Allergy 1981, 36, 435–436

Short Communication

Possible Role of Histamine in Rheumatoid Arthritis

Treatment with Cimetidine and Mepyramine

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Basophilocytes from patients with rheumatoid arthritis (RA) responded to leukocyte nuclei from normal persons with histamine release; a similar histamine release induced by the nuclear components RNA and DNA has been demonstrated previously. A role of histamine in RA is also supported by the findings of clinical improvement during treatment with H_1 and H_2 antihistamines in six of 12 patients with RA in active phase, whereas four showed definite deterioration.

Key words: antihistamines; basophilocytes; cimetidine; histamine release; leukocyte nuclei; mepyramine; rheumatoid arthritis.

Accepted for publication 19 August 1981

Some observations indicate a possible role of histamine in rheumatoid arthritis (RA). We investigated 12 patients (10 female and 2 male), age 18–64 years (mean 48 years) with classical RA (6). All the patients had active disease. Blood leukocytes with approximately 2% basophilocytes isolated by the Ficoll-Hypaque gradient method (7) were incubated in the absence of serum at 37°C for 40 min with sonicates of leukocyte nuclei from normal non-atopic persons. In contrast to normal individuals, cells from RA patients responded to human leukocyte nuclei with histamine release. Thus, the RA patients showed a percentage of histamine release of 18.4 ± 2.9 (SD) in contrast to 4.9 ± 4.1 in the age- and sex-matched controls. A similar release of histamine was previously demonstrated in our laboratory, when cells from patients with RA of moderate and severe activity were exposed to the nuclear constituents RNA and DNA (4). In the allergic type I reaction, antigen reacts with antibody bound to mast cells and basophilocytes, and this interaction, which does not activate complement, leads to histamine release. The observations suggest an involvement in the pathogenesis of RA of an autoimmune type I reaction directed against normal nuclear components. This is supported by the finding of IgE-granulocyte-specific antinuclear antibodies in RA patients (5). Histamine and other inflammatory mediators released from mast cells and basophilocytes may therefore be contributory factors to the inflammatory reactions in RA. A role of histamine in active phases of RA is also supported by the associated finding of increased urinary excretion of the main histamine metabolite, 1-methyl-4-imidazole-acetic acid (2).

Antihistamines might therefore be a new approach in the treatment of RA. In dogs histamine-induced increase of synovial perfusion is abolished by blockade of vascular histamine H_2-receptors with H_2-antihistamines (3). Vascular H_2-receptor blockade might thus contri-

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Table 1

Treatment of rheumatoid arthritis with antihistamines

Duration of treatment		No. of patients	Clinical effect: Improvement	Clinical effect: Deterioration
Ci	1 month	4	1	1
	3 months			
Ci	1st month			
Ci + Me	2nd month	8	5	3
Ci	3rd month			

Ci: cimetidine 1 g/day; Me: mepyramine 150–200 mg/day.

bute to a reduction of inflammatory reactions in RA patients. Modulation of a variety of leukocyte functions by altered stimulation of their surface H_2-receptors might result in pro- or antiinflammatory effects (1), and the dose of antihistamines might therefore be of importance for the clinical effect observed.

In an open study we followed the present RA patients during treatment with the H_2-antihistamine cimetidine, and the combination of cimetidine and mepyramine (see Table 1), while all other medication was kept constant. Clinical improvement was seen in half of the patients, especially with the combination of H_1- and H_2-antihistamines, but definite deterioration was seen in four patients, with relief during the first few days after cessation of treatment. These observations are still preliminary; however, it seems important to define which RA patients will benefit from treatment with antihistamines and which patients will deteriorate, and to determine the role of the dosages employed.

ACKNOWLEDGEMENTS

This study was supported by the following grants: Danish Medical Research Council (grant No. 12-2344), National Association against Rheumatic Diseases (grant No. 233–165), and Daell Fonden.

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