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IMMUNOHISTOCHEMICAL CHANGES IN REGIONAL LYMPH NODES IN THE PROCESS OF INFLAMMATION CHRONICITY

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Key words: inflammation; chronicity; immune reaction; lymph nodes

The immunohistochemical changes in regional lymph nodes in the acute infectious inflammation and in the process of inflammation chronicity, namely in the secondary chronic inflammation, primary chronic non-immune and primary chronic immune inflammation have been studied. The research was performed using 246 rats. Acute infectious inflammation was induced by introduction of Staphylococcus aureus daily culture containing 2 milliard microbial bodies in 1 ml of the isotonic solution of sodium chloride into the thigh. The secondary chronic inflammation was reproduced by subcutaneous introduction of 5ml of λ-carageenen in 1 ml of the isotonic solution of sodium chloride into the thigh. The primary chronic granulomatous inflammation was induced by introduction of sephadex A-25 in the dose of 1 mg in 1 ml of the isotonic solution of sodium chloride into the thigh. The chronic immune inflammation of the adjuvant arthritis type was reproduced by subplantar introduction of the total Freund adjuvant in the dose of 0.1 ml. Immune cells and immunoglobulins were differentiated with the help of rat monoclonal antibodies (MCA) labeled by FITC to CD3 antigens (general T-lymphocytes), CD4 (helper T-lymphocytes), CD8 (cytotoxic suppressor T-lymphocytes), CD45RA (B-lymphocytes), ED (macrophages) and IgE and IgG. It has been found that in the chronic inflammation the activation of regional lymph nodes is more expressed, longer and phasic than in the acute one. This is evident by increase of intensity of cellular immune responses and decrease of humoral responses, increase of the suppressor activity and reduction the helper activity, increase of the macrophagal reaction as compared with the control, increase of amount of lymphocytes - producers of IgG and IgE.

Recently because of deterioration of the ecological situation in the world the immunological responsiveness of the human organism has changed and, as a result, the frequency of the chronic acute inflammation has increased. It is known that at the beginning of an inflammatory process irrespective of any etiological factor the changes in the immune system organs take place. Such organs, first of all, are lymph nodes [9]. It has been proven that the reaction of regional lymph nodes to introduction of phlogogen is more pronounced than those lymph nodes that are distant from the focus of inflammation [6, 10]. In this regard the aim of our research was to study immunohistochemical changes in the regional lymph nodes in the acute infectious inflammation and in the process of inflammation chronicity, namely in the secondary chronic inflammation, primary chronic non-immune and primary chronic immune inflammation.

Materials and Methods

The research was performed using 246 male Wistar rats with the body weight of 180-200 g. Acute infectious inflammation was induced by introduction of *Staphylococcus aureus* daily culture containing 2 milliard microbial bodies in 1 ml of the isotonic solution of sodium chloride into the thigh [7]. The secondary chronic inflammation was reproduced by subcutaneous introduction of 5 ml of λ-carageenen in 1 ml of the isotonic solution of sodium chloride into the thigh [1]. The primary chronic granulomatous inflammation was induced by introduction of sephadex A-25 in the dose of 1 mg in 1 ml of the isotonic solution of sodium chloride into the thigh [5]. The chronic immune inflammation of the adjuvant arthritis type was reproduced by subplantar introduction of the total Freund adjuvant in the dose of 0.1ml [8].

The research was conducted in detailed dynamics of inflammation beginning from 6 h to 28 days. Immune cells and immunoglobulins were differentiated with the help of rat monoclonal antibodies (MCA) labeled by FITC to CD3 antigens (general T-lymphocytes), CD4 (helper T-lymphocytes), CD8 (cytotoxic suppressor T-lymphocytes), CD45RA (B-lymphocytes), ED (macrophages) and IgE and IgG.

Results and Discussion

The humoral immune responses in lymph nodes (containing CD45RA+-cells) depending on the kind of inflammation are expressed in such way: acute inflammation > primary chronic immune inflammation > secondary chronic inflammation > primary chronic non-immune inflammation. It is possibly connected with the fact that acute inflammation is humoral, in the immune inflammation the immune responses are especially tense, and that is why in the primary chronic immune inflammation the humoral immune responses are rather pronounced; in the secondary chronic inflammation the humoral immune responses are tense, apparently, as a compensatory reaction directed to prevent the process chronicity, and primary chronic non-immune inflammation is cellular [2-4].

The cellular immune responses in lymph nodes (the amount of CD3+-lymphocytes) depending on the kind of inflammation are expressed in such way: primary chronic immune inflammation > pri-

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mary chronic non-immune inflammation > secondary chronic inflammation > acute inflammation. It corresponds to the regularity of lymph nodes involvement in general and shows that involvement of lymph nodes to chronic inflammation is based on the necessity of implementation of cellular immune responses, first of all.

The helper activity in cellular immune responses of lymph nodes (containing CD4+-cells) in different kinds of inflammation has the following dependence: acute inflammation > primary chronic non-immune inflammation > secondary chronic inflammation > primary chronic immune inflammation, but the suppressor activity (the amount of CD8+-lymphocytes) is expressed in reversed manner. Thus, in the first case IRI is significantly increased and it indicates a visible helper activity, but in other cases – the increase is less or reduced in the same way; it testifies about increase of the suppressor activity in the chronic inflammation. Since the acute inflammation is humoral, the marked helper activity in this case is likely to be caused by the reaction of Th2-lymphocytes, but in other cases this reaction is less [2-4].

The macrophagal reactions in lymph nodes (the content of ED1+-cells) depending on the type of inflammation are expressed in such way: the primary chronic non-immune inflammation > the secondary chronic one > acute inflammation > the primary chronic immune inflammation, which is likely to be interconnected with the fact that the granulomatous inflammation is mainly macrophagal. In the secondary chronic inflammation the macrophagal reaction is considerably intense compared to the acute one, first of all, compensatory because of the insufficient neutrophilic reaction. In the primary chronic immune inflammation the lymphocytic reaction dominates over the macrophagal reaction [2-4].

In the chronic inflammation the amount of lymphocytes-producers of Ig G and Ig E increases in lymp nodes. It is most pronounced in the secondary chronic inflammation, apparently again as a compensatory reaction, aimed at preventing the process chronicity, and the content of IgE-producers in all types of the chronic inflammation increases earlier and more than in the acute one; it probably testifies about a greater antigenic load and sensibilization, including autoimmunization in the chronic inflammation compared to the acute one.

CONCLUSIONS

1. In the chronic inflammation the activation of regional lymph nodes is more expressed, longer and phasic than in the acute one.

2. As far as the chronic inflammation grows, the intensity of cellular immune responses in lymph nodes increases; it testifies that involvement of lymph nodes in the chronic inflammation is based on the need for cellular immune responses.

3. Humoral immune reactions are intensified compared to the control, and less than in the acute inflammation.

4. In the chronic inflammation the suppressor activity in lymph nodes increases not only as compared with the acute inflammation, but also with the control. The helper activity is reduced.

5. The macrophagal reaction in lymph nodes in the chronic inflammation increases compared to the control.

6. In the chronic inflammation compared to the acute one the amount of lymphocytes – producers of Ig G and Ig E increases in lymp nodes.

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ІМУНОГІСТОХІМІЧНІ ЗМІНИ У РЕГІОНАРНИХ ЛІМФОВУЗЛАХ У ПРОЦЕСІ ХРОНІЗАЦІЇ ЗАПАЛЕННЯ

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Ключові слова: запалення; хронізація; імунні реакції; лімфовузли

Вивчені імуногістохімічні зміни у регіонарних лімфовузлах при гострому інфекційному запаленні та в процесі хронізації запалення, а саме, при вторинно хронічному, первинно хронічному неімунному та первинно хронічному імунному запаленні. Дослідження виконані на 246 щурах. Гостре інфекційне запалення викликали введенням у ділянку стегна добової культури Staphylococcus aureus, штам АТСС-25923, що містить 2 млрд мікробних тіл в 1 мл ізотонічного розчину хлориду натрію. Вторинно хронічне запалення відтворювали підшкірним уведенням у ділянку стегна 5 мг λ-карагеніну в 1 мл ізотонічного розчину хлориду натрію. Первинно хронічне гранулематозне запалення викликали введенням у ділянку стегна сефадексу А-25 у дозі 1 мг в 1 мл ізотонічного розчину хлориду. Хронічне імунне запалення відтворювали субплантарним уведенням повного ад'юванту Фрейнда в дозі 0,1 мл. Імунні клітини та імуноглобуліни диференціювали за допомогою щурячих моноклональних антитіл (МКА), мічених ФІТЦ, до антигенів CD3 (загальні Т-лімфоцити), CD4 (Т-лімфоцити-хелпери), CD8 (Т-лімфоцити-супресори цитотоксичні), CD45RA (В-лімфоцити), ED1 (макрофаги), а також до IgG та IgE. Було встановлено, що при хронічному запаленні активація регіонарних лімфовузлів є більш вираженою, тривалішою та фазною, ніж при гострому. Про це свідчать: зростання вираженості клітинних імунних реакцій та послаблення гуморальних, підвищення супресорної активності та зниження хелперної, зростання макрофагальної реакції у порівнянні з контролем, зростання кількості лімфоцитів-продуцентів IgG та IgE у лімфовузлах по мірі хронізації запалення.

ИММУНОГИСТОХИМИЧЕСКИЕ ИЗМЕНЕНИЯ В РЕГИОНАРНЫХ ЛИМФОУЗЛАХ В ПРОЦЕССЕ ХРОНИЗАЦИИ ВОСПАЛЕНИЯ

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Ключевые слова: воспаление; хронизация; иммунные реакции; лимфоузлы

Изучены иммуногистохимические изменения в регионарных лимфоузлах при остром инфекционном воспалении и в процессе хронизации воспаления, а именно, при вторично хроническом, первично хроническом неиммунном и первично хроническом иммунном воспалении. Исследования выполнены на 246 крысах. Острое инфекционное воспаление вызывали введением в область бедра суточной культуры Staphylococcus aureus, содержащей 2 млрд микробных тел в 1 мл изотонического раствора хлорида натрия. Вторично хроническое воспаление воспроизводили подкожным введением в область бедра 5 мг λ-карагенина в 1 мл изотонического раствора хлорида натрия. Первично хроническое гранулематозное воспаление вызывали введением в область бедра сефадекса А-25 в дозе 1 мг в 1 мл изотонического раствора хлорида натрия. Хроническое иммунное воспаление воспроизводили субплантарным введением полного адъюванта Фрейнда в дозе 0,1 мл. Иммунные клетки и иммуноглобулины дифференцировали с помощью крысиных моноклональных антител (МКА), меченых ФИТЦ, к антигенам CD3 (общие Т-лимфоциты), CD4 (Т-лимфоциты-хелперы), CD8 (Т-лимфоциты-супрессоры цитотоксические), CD45RA (В-лимфоциты), ED1 (макрофаги), а также к IgE и IgG. Было установлено, что при хроническом воспалении активация регионарных лимфоузлов является более выраженной, продолжительной и фазной, чем при остром. Об этом свидетельствуют: нарастание выраженности клеточных иммунных реакций и ослабление гуморальных, повышение супрессорной активности и снижение хелперной, нарастание макрофагальной реакции по сравнению с контролем, возрастание количества лимфоцитов-продуцентов IgG и IgE в лимфоузлах по мере хронизации воспаления.