OBSERVATION OF IMMUNOLOGICAL CHANGES DURING CLINICAL CYCLES OF SKIN LEISHMANIOSIS

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Abstract: In this article, statistics were obtained from patients with cutaneous leishmaniasis, with particular emphasis on the specific course of clinical cycles and immunological changes. Immunological changes showed a decrease in lymphocytes, a significant increase in IgA, IgM, IgG and CIC. These indicators help patients choose the right treatment.

Keywords: Leishmaniasis, IgM, IgG, Lymphadenitis, parasites, viscerotropic.

INTRODUCTION

Relevance

Leishmaniasis is a tropical anthropozoonosis caused by protozoan parasites of the genus Leishmania, which are both viscerotropic and dermotropic. The infection has a wide clinical spectrum, ranging from cosmetically disfiguring cutaneous and mucosal variants to devastating and fatal visceral forms [1]. Cutaneous leishmaniasis (CL) is the most common type, with a global prevalence of about 12 million cases and an annual incidence of 0.6-1 million cases. The prevalence of the disease is highest in Central and South America, Southern Europe, Central Africa and parts of South and Central Asia [2]. The zoonotic form of cutaneous leishmaniasis (CL) in recent years is most often observed in Turkmenistan and Uzbekistan [3,4]. In recent years, CL has become much more common in the republic, mainly in areas bordering Afghanistan and Uzbekistan. More than 20 Leishmania species have been involved in the etiology of the disease; they are divided into two groups: old world species such as L. major, L. infantum and L. tropica, and new world species such as L. amazonensis, L. mexicana, L. panamensis, L. braziliensis and L. Guyanensis [5.6]. Among the species of the Old World, L. tropica (urban / dry type) and L. major (rural / wet type) predominate. Infected female sand flies of the genus Flebotomus act as carriers of the disease in old world leishmaniasis, while females of the genera Lutzomyia and Psychodopygus are carriers of new world leishmaniasis [7,8]. In recent years, experimental studies [9,10,11] have established an important role of cellular factors in the development of post-infectious immunity in CL. The addition of secondary infection and incomplete scarring is a complication of cutaneous leishmaniasis [12]. In the literature there are isolated works, mainly by researchers from far abroad, on the study of the state of indicators of cellular and humoral immunity in patients with CL [13, 14], the results of which are contradictory. To assess the state of cytokine indices in patients with cutaneous leishmaniasis, we studied the indices of the anti-inflammatory cytokine IL-4 and the pro-inflammatory cytokine IL-8 and TNF-α, as well as gamma-interferons. In this pathology, these cytokines are more affected by changes than other cytokines, and the quantitative determination of their level is of great importance in assessing the immune status of the organism [15].

Purpose of the study

Observation of immunological changes depending on the clinical signs of rural cutaneous leishmaniasis.

Material and research methods

70 patients with a rural form of CL were under observation, including 26 (37.1%) men and 54 (62.9%) women (ratio 1:2.5). The age of the patients ranged from 16 to 50 years or more. As can be seen, adults of all age groups suffer from acute necrotizing CL, the largest number of patients were aged 21-30 years – 18 (25.7%) and 16-20 years – 15 (21.4%), the smallest – aged over 50 years– 10 (14.3%). All patients were residents of border areas of rural areas. Among the male agricultural workers there were 5 people, students – 7, non-working-8. The contingent of sick women: housewives – 46, students-3, teacher-1. Most of the patients sought medical help in the fall and summer, less often in winter. In August, 33 (47%) patients were treated, in September-October– 28 (40%), in November-December – 9 (13%). The incubation period ranged from 5-7 days to 2 months (in most cases 2-3 weeks).

The duration of the disease ranged from 2 weeks to 3 months or more. The clinic of the disease in all patients was characterized by the presence of ulcers on the surface of the skin. In 35 (50%) patients, the lesions were localized in open areas of the body (face, neck, upper chest, arms, back of the foot), in 21(30%) – in closed areas, in 14(25%) – in closed and open areas.

The number of ulcers ranged from 1 to 12.Figure 3 shows that 31.3% (22) of patients had 1 ulcer, 28.7% (20) – 2-3, 18.8% (13) – 4-6, 16.3% (11) – 7-9, 5% (4) – from 10 to 12. The size of the ulcers ranged from 1x1 cm to 10x11 cm. Single ulcers, as a rule, in most cases were larger than multiple ulcers. In most patients, the ulcers were rounded or oval, in some – irregular. The ulcers had steep, covered, scalloped, sometimes even edges, in some patients the edges hung over the bottom of the ulcer, forming pockets. Around the ulcers, most patients had a wide area of infiltrate with inflammatory edema. In some patients, the infiltrate was quite pronounced, rising above the ulcer in the form of a roller, which, as it moved away from the ulcer, gradually became flat, aligning with the skin. In patients with relatively fresh ulcers, the bottom was covered with necrotic masses. In patients with ulcers for more than 4-5 weeks, the bottom of the ulcers was gradually cleared of necrotic layers, grew in granulations in the form of papillae. The papillae were covered with a whitish coating, and when pressed, a serous-purulent fluid was released. In patients with a disease duration of more than 2 months, the ulcers, almost completely cleared of necrotic masses, were covered with islands of granulations like pomegranate seeds. In some patients, granulations covered the entire bottom of the ulcer. The infiltration around the ulcers gradually decreased.In 24 patients, the leishmaniasis process was accompanied by complications in the form of lymphangiitis, in 11 of them, lymphadenitis was also observed. In all patients, immunological studies were conducted to determine the state of the main indicators of cellular and humoral immunity. Quantitative content of total immunoglobulins A, M and G in blood serum – by the enzyme immunoassay, circulating immune complexes – CIC) - by the method of polyethylene glycol precipitation according to Yu.A. Grinevich and A. I. Alferov (1981). The control group consisted of 25 healthy individuals aged 16 to 50 years. The age and gender of the patients and the control group were comparable. Statistical processing was performed using the application program "Statistica 6.0". The paper studied quantitative indicators, which were presented in the form of an average value and a statistical error. The differences were considered statistically significant at $p<0.05$.

Results and discussion

As can be seen from the above data, in patients with CL compared with healthy people, there is an inhibition of the activity of the cellular link of immunity, a tendency to reduce the absolute and relative number of lymphocytes (by 10%) of peripheral blood.

Indicators	Control No. 25	Patients No. 70	**p**
Lymphocytes %	29,9±1,8	26,1±1,4	< 0,05
IgA g/l	2,08±0,15	2,35±0,18	< 0,05
IgM g/l	1,56±0,14	2,45±0,16	< 0,001
IgG g/l	10,8±0,9	14,9±1,1	< 0,001
CIC g/l	1,89±0,15	2,75±0,14	< 0,001

Note: p is the statistical significance of the differences between the groups (according to the Mann Whitney U-test).

On the part of the indicators of humoral immunity, an increase in its activity was revealed, which was determined by an increase in the content of immunoglobulins M and G in the blood serum (1.5 and 1.3 times, respectively, by 47% and 33%), the IgM level in 35 (50%) patients with CL was higher than in healthy people, in 24 (34.3%) – within the normal range, in 11 (15.7%) - below the norm. The content of serum IgG in 28 (40%) patients was higher than in the control group, in 25 (35.7%) – corresponded to normal values, in 17 (24.3%) – was reduced. There were clear violations on the part of circulating immune complexes (CIC), the content of which in patients with CL was 1.5 times higher (by 47%) than in healthy people. An increase in the CEC content was observed in 31 (44.3%) patients, a decrease – in 15 (21.4%), within the normal range – in 24 (34.3%).

The activity of immunological parameters in patients with CL depended on the duration of the leishmaniasis process. In patients with the duration of the ulcerative stage of the disease up to 1.5-2 months (the period of disease progression), compared with healthy people, there were profound changes in the cellular immunity. With an increase in the duration of the ulcerative stage of the disease over 2 months, when the vast majority of patients began the process of reverse development of leishmanioma, characterized by a gradual cleansing of the bottom of the ulcers from necrotic masses, there was a positive trend from immunological disorders, which was expressed, first of all, in an increase in the activity of the cellular immunity suppressed during the height of the disease. During the progression of clinical symptoms of cutaneous leishmaniasis, the high activity of humoral immune system during the reverse development of the ulcerative stage of leishmaniasis begins to decrease, as evidenced by the normalization of serum IgG levels (14.9±1.1 g / l, $p>0.05$) and the tendency to normalize the increased IgM and CEC levels, but their concentration continued to exceed normal values ($p<0.05$). The severity of the degree of suppression of the activity of the cellular department of immunity and an increase in the activity of the humoral during the height of the ulcerative stage of leishmaniomas compared with the period of their reverse development is indicated by significantly high IgM (2.67±0.15 g/l $p<0.05$) and CEC (3.02±0.17 g/l and 2.46±0.17 g/l, $p<0.05$) in patients during the progression of the ulcerative stage compared with the data of patients who are in the period of gradual improvement of the pathological process. We compared the state of the main immunological parameters in patients with CL with complications (presence of lymphangiitis, 23 patients) and without them (47 patients). Studies have shown that in patients with CL, whose infectious process proceeds without complications, immunological disorders on the part of the cellular department of immunity were determined by an increase in the activity of the humoral department of immunity was confirmed by an increase in the serum content of IgM (2.23±0.16 g/l, $p<0.05$), CEC (2.64±0.20 g/l, $p<0.05$), a tendency to increase the amount of IgG. More profound

immunological disorders were found among patients whose disease was complicated by lymphangiitis, in some patients (11 people) and lymphadenitis. Their content of all 3 main indicators of cellular immunity was high, the activity of the humoral immunity was high, as evidenced by an increase in IgM content by 68% (2.79±0.17 g/l, p<0.001), IgG – by 62% (17.9±1.4 g/l, p<0.01), CEC – by 69% (3.19±0.19 g/l and 2.53±0.19 g/l, p<0.001). When comparing the immunological parameters in patients with CL of different age groups with single and multiple leishmaniomas, as well as between men and women, no changes were found (the differences are not statistically significant).

Conclusion

Thus, studies have shown that patients with cutaneous leishmaniasis had immunological disorders from both the cellular and humoral parts of the immune system, which depended on the duration of the process and the presence of complications.

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