myosin genes in MF. Thus the action of trophic factors and spike activity of motor neurons evidently regulate synthesis of contractile proteins by independent mechanisms.

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MORPHOMETRIC AND IMMUNOHISTOCHEMICAL FEATURES OF THE GASTRIC AND DUODENAL MUCOSA IN SYSTEMIC LUPUS ERYTHEMATOSUS

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KEY WORDS: systemic lupus erythematosus; gastric and duodenal mucosa; morphometry; immunohistochemistry

The overwhelming number of publications devoted to the state of the gastrointestinal tract in systemic lupus erythematosus (SLE) in adults and children have been based on studies of autopsy material [1-3, 6, 7, 3]. The morphometric and immunohistochemical features of the gastric and duodenal mucosa in SLE have not yet been studied.

With this aim we undertook morphometric and immunohistochemical investigations of 108 biopsy specimens of mucosa from the body and antrum of the stomach, and the bulk and descending portions of the duodenum from 27 children with SLE. The disease in 17 children was categorized as the II degree of activity, whereas in 10 it was in the stage of remission. The comparison group consisted of 36 biopsy specimens of mucosa from the same parts of the stomach and duodenum from 12 children with exacerbation of chronic gastroduodenitis.

EXPERIMENTAL METHOD

The biopsy specimens of the mucosa were fixed in 10% neutral buffered formalin and embedded in paraffin wax. Sections were stained with hematoxylin and eosin. The PAS reaction revealed neutral glycosaminoglycans. Parameters character-

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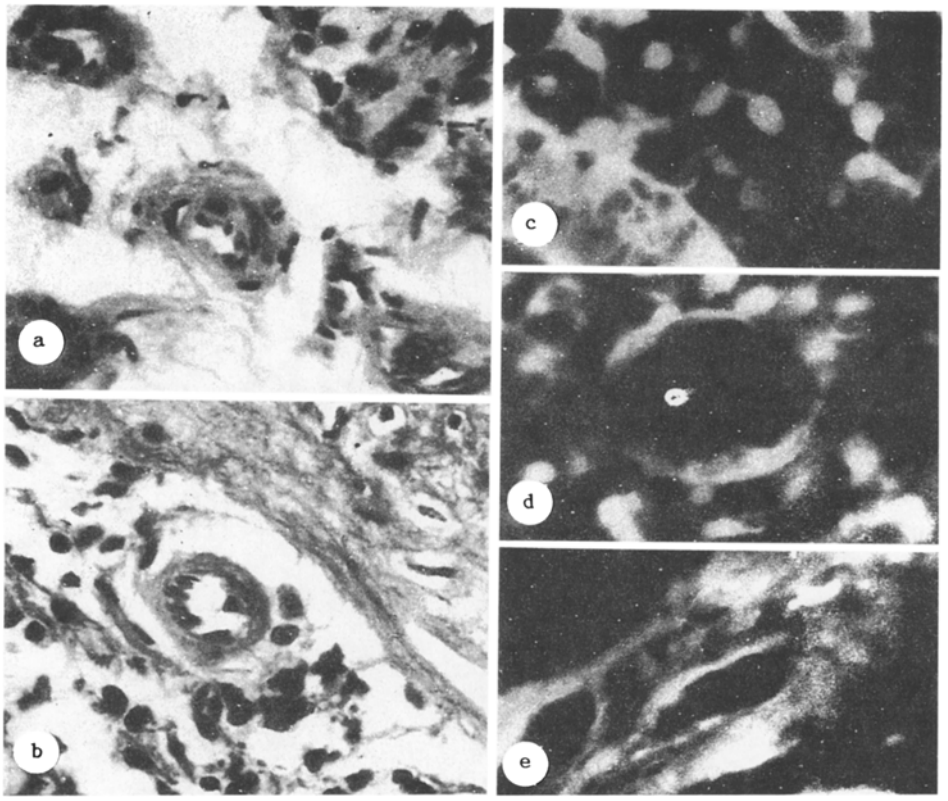

Fig. 1. Morphological changes in gastroduodenal mucosa in SLE. a) marked thickening of vascular wall and hypertrophy of endothelium of intima during exacerbation of disease. Hematoxylin and eosin, 320×; b) weakening of reaction of endothelium and decrease in thickness of vessel wall during clinical-laboratory remission. Hematoxylin and eosin, 320×; c) increase in number of IgG-producing cells during exacerbation. Direct immunofluorescence method, 720×; d) specific fluorescence of immune complexes of IgG in vessel wall during exacerbation. Direct immunofluorescence method, 720×; e) weakening of specific fluorescence of IgG during remission. Direct immunofluorescence method. 720×.

izing the state of the epitheliocytes and the degree and character of infiltration of the epithelium and of the lamina propria of the mucosa were determined by morphometric investigations. The number of cells producing immunoglobulins of classes IgA, IgM, and IgG per square millimeter of tissue [8] was determined in paraffin sections treated with 0.01% trypsin solution by a direct immunofluorescence method [5]. The level of IgA, IgM, and IgG and of circulating immune complexes in the blood was determined by radial immunodiffusion by Mancini's method. The experimental results were subjected to statistical analysis, differences being regarded as significant at the $p < 0.05$ level. Paired correlations between some parameters were identified.

EXPERIMENTAL RESULTS

In all ten biopsy specimens of the mucosa studied from children with a clinical or laboratory remission of SLE, chronic superficial fundal gastritis and stage I-II duodenitis were found, and in 8 cases chronic superficial antral gastritis was found with no signs of exacerbation (according to Whithead [10]).

In SLE with the II degree of activity, chronic superficial fundal gastritis without exacerbation was found in only three cases, and in all the rest it was accompanied by exacerbation. Chronic diffuse, in 12 cases, and superficial antral gastritis with exacerbation in 5 cases, were found in the mucosa of the gastric antrum. Investigation of the duodenal mucosa revealed chronic duodenitis of the II degree with exacerbation in all 17 cases. In 12 of them it was accompanied by marked hypertrophy of Brunner's glands. In all parts of the mucosa of the gastroduodenal zone, marked thickening of walls of the arterioles in the depth of the mucosa and marked hypertrophy of the endothelium were found (Fig. 1a). These changes were less marked and less frequent in the presence of a clinical laboratory remission (Fig. 1b).

TABLE 1. Morphometric Parameters of Lamina Propria of Mucosa in Antral Region of Stomach and of Duodenum in Children with SLE and Gastroduodenitis

Number/mm^2	Gastric antral mucosa			Duodenal mucosa		
	SLE (exacerbation; n = 17)	SLE (remission; n = 10)	gastroduodenitis (exacerbation; n = 12)	SLE (exacerbation; n = 17)	SLE (remission; n = 10)	gastroduodenitis (exacerbation; n = 12)
Cell density	11 755±569	10 151±832	14 857±1 256*	13 341±528	10 627±645**	20 026±1487*
	8 707±817	7 193±765	6294±470*	16 021±552	11 185±646**	26 364±2043*
Lymphocytes	3754±331	3214±116	5242±342*	4181±309	4032±248	6884±381*
	3031±348	2303±342	2469±195	5294±591	3526±308**	8036±422*
immature plasma	1216±167	729±133**	1441±160	2132±211	1498±305	2607±481
	220±47	71±49**	290±49	2158±383	1165±265**	5164±738*
mature plasma	1322±126	1005±135	1678±178	1758±175	1354±116	3067±201*
	506±114	382±205	422±69	2629±243	1826±186**	4980±395*
Macrophages	550±109	282±63**	193±75*	601±149	459±111	422±80
	191±72	132±68	132±38	560±108	206±81**	633±107
Fibroblasts	2005±248	2092±209	3460±222*	1691±193	1457±135	3529±321*
	2063±319	1825±262	1422±157	2181±246	2090±400	4189±369*
Fibrocytes	2775±215	2750±331	2732±164	2528±258	1641±380	3047±201
	2614±413	2468±413	1267±51*	2943±232	2253±344	3320±184
Eosinophilic granulocytes	123±46	69±58	119±15	208±71	186±127	421±60*
	73±45	12±9	32±6	233±90	118±76	606±106*
Neutrophilic granulocytes	12±6	10±11	15±15	43±24	0±0	221±40*
	9±9	0±0	0±0	23±18	0±0	185±26*
IgA	848±109	630±87	1193±96*	927±84	931±36	1216±97*
IgM	612±63	402±52**	684±69	704±63	573±52	946±109
IgG	605±70	273±37**	131±21*	533±74	302±17**	163±35*

Legend. Top line denotes superficial part and villi; bottom line shows deep part and intercryptal space. *p < 0.05, SLE (exacerbation) and gastroduodenitis; **p < 0.05, SLE in exacerbation and remission.

Analysis of the morphometric data showed that the principal statistically significant differences between the clinical-laboratory remission group and the group with II degree of activity of SLE were observed in the mucosa of the antrum of the stomach and of the duodenum.

For instance, during exacerbation of SLE more than during its remission, the lamina propria of the antral mucosa of the stomach was infiltrated, and among the infiltrating cells there were more macrophages and immature plasma cells (Table 1). Compared with the control group, in the area of inflammatory infiltration of the deep part of the mucosa, young and mature fibroblasts were more numerous. A characteristic feature of SLE was a change in the ratio between young and mature fibroblasts, with predominance of adult forms of these cells, whereas in children with both an unchanged mucosa and with chronic inflammation, young fibroblasts always predominated (Table 1). In our investigations on children in the comparison group the ratio of young to mature fibroblasts exceeded unity (1.27), in SLE in the exacerbation phase it was 0.72, and during a remission 0.66. Correlations of these cells varied depending on the phase of the disease: in the exacerbation period correlation was close (R_0 = 0.60), whereas during a remission it weakened to 0.46.

In the duodenal Mucosa the cell density of the infiltrating tissue in the lamina propria, which contained more lymphocytes, plasma cells, and macrophages, was more marked in the exacerbation phase than during remission. However, these features of inflammation, as well as the degree of infiltration of the epithelium by lymphocytes and neutrophilic infiltration of the lamina propria, were less marked during exacerbation than in the comparison group. The ratio of young and mature fibroblasts in the duodenal mucosa also varied, with predominance of mature forms, as a result of which the ratio between young and mature fibroblasts was under unity (0.67 for exacerbation and 0.89 for remission).

The IgA and IgM levels in the blood serum were statistically significantly higher in the blood serum that normally [2] (1.42 ± 0.03 and 1.07 ± 0.03 g/liter) in the period of exacerbation of SLE, reaching 2.22 ± 0.31 and 1.76 ± 0.12 g/liter respectively. In the convalescence period, compared with the exacerbation period, the IgM level was statistically significantly lower, whereas the IgA level remained high. The level of circulating immune complexes was statistically significantly higher both during exacerbation and during remission, amounting to 0.174 ± 0.02 and 0.163 ± 0.02 unit respectively, compared with the normal value of 0.09 ± 0.006 unit. Meanwhile, immunohistochemical investigation of biopsy specimens of the mucosa showed that, during both exacerbation and remission, the number of cells producing immunoglobulins of all three classes was increased. A sharp increase in the number of cells producing IgG was unusual, and could reach 25% of the total number of cells producing

immunoglobulins (Fig. 1c). The number of IgG cells in the unchanged mucosa and in the mucosa in chronic gastroduodenitis usually do not exceed 10%.

In the exacerbation phase immune complexes belonging mainly to IgG, and to a lesser degree to IgM, were discovered in the walls of the blood vessels in the deep zones of the lamina propria (Fig. 1d). In the remission phase specific fluorescence of the vessels was reduced (Fig. 1e), whereas the level of circulating immune complexes in the blood serum was reduced, although these differences were not statistically significant.

The histological, morphometric, and immunohistochemical investigations of biopsy material for the gastric and duodenal mucosa thus show that the level of inflammatory changes in the gastric and duodenal mucosa is related to the degree of activity of SLE. The severity of the inflammation and involvement of the local immune system are significantly less during SLE than in chronic gastroduodenitis, and do not correlate with SLE, a fact which can be explained by therapeutic procedures [4]. There is no doubt about the involvement of fibroplastic processes in the changes in the mucosa. Deposition of the immune complexes in the wall of the vessels aggravates the changes in the mucosa. The unusually high local IgG production may perhaps arise as a result of structural changes in the vessels and may create a local immunodeficiency, for IgG are not protected by a secretory component, unlike the principal immunoglobulins of the mucosa — IgA and IgM. Changes in the serum immunoglobulin levels do not correlate with local immunoglobulin production.

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