Acta Dermatovener (Stockholm) 53: 35–38, 1973

LEUKOCYTE MIGRATION TEST IN RECURRENT ERYSIPELAS

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Abstract. Cellular immunity has been studied by the leukocyte migration test in acute and recurrent forms of erysipelas. Streptolysin-O added to leukocyte cultures did not inhibit migration in 21 of 25 relapsing cases, but did so in the remaining 4 cases and in all 13 cases of acute erysipelas as well. It appears that in the majority of cases with recurrent erysipelas there is no cellular hypersensitivity to Streptolysin-O. The probable circumstances of the reappearance of recurrent erysipelas are discussed in the light of these findings and data from the literature.

Some patients are known to recover completely from acute erysipelas, while others have relapses and clinical findings cannot account for the true causes of recurrences. Rajka et al. (17) and Korossy et al. (13) have postulated on the basis of clinical observation, circulating antibody titre measurements, bacteriological examinations and skin tests that the frequent reappearance of the disease may be due to a partial defect of delayed-type immune reactions.

Thor, Søborg & Bendixen have demonstrated specific inhibition of capillary tube migration of sensitized human lymph node cells and peripheral blood leukocytes by antigens inducing the delayed-type of hypersensitivity. With this method, further investigations succeeded in proving the existence of cellular hypersensitivity with the help of various bacterial antigens—such as Streptolysin-O—chemical materials and in certain autoimmune diseases with that of proper tissue extracts (1, 2, 7, 8, 10, 15, 24, 25, 27).

METHODS

The leukocyte migration test was carried out as previously described (10). Serum-containing leukocytes and erythrocytes were separated from citrated blood by sedimentation. The leukocyte-containing serum was centrifuged, and after the cell sediment had been washed in Parker 199 medium, it was withdrawn into a capillary tube. Four of these cultures were prepared parallel from each sample. To two cultures 0.2 IU/ml Streptolysin-O (Humán, Budapest) was added (10), the other two served as controls. Migration of cells from the capillary tube was assessed by planimetry after culturing in Parker 199 medium for 24 hours. A migration index, corresponding with the quotient of migration figures for antigen-containing and control cultures, was used to express the effect of Streptolysin-O.

The anti-streptolysin titre (AST) was determined by the method by Böszörményi (4).

Patients

The leukocyte migration test was carried out in the cases of 25 patients with recurrent erysipelas; the number of relapses varied from 2 to 20 and in every case the lower extremity was affected. Thirteen patients—2 with facial, 11 with crural erysipelas—having the disease for the first time, have been examined; in this group the tests were always carried out during the manifestation of the acute symptoms.

RESULTS

In 21 of the 25 cases with recurrent erysipelas Streptolysin-O had no significant influence on leukocyte migration: the migration index varied between 0.7–1.3, irrespective of the AST-values (Table I). In the remaining 4 cases the Streptolysin-O did inhibit leukocyte migration, but the clinical symptoms, laboratory tests and number of relapses were similar to those of the former group.

In every case, the Streptolysin-O inhibited cell migration in leukocyte cultures of patients with acute erysipelas and the migration index never exceeded 0.4. In this group, too, the migration index and AST value were conspicuously unrelated (Table I).

Table 1. *Effect of streptolysin-O on leukocyte migration of patients with acute and recurrent erysipelas*

No.	Diagnosis	Migration index	AST	Acute symptomes at the time of examination	No. of rec.
1	Erysipelas rec.	0.9	3 733	−	3
2	Erysipelas rec.	0.7	1 920	−	6
3	Erysipelas rec.	1.1	1 920	+	20
4	Erysipelas rec.	1.3	1 344	−	5
5	Erysipelas rec.	1.2	1 344	−	15
6	Erysipelas rec.	1.3	1 120	−	20
7	Erysipelas rec.	1.0	1 120	+	20
8	Erysipelas rec.	1.0	960	−	9
9	Erysipelas rec.	1.2	800	−	2
10	Erysipelas rec.	1.1	800	−	4
11	Erysipelas rec.	0.02	672	+	2
12	Erysipelas rec.	1.2	480	+	5
13	Erysipelas rec.	1.3	480	−	2
14	Erysipelas rec.	0.06	400	+	11
15	Erysipelas rec.	1.0	400	−	6
16	Erysipelas rec.	1.0	400	−	9
17	Erysipelas rec.	0.43	400	−	3
18	Erysipelas rec.	0.02	400	+	3
19	Erysipelas rec.	0.8	336	−	2
20	Erysipelas rec.	1.2	336	−	2
21	Erysipelas rec.	1.0	286	−	5
22	Erysipelas rec.	0.9	286	+	2
23	Erysipelas rec.	0.9	286	+	2
24	Erysipelas rec.	1.3	170	+	3
25	Erysipelas rec.	1.0	120	+	2
1	Erysipelas ac.	0.08	1 920	+	—
2	Erysipelas ac.	0.01	1 120	+	—
3	Erysipelas ac.	0.28	672	+	—
4	Erysipelas ac.	0.01	570	+	—
5	Erysipelas ac.	0.35	480	+	—
6	Erysipelas ac.	0.15	480	+	—
7	Erysipelas ac.	0.01	480	+	—
8	Erysipelas ac.	0.20	466	+	—
9	Erysipelas ac.	0.40	400	+	—
10	Erysipelas ac.	0.40	336	+	—
11	Erysipelas ac.	0.22	143	+	—
12	Erysipelas ac.	0.12	n.i.	+	—
13	Erysipelas ac.	0.10	n.i.	+	—

n.i. = not investigated.

DISCUSSION

Many investigators have been searching for the cause of relapses in erysipelas. Histologically, lymphangitis, endolymphangitis and perilymphangitis were found in the dermis and subcutis, especially if there was oedema too (16, 18, 23, 26). Histochemically, the mitochondrial enzyme activity and ATP-ase activity were found to have increased in endothelial cells of lymph vessels (22) and electron-microscopically cystic bodies, mitochondrial swelling and, in lymphangiectasia, partial opening of the interendothelial junctions could be seen (21). Kaindl demonstrated by lymphography a complete obliteration of lymph vessels in all cases of erysipelas (11, 12), whereas Thury et al. (28) observed intact lymph vessels or radiological signs of varicosity and recovery of lymphangitis. We suggest that both the morphological and radiological changes are secondary, being consequences rather than causes of the recurrent inflammation.

Apart from pathological investigations, many authors have chosen the immunological approach to the problem of relapse in erysipelas. Busila et al. observed hypogammaglobulinaemia and, in some cases, even the absence of certain immunoglobulin fractions of recurrent erysipelas (6). Schneider et al., however, failed to demonstrate

any notable alteration of immunoglobulin fractions by titration immunelectrophoresis (20). On the other hand, increase of certain serum glycoprotein fractions could be observed in most of the cases like that of other chronic inflammations. Like Brandao (5) and Korossy et al. (14), we also found the AST value to be increased. Our previous studies by means of lymphocyte transformation tests using different streptococcus antigens failed to disclose immunological alterations of such an extent as could be held responsible for the relapses (19).

The present investigation has shown that Streptolysin-O inhibits the migration of the leukocytes of patients with acute erysipelas (Table I) to the same high degree as it did in certain non-streptococcal diseases studied earlier (10). But in 21 of 25 cases of recurrent erysipelas, the same antigen did not significantly suppress cell proliferation; migration indexes varied between 0.7–1.3 (Table I), suggesting that no cellular hypersensitivity to Streptolysin-O could be observed in recurrent erysipelas.

The toxic effect of Streptolysin-O on macrophage cultures is well-known, though in our opinion it is not the toxic effect of the antigen that inhibits the cell migration of patients with acute erysipelas as it has only a very slight influence on leukocyte migration of patients with recurrent erysipelas.

The results of the leukocyte migration tests being in coincidence with those of clinical investigations of Rajka et al. (17) and Korossy et al. (13) indicate that patients with recurrent erysipelas have a partial cellular immune defect to streptococcal antigens. It is suggested that the reduction of the immune reactivity together with the known localizing factors (macro- and microtraumata, interdigital mycosis, aplasia or hyperplasia of lymph vessels, lymph stasis, lymph vessel changes establishing during the acute stage, local persistence of bacteria (3, 9), scars, etc.) form the milieu that can be held responsible for the frequent relapses.

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Received May 23, 1972

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