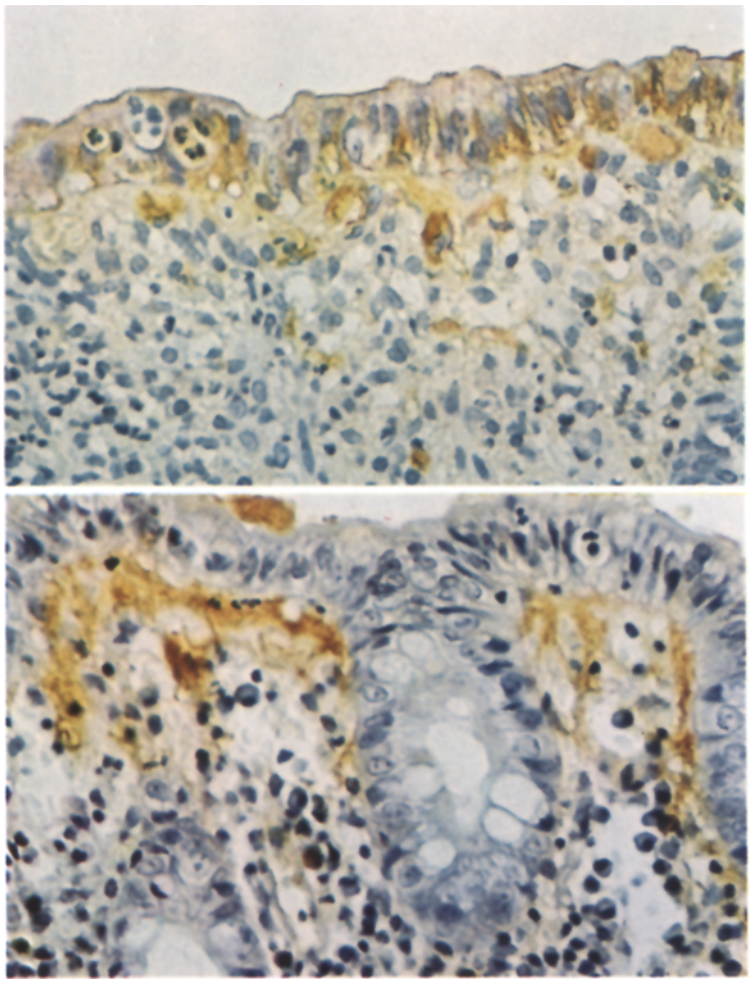

Figs. 1 and 2. Surface mucosa in ulcerative colitis with granulocytic infiltrates. **Fig. 1.** Demonstration of IgG by the indirect immunoperoxidase method. Note distinct brownish deposits of the reaction product at those sites were specific anti-human-IgG-antibodies are bound: basement membrane, intercellularly within the mucosa and in the capillaries. **Fig. 2.** Demonstration of complement (*C3*) in form of brownish reaction products at the sites where IgG is demonstrated by the same method

demonstrated and is also found in the intercellular space of the surface epithelium (Fig. 2). This latter finding is seen only in cases of acute relapse of the disease. Ultrastructurally distinct morphological alterations of the plasma cells are seen: Russell bodies, Mott cells and numerous necrobiotic plasma cells occur. This latter finding explains the deposits of interstitial Ig (Gebbers and Otto, 1976).

Close topographical relationships of lymphocytes and macrophages occur; both cell types appear activated. Lymphocytes and plasma cells are clustered around activated macrophages. This may be the morphological expression of a functional involvement of macrophages in the local B-cell response, as macrophages are able to induce immunological processes (Nelson, 1976). The number

of interepithelial lymphocytes is increased in UC; they are frequently found to be activated. The surface membranes of the adjacent epithelial cells show an intensive folding, which may be an indication of a rapid intrusion of lymphocytes into the lamina epithelialis mucosae. The perilymphocytic space is characterized by distinct staining with ruthenium red.

Depending on the activity of the disease infiltrates of granulocytes in the surface epithelium can be demonstrated, notably in cases with an acute relapse. Often groups of two to four granulocytes are lying within small cavities in the epithelium. At the site of these "micro abscesses" IgG and complement can be demonstrated (Figs. 1 and 2).

Discussion: These observations suggest a cellular and humoral immune reaction and could be discussed in terms of a local immunopathogenesis in UC. In particular, the findings of a locally increased production of IgG with intercellular deposits and demonstration of activated complement (C3) in the tissue is of immense interest. IgG antibodies, IgG-antigen-complexes and antibodies complexed to target cells are able to induce cytotoxic activities in "nonspecific" lymphocytes by interaction with membrane receptors through the Fc portion or through activated complement (C3). In addition, IgG-antigen-complexes are effective complement activators, and lead to local immune complex disease (for discussion see: Brandtzaeg and Baklien, 1976; Gebbers and Otto, 1977; Otto et al., 1976).

Conclusions: These findings provide more evidence for the suggestion that immune complexes occur *locally* in UC and play, at least in part, an important role in the pathogenesis of UC. We think that we are approaching an answer for the provocative question of W.R. Thayer (1976): "Are the inflammatory bowel diseases immune complex diseases?"

The authors are indebted to Prof. Dr. K. Müller-Wieland, 1. Medical Dept., University of Hamburg, for gaining the biopsies, and we gratefully acknowledge the technical assistance of Miss C. Schürmann and the undertaking of the additional printing expenses of the coloured figures by Deutsche Pharmacia GmbH, Freiburg.

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Received January 22, 1977