

Research Article

The Prognostic Value of the Change in the Concentration of C–Reactive Protein in the Oral Liquid of Patients with Acantholytic Pemphigus, in Varying Degrees of the Acantholytic Process Severity on the Mucous Membrane of the Oral Cavity

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Abstract

The interconnection of changes in the concentration of C-reactive protein with the severity degree of the acantholytic process on the mucous membrane of the oral cavity in patients suffering from acantholytic pemphigus is described in the article.

Objective of the study – is to determine the correlation between the concentration of C-reactive protein in the oral liquid of patients with acantholytic pemphigus with the severity degree of the acantholytic process during the period of exacerbation of the disease in order to predict the assessment of general and local therapy, as well as the dynamics of the course of pathological processes on the oral mucous membrane.

Materials and methods. A complex of studies was performed in patients with acantholytic pemphigus, aged from 45 to 63 years, which included oral liquid examination in order to determine the CRP level, and determination of the acantholytic process severity degree on the mucous membrane of the oral cavity (utility model patent #101844).

Results and discussion. There was a clear correlation between the level of CRP concentration in the oral liquid of patients with acantholytic pemphigus with the severity degree of acantholytic process on the mucous membrane of the oral cavity, during different periods of the disease exacerbation. During the first day of exacerbation, the level of CRP was 384 (mg/ml), or higher in 41 individuals, with the third (III) severity degree of the acantholytic process on the mucous membrane of the oral cavity, which was a 73.21% of the total number of examined patients. During the 7th day, the CRP concentration level decreased to values of ≥ 24 and ≥ 48 (mg/ml), and during the 14th day – to the values of ≥ 12 and ≥ 24 (mg/ml).

Conclusions. The obtained results showed that the change in the concentration of CRP in the oral liquid of patients with acantholytic pemphigus has a reliable prognostic value and is an important characteristic of local and general diagnostic parameters of the disease.

Keywords

acantholytic pemphigus; diagnostics; C-reactive protein; acantholysis; severity degree

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Problem statement and analysis of the latest research

Acantholytic pemphigus – is a group of diseases with the damage of the skin and mucous membrane that have a malignant course. Treatment of patients with pemphigus is one of the most difficult problems of dermatology. Mortality during the first 2 years from the onset of the disease reaches 30% [1]. Without the use of glucocorticosteroid medicines, death in these terms is virtually inevitable. Remissions are unstable; even while performance of the permanent maintenance therapy with glucocorticosteroid medicines.

Damage of the mucous membrane may be the only symptom of the disease for a long time from 1 month to 2-3 years.

Most lesions are localized on the soft palate, in the retro-molar area of the cheeks, at the bottom of the oral cavity, in the lips, gums (desquamative gingivitis) and throat [6]. Acantholytic process on the mucous membrane of the oral cavity (MMOC) can cause the emergence of a distant symptom of Nikolsky (detachment of the superficial layers of the epithelium with the formation of erosions) due to the mechanical influence of the prosthetic base on the tissues of the prosthetic bed. This, in turn, prevents the use of removable denture structures during the period of exacerbation of bullous dermatoses [4].

The acantholytic process of various degrees of severity depends on the duration of the disease and on the intensity of glucocorticoid therapy. An increase of the severity of the acantholytic process on MMOC requires an increase of the

daily dose of glucocorticosteroids. And an increase of the daily dose of hormonal medicines, will negatively affect the condition of the tissues of the prosthetic bed and periodontium in particular. That is why timely diagnosis and monitoring of laboratory parameters are important in the careful administration of medicines and, partially, the replacement of them with external means, as well as the use of various methods of local therapy of lesions of MMOC, to regulate the severity of the acantholytic process.

C-reactive protein (CRP) refers to the so-called acute-phase proteins, a sensitive indicator of tissue damage in necrosis, inflammation, and trauma. CRP, linked to a complex with phosphatidylcholine molecules on the surface of many bacteria, is a potent opsonin for monocytes, stimulating the digestion of the involved organisms, and also takes part in the interaction of T- and B-lymphocytes, activates the classical complement pathway [6, 7]. This nonspecific protein is synthesized mainly in the liver and is available in many biological fluids (pleural, peritoneal, pericardial, synovial, oral). Data on the level of CRP can be interpreted as an indicator of the dynamics of treatment of autoimmune diseases. [2] Taking into account the general biological function of CRP, it should be considered logical detection of this protein directly in the "foci of the damage" [3]. Taking into consideration the direction of the work, we decided to measure the content of CRP directly in the oral liquid of patients with acantholytic pemphigus, as the content of CRP in blood serum can be "masked" due to the administration of significant doses of glucocorticosteroids (GCS) during the period of exacerbation of the disease and the presence of significant traumatic tissue damage of MMOC due to the acantholytic changes.

1. Materials and Methods

In the course of study, there were examined 56 patients with acantholytic pemphigus aged from 45 to 63 years who were using removable dentures. The complex of examination, which included the oral liquid sampling for determination of the level of CRP and the determination of the severity of the acantholytic process at the MMOC (utility model patent #101844), was performed for three times during the period of acantholytic pemphigus, and its manifestations on the mucous membrane: during the 1st, 7th, 14th days.

The content of C-reactive protein in the oral liquid was determined using the Express-Test to determine the level of CRP.

he method is as follows: in each of 10 test-tubes, 0.1 ml of physiological saline was added. Into the test-tube #1, 0.1 ml of oral fluid was added. The dilution in this test-tube was 1:1 and the CRP concentration was ≤ 6 mg/ml. 0.1 ml of solution was poured into a test-tube #2 from the test-tube #1 using pipette, thus changing the dilution to 1:2 and the concentration of CRP = 12 mg/ml. Similarly, 0.1 ml of solution from test-tube #2 was transferred to a test-tube #3, with a change in the CRP concentration to 24 mg/ml, etc. The concentration of CRP (mg/ml) was determined according to the Table 1. Then from



Figure 1. Express-Test to determine the level of CRP

each of 10 test-tubes, 0.1 ml of solution was collected and dripped on a slide circle. Also, 0.1 ml of "CRP-Reagent" was added to this. Reagents were mixed with spatula and we observed, at which of the last dilutions the process of precipitation began. This value corresponds to the value of CRP of the oral fluid.

Table 1

Dilution	1:1	1:2	1:4	1:8	1:16	1:32	1:64
Oral liquid, ml	0.1	-	-	-	-	-	-
Diluent, or normal saline, ml	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Concentration of CRP (mg/ml) in a sample	6	12	24	48	96	192	384

Detection and determination of the degree of severity of the acantholytic process on the mucous membrane of the oral cavity in patients with acantholytic pemphigus according to the method offered by us.

The essence of the method is to determine the distant symptom of Nikolsky turn-by-turn using working surfaces of spatulas from the first to the third ones, the working surfaces of which have different relief. The working part of the spatula #1 has a smooth working surface; spatula #2 – has a hilly relief of the working surface, spatula #3 – has a slightly sharpened, most aggressive relief. With the appearance of a positive symptom after irritation with spatula #1, we offered



Figure 2. A set of spatulas to determine the degree severity of the Nikolsky symptom

to consider the severity of the acantholytic process as severe or the third (III) one. If there is no epithelial detachment in the irritation with spatula #1, we used the spatula #2. In a positive symptom in this case, we offer to consider the acantholytic process as the process of moderate severity or the second (II) one. If the violation of the epithelium integrity is not observed while using spatula #2, the spatula #3, with the most aggressive working surface, was used. In a positive symptom in this case, the degree of severity of the acantholytic process should be taken as mild or first (I) one.

If the distant symptom of Nikolsky was negative in all three cases, we noted the absence of acantholytic process in patients currently in the course of the disease. For the accuracy of the study results, the symptom is determined in various areas of MMOC.

2. Results and Discussion

Having analyzed the results of the study, the following data were obtained. According to the express-test of CRP concentration, and the definition of the severity of acantholytic process in patients with acantholytic pemphigus, during the first day of exacerbation, the CRP level was 384 (mg/ml) or higher in 41 patients, with the third (III) degree of acantholytic process at MMOC, which was 73.21% of the total number of the studied persons. Other values of the CRP concentration relative to the degree of acantholytic process are shown in the Table 2.

Table 2

Amount of patients		CRP concentration (\geq)					
		12	24	48	96	192	384
Degrees of acantholysis severity	I	-	-	-	-	-	-
	II	-	-	2	3	4	2
	III	-	-	-	-	4	41

The above-mentioned results clearly indicate a sharp increase of the values of CRP concentration in the oral fluid in patients during the first day of exacerbation of acantholytic pemphigus. The reason for this is the sharp deterioration of local traumatic status due to the complication of the acantholytic process at the MMOC. According to the data presented in the table, we can see that in some patients, the level of CRP 192 (mg/ml) was noted, which corresponded to the severity of the acantholytic process II and III. Due to the low number of such indicators, we can state the statistical insufficiency of such data, which may be caused by a number of reasons.

Indicators of the CRP concentration relative to the degree of severity of the acantholytic process during the 2nd and 14th days are given in Tables 3 and 4, respectively.

Table 3

Amount of patients		CRP concentration (\geq)					
		12	24	48	96	192	384
Degrees of acantholysis severity	I	-	-	6	-	5	-
	II	-	24	12	3	3	-
	III	-	-	-	1	2	-

Table 4

Amount of patients		CRP concentration (\geq)					
		12	24	48	96	192	384
Degrees of acantholysis severity	I	36	12	3	2	-	-
	II	-	-	2	1	-	-
	III	-	-	-	-	-	-

According to the above-mentioned results, we can see that during the 7th day, the level of CRP concentration is rapidly reduced to the values ≥ 24 and ≥ 48 (mg/ml), and during the 14th day to the values ≥ 12 and ≥ 24 (mg/ml). The degree of severity of the acantholytic process decreases more smoothly. During the 7th day, 75.00% of patients were diagnosed with the second (II) degree of severity, of them in 21.23% the level of CRP was ≥ 48 (mg/ml) and 42.85% ≥ 24 (mg/ml). During the 14th day, 85.71% of patients with acantholytic pemphigus were diagnosed the first (I) degree of acantholytic process severity, and a decrease of CRP concentration to ≥ 24 and 12 (mg/ml).

The relationship between the degree of severity of the acantholytic process and the level of CRP concentration according to the time intervals and statistical reliability are observed in the diagrams (Figures 3 and 4).

3. Conclusions

The obtained results showed that the change of the CRP concentration level in the oral liquid of patients with acantholytic pemphigus correlates with changes in the severity of acantholytic process at MMOC, which allows monitoring the

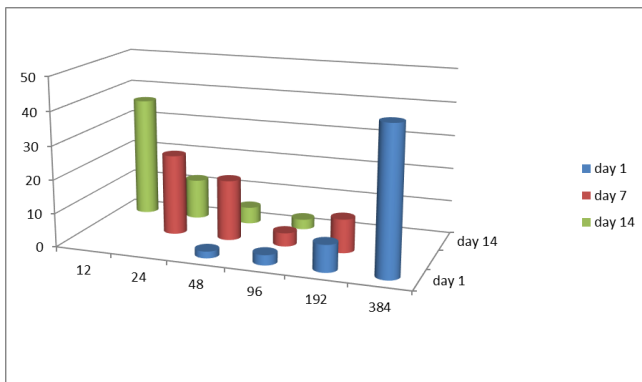


Figure 3. Changes in the level of CRP concentration

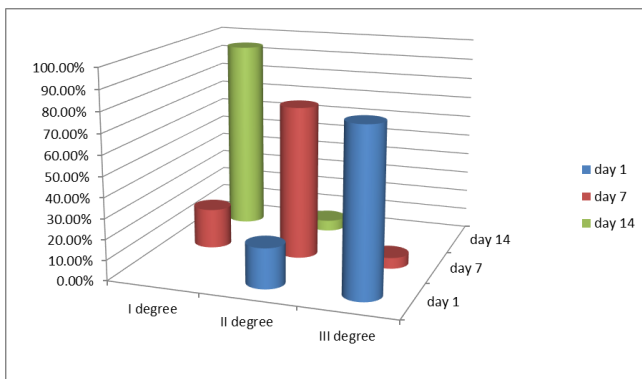


Figure 4. Changes of the severity degree of the acantholytic process at MMOC

efficacy of both systemic and local therapy of the disease by express-testing, which has an important prognostic value. Rapid reduction of CRP level is primarily due to GCS therapy, and indicates the rapid completion of the acute phase of the disease, with further stabilization of the process, and transition to the levels close to the norm. The degree of severity of the acantholytic process decreases gradually, due to the influence of the external factors on MMOC, which leads to the complications of epithelization of lesions. The rate of change in the degree of severity of the acantholytic process on MMOC is largely influenced by the local therapy of lesions, along with the correction of the algorithms of systemic treatment.

Reduction of the CRP level, without apparent reduction of the severity of acantholysis, indicates the "masking" of its concentration against the background of GCS therapy, rather than the positive dynamics of treatment. Therefore, it is important to have a comprehensive diagnosis of local and general diagnostic parameters.

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Received: 2018-10-9

Revised: 2018-11-30

Accepted: 2018-12-10