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Review article

Some Immunological and Genetic Aspects of the Development of Traumatic Osteomyelitis: a Review of the Literature

Umidjon Kholmurodov [1], Nodir Kobilov [2], Murodulla Karimov [3]

[1] *3rd year basic doctoral student of the Department of Traumatology, Orthopedics and Military Field Surgery, Tashkent Medical Academy, Tashkent, Uzbekistan. E-mail: ukholmurodov@gmail.com*

[2] *Assistant of the Department of Traumatology, Orthopedics and Military Field Surgery, Tashkent Medical Academy, Tashkent, Uzbekistan. E-mail: 1202nodir@gmail.com*

[3] *Head of the Department of Traumatology, Orthopedics and Military Field Surgery, Tashkent Medical Academy, Tashkent, Uzbekistan. E-mail: m.karimov@mail.ru*

Abstract

This review summarizes features of the pathophysiological course of post-traumatic osteomyelitis. Options for the development of traumatic osteomyelitis in patients with immunological and genetic predispositions are considered. Along with a description of the pathophysiology and conditions for the occurrence of these processes, the features of the pathophysiological course of this disease are described in detail.

Molecular genetic studies devoted to the search for an association between polymorphic gene variants and the development of chronic traumatic osteomyelitis are not sufficiently reflected in domestic and foreign literature, which confirms the relevance of this work.

Key words: traumatic osteomyelitis, pathophysiology, predisposition, molecular genetic studies.

Corresponding author: Murodulla Karimov, Head of the Department of Traumatology, Orthopedics and Military Field Surgery, Tashkent Medical Academy, Tashkent, Uzbekistan.
Postal code: 100109
Address: Uzbekistan, Tashkent, Farobiy 2
Phone: +998 90 959 86 16
E-mail: m.karimov@mail.ru

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Introduction

Traumatic osteomyelitis is a multifactorial disease, the nature of the development of which depends on the dose, pathogenicity, virulence of a pathogen, and the immunoreactivity of an organism in relation to environmental conditions [1].

The proportion of patients with chronic osteomyelitis is 3-5% of the number of patients with bone diseases in general. In this case, the disability of patients reaches 50-90% [2,3].

It has now been proven that almost any injury or surgical intervention has an adverse effect on the immune system and causes the development of immunodeficiency, the main manifestation of which is infectious complications [4-6].

The problem of chronic osteomyelitis requires an interdisciplinary approach with the mandatory participation of not only orthopedic traumatologists, but also clinical pharmacologists, microbiologists, specialists in the field of biochemistry and osteoporosis [1,7].

Thus, chronic post-traumatic osteomyelitis remains one of the most severe diseases of the musculoskeletal system, despite the achieved level of development of medical care.

The aim of the study: is to study options for the development of traumatic osteomyelitis in patients with immunological and genetic predispositions and to summarize features of the pathophysiological course of post-traumatic osteomyelitis.

Immunological Aspects

A general immune response in patients with purulent-septic complications can proceed in 2 phases: the 1st is the activation of monocytes with the increased production of proinflammatory cytokines by them (clinically corresponds to the picture of acute inflammation); the 2nd is immunological tolerance (an areactive or chronic stage of the disease) - decrease in the level of proinflammatory cytokines begins [3,8]. The development of immunological tolerance is considered as an adaptive mechanism aimed at limiting hyperinflammation, which weakens the macroorganism. However, the persistence of this state leads to the inhibition of T-cell functions [9].

The components that make up the endotoxin of most gram-negative bacteria or exotoxins produced by gram-positive microorganisms play an important role in the initiation of immune response in a developed surgical infection [10,11].

It is known that gram-negative bacteria contain lipopolysaccharides, which are immunomodulators with a wide spectrum of action. At the same time, lipopolysaccharide complexes of endotoxins interact with all types of antigen-presenting cells – dendritic cells, monocytes, B-lymphocytes, neutrophils, endothelial, and others involved in the activation of the systemic inflammatory response syndrome. Under the influence of endotoxin, the synthesis of cytokines by macrophages is induced, the adhesion of microbes to endothelial cells and lymphocytes increases, expression of co-receptor lymphocytes (CD80, CD86) increases, the efficiency of microbial antigen presentation to T-lymphocytes increases, and the alternative and classical pathway of complement activation is stimulated [12,13].

Exotoxins produced by gram-positive microorganisms have the properties of superantigens through hyperactivation of up to 20-30% of T-lymphocytes with excessive cytokine induction. Activated T-lymphocytes undergo apoptosis, which contributes to the formation of secondary immunodeficiency of the T-cell link [14].

In gram-negative bacteria, the main component that activates inflammatory response is lipopolysaccharide (LPS), which contains lipid A, a ligand for TLRs, and is responsible for the toxic, mitogenic, and immunomodulatory properties of the pathogen. Gram-positive bacteria are characterized by several potentially biologically active cell wall molecules: peptidoglycan, lipoteichoic acid, and lipopeptides [15, 16].

Numerous experimental data have confirmed the involvement of TLRs in the development of the inflammatory response. It has been established that genetically determined hyperactivation of TLR4 activates the genes of pro-inflammatory interleukins IL-1, IL-6, IL-8, and TLR2 stimulates the production of IL-12 and TNFα. This synthesis of interleukins ensures the development of an inflammatory response and regulates adaptive immunity responses [17-19].

Following the recognition of the central role that TLRs play in innate immunity, it has come to be understood that an increase or decrease in the function of these receptors contributes to the pathogenesis of many infectious or immune-mediated diseases [20].

It has been proven that after injury there is an increase in the number of neutrophilic granulocytes in the peripheral blood, which positively correlates with the level of adrenaline and cAMP in the blood plasma, which suggests that the process depends on β-adrenergic stimulation. Along with the release of cellular elements from the depot, activation of stem cells precursors of granulomonocytopoiesis occurs [21]. Thus, leukocytosis is formed due to the “marginal” pool of leukocytes, and the subsequent ones are the result of the stimulation of hematopoiesis [22].

According to B. Kuznik et al. (2008), when studying the state of the immune system in patients with fractures of long tubular bones, they noted an increase in the number of leukocytes and lymphocytes, a decrease in the absolute and relative number of T-total and T-active lymphocytes, a reduction in the percentage of B-lymphocytes, a decrease in the concentration of IgG, an increase in the content IgA and a clear upward trend in IgM. The presented facts indicate secondary T-cell immunodeficiency and an imbalance of various classes of immunoglobulins [23].

There are few data on changes in the homeostasis system in patients with chronic traumatic osteomyelitis. Convincing evidence has been obtained that chronic traumatic osteomyelitis, in contrast to uncomplicated trauma, is accompanied by a combination of hyperactivation of phagocytic leukocytes. Meanwhile, hyperactivation of the T-link of the immune system is characterized by increased T-lymphoproliferation and severe hyposuppression in the T-cell immunoregulation system, which may be a significant predisposing factor in the development of chronic inflammation [5, 24-26].

Suppression of Th1 and activation of the Th2 subpopulation leads to a decrease in the production of anti-inflammatory cytokines and, consequently, to a more "sluggish" course of the inflammatory response, and an excessive predominance of Th1 over Th2 is accompanied by increased production of pro-inflammatory cytokines with the possible development of septic shock [27].

According to B.Kuznik et al. (2008), there is a sharp decrease in the number of lymphocytes in patients with a complicated course of fractures of long tubular bones. The number of cells with CD2+ and CD2+-HLA-DR+ markers in the patients was reduced by two times compared to healthy people, the number of CD4+ and CD8+ lymphocytes was reduced by two times, and the CD4/CD8 ratio was reduced, which indicates suppression of cellular immunity reactions [23].

According to other data, it was found that during the first week of the post-traumatic period, there were no significant differences in the Th1/Th2 ratio compared to healthy donors. On the 10th day, with an uncomplicated course of the traumatic disease, the CD8+ content was within the normal range. With the development of purulent complications, a decrease in the content of CD4+ was observed with a simultaneous increase in the number of CD8+, which persisted in patients with an unfavorable outcome of the disease [27].

The imbalance of T-lymphocyte subpopulations was proved in the work of A. Kamek and S.Leonova (2008), in a comparative analysis of the initial parameters of the immune system in patients with chronic traumatic osteomyelitis [28].

Changes in the content of B-lymphocytes during trauma are not detected in most cases. Therefore the indicators of humoral immunity (the number of B-lymphocytes and the range of the main classes of immunoglobulins) are proposed to be uninformative [24,25].

Some authors observed a decrease in the number of B-lymphocytes in patients with traumatic osteomyelitis, along with an increase in the production of immunoglobulin A in the blood and a reduction in the concentration of immunoglobulin M [29]. At the same time, according to the results of studies by other authors [30], hyperactivation of the B-link of the immune system is noted in osteomyelitis.

M.Chepeleva and N.Klyushin (2012) in their work conducted a comparative analysis of cellular immunity in patients with chronic traumatic osteomyelitis, depending on the stage. The immunological features of chronic post-traumatic osteomyelitis at the stage of remission and with the development of a fistulous form of the disease were revealed. Regardless of the pathological process stage, osteomyelitis is characterized by moderate leukocytosis, an increase in the number of monocytes and neutrophils, and an increase in the number of CD25 and HLADR-positive T-lymphocytes. The stage of remission in patients with osteomyelitis is accompanied by a moderate activation of humoral immunity (an increase in the number of B-lymphocytes (CD19+) and IgG production). A decrease in the number of lymphocytes, as well as the expression of HLAII-DR on monocytes, creates prerequisites for the development of a fistulous form of osteomyelitis and may serve as an indication for the use of immunomodulatory drugs [31].

It has been established that a pronounced autoimmune reaction can also accompany chronic traumatic osteomyelitis [32].

According to V. Slesarev (2002), chronization of osteomyelitis is associated with the formation of secondary post-infectious immunodeficiency caused by the immunosuppressive effect of microbial pathogens and the features of the immunological reactivity of the host organism [33].

Immune cells secrete numerous soluble mediators (cytokines), some of which are highly specific. Increased cytokine synthesis begins in response to microbial entry or tissue damage [21].

Synthesized in the focus of inflammation, cytokines affect all cells involved in the development of inflammation - granulocytes, macrophages, fibroblasts, endothelial and epithelial cells, T- and B-lymphocytes. Within the immune system, cytokines mediate the relationship between specific defense responses and specific immunity. In case of failure of local defense reactions, cytokines enter the circulation, which leads to the development of an acute phase response at the level of the organism [21,24].

In addition, at the level of the organism, cytokines communicate between the immune, nervous, endocrine, hematopoietic, and other systems and serve to involve them in the organization and regulation of a single protective reaction [21,24,25].

Cytokines in low concentrations are needed for the correct formation of local inflammation, higher doses cause the development of a systemic inflammatory response, and pathologically high concentrations lead to a state of septic shock, multiple organ failure and death of the body. Currently, about 200 individual polypeptide substances have been discovered and described, each of which plays an essential role as a link in the body's adaptive reactions [27].

The activity of the inflammatory process is one of the indicators most commonly used in diagnosing many diseases. Diagnostic approaches to its assessment are diverse, but there is a general trend toward developing and improving methods. One of these methods is the study of the cytokine profile in the dynamics of the development of pathology with an inflammatory component [21-27].

In the work of Magomedov P. et al. (2010), an analysis was made of the relationship between clinical and immunological parameters in patients with pyoinflammatory diseases of the pelvic organs. As a result of the studies, an increase in the content of cytokines due to pro-inflammatory cytokines (TNF-α, IF-γ, IL-1β, and IL-8) was established. It was also found that the nature of changes in the concentration of blood cytokines has a clear tendency to increase from the initial to the final stage of the disease, from mild to severe, complicated course of the disease [34].

In the studies of E.Kirdey et al. (2000) revealed changes in the immunocytokine status in patients with chronic osteomyelitis towards increased production of pro-inflammatory mediators (IL-1, TNF-α) and their important role in the chronicity of the inflammatory process [35].

V. Khavinson et al. (2001), in their studies on patients with fractures of long tubular bones complicated by osteomyelitis, established changes in the content of pro-inflammatory and anti-inflammatory cytokines. It was noted that in patients in the first days after injury, not only a decrease in the number of T- and B-lymphocytes are observed but also a significant decrease in the level of immunoglobulins, the more the concentration of IgG

and IgA falls, the worse the prognosis for mechanical injury. The revealed shifts indicate the development of the inflammatory process and the excessive tension of the body's defenses [36].

A. Ovdenko and A. Golubeva (2003) studied the level of pro-inflammatory cytokines in patients with gunshot osteomyelitis in an acute and chronic course. It has been established that the most significant in the acute course of a purulent process is IL-1α and, in particular, IL-1β, which increase several times in the blood serum. TNF-α is a modifier of the inflammatory response, increasing in the blood serum during the acute course of the purulent process and remaining slightly above the norm in the chronic course [37].

Other authors studied the level of IL-4 and IFγ in blood serum in chronic recurrent furunculosis and chronic osteomyelitis in patients with different levels of total IgE. It was found that an increase in the concentration of IL-4 in the blood serum of patients with chronic recurrent furunculosis and chronic osteomyelitis does not depend on the level of total IgE [38].

Thus, cytokines are an organizing system that forms and regulates the entire complex of protective reactions of the body upon the introduction of pathogens and play a leading role in the development of inflammation.

Genetic Aspects

Molecular medicine is one of the most intensively developing branches of modern medicine. It is aimed at correcting the pathological process in a particular person, taking into account the unique features of his genome.

Since cytokines are mediators of inflammation, it is important to study the genes that control their activity. This fact is significant not only in studying the mechanisms of development and course of various diseases but also in identifying predispositions to them. It has been proven that interleukin genes have an excessively high degree of polymorphism [39].

At present, not only the polymorphism of the genes of many cytokines has been established, but the influence of various gene variants on the properties and functioning of the protein products of their expression has also been noted [40].

IL-1 is a cytokine with a wide range of biological and physiological effects. The IL-1 gene family consists of three homologous genes IL1A, IL1B, and IL1RN, is localized on chromosome 2q13-21, and encodes the cytokines IL-1α, IL-1β, and their receptor antagonist IL-1RN. In the study of polymorphic markers of family genes, an association of specific genotypes with the risk of developing diseases characterized by chronic inflammation was found. The balance between the production and inhibition of the synthesis of proteins of the IL-1 family plays one of the key roles in the development, regulation, and outcome of the inflammatory process [41-43].

It has now been established that the -511T/C polymorphism, which affects the level of cytokine expression, has been found in the IL-1β gene promoter. The -511C- allele is a genetic marker of the risk of developing hepatocellular carcinoma in patients with chronic HBV and HCV infection in Iranian residents. The level of IL-1β is elevated in the hepatic tissue around the tumor and acts as a tumor growth factor. The frequency of the -511C- allele of the IL-1β gene is increased in patients with HCV-associated hepatitis cell carcinoma compared with patients with chronic hepatitis C [44].

Studies in the United States have shown that the -511T allele of the IL1B gene, in combination with the -ILRN1 allele is a risk factor for the development of chronic obstructive pulmonary disease [45]. In the study of the distribution of alleles of these polymorphic markers in non-smoking patients with asthma, an association of -511T- alleles of the IL1B gene and -ILRN2 in the IL1RN gene with a rapid decline in respiratory function was found [46].

IL-6 is one of the key participants in the cytokine network. The IL6-174G>C gene polymorphism downregulates gene transcription and is associated with chronic inflammation and severe sepsis. The -174C allele of the IL-6 gene is a marker of an increased risk of acute respiratory distress syndrome, generalized inflammation syndrome, and severe sepsis [87]. At the same time, the high-producing allele, 174G, of the IL-6 gene is associated with the risk of developing Kaposi's sarcoma caused by HIV infection [47]. Heterozygosity for IL6-4272C>T is associated with a low level of production of antibodies against the measles pathogen and in response to vaccination with a trivalent vaccine against paramyxoviruses [48].

Some studies have found an association of the -174C- allele of the IL-6 gene with some multifactorial diseases, for example, chronic arthritis, osteoporosis, and some oncological diseases [49,50].

The IL-8 gene is mapped on chromosome 4 (4q12-13) and encodes the neutrophilotropic chemoattractant IL-8 (CXCL8), which is the primary mediator of chemotaxis and activation of neutrophils and phagocytes in response to bacterial antigens. The IL8-251A>T gene polymorphism is associated with an increased level of neutrophilic infiltration of the gastric mucosa and IL-8 production, a high risk of atrophic gastritis and gastric cancer in individuals with H. pylori infection [51], especially in homozygous -251A/A genotypes of the IL8 gene and -1082G/G IL10 gene [52].

One of the hallmarks of RSV-associated bronchiolitis is airway neutrophil infiltration, as RSV-infected airway epithelial cells secrete high levels of IL-8 and other pro-inflammatory cytokines. The SNP allele -251A- of the IL-8 gene is associated with increased gene expression and RSV-associated bronchiolitis. In their works, researchers from the UK showed that the carriage of the -251A- allele is associated with an increased level of IL-8 production, which is a risk factor for developing severe complications when exposed to viral infections [53].

Cytokine IL-12 is involved in regulating IFN-γ secretion by Th1 cells and natural killer cells. Several monogenic defects in the IFN-γ/IL-12 axis confer a predisposition to transient, severe, and fatal infectious diseases caused by common pathogens [54]. For example, among HBV-infected individuals, individuals with low IFN-γ activity are at particularly high risk of developing hepatocellular carcinoma. IL-12 is produced by hepatocytes of HBV-infected individuals, promotes Th1 cell production of IFN-γ, and inhibits Th2 cell differentiation and HBV replication. Homozygosity for the -1188A allele of the IL12 polymorphism -1188A>C is associated with increased expression of IL-12 by lymphocytes and spontaneous clearance of HBV. One of the main cytokines secreted by Th2 cells is IL4, which suppresses the Th1-type immune response and antagonizes the effect of IFNγ on

Th1 cell differentiation. The IL4-598C>T gene promoter polymorphism, which enhances IL-4 production and shifts the immune balance towards Th2, is associated with suppression of the immune response to viral antigens and severe respiratory infection [55], and -589T- is the allele of the IL4 promoter polymorphism IL4 -589T>C - with RSV (respiratory syncytial virus)-associated diseases [56] and recurrent trachoma caused by chlamydia [57].

IL-4 regulates the expression of co-receptors CCR5 and CXCR4 used by the HIV virus to penetrate into a human cell: it reduces the level of CCR5 and increases the level of CXCR4 on the surface of CD4+ cells, respectively, reduces the replication of R5 strains and enhances the replication of X4 strains. The mutant allele -589T- of the IL4 gene, which is more common in HIV-negative individuals, has a protective effect in the transmission of infection through heterosexual contact and slows down the progression of AIDS [58].

Th2-type cytokines include the immunosuppressive anti-inflammatory cytokine IL-10, which inhibits the secretion of pro-inflammatory Th1-type cytokines by lymphocytes and activated macrophages. In patients with chronic HBV and HCV infection, especially those with elevated ALT levels, the predominant cytokine pattern is associated with abnormally elevated IL-10 production. The frequency of alleles -8I9T- and -592A- of the IL10 gene in asymptomatic carriers of the infection is significantly higher than in patients with chronic progressive hepatitis [59].

Functional polymorphisms -592A>C, -819T>C, and -1082G>A associated with the level of cytokine production and the pathogenesis of HCV infection were found in the IL10 gene promoter. Haplotypes ACC/ACC, ACC/ATA, and ATA/ATA (genotype AA) are associated with a low level of production, GCC/ACC and GCC/ATA (genotype GA) - with an intermediate level, and GCC/GCC (GG genotype) - with a high level of IL-10 production [60].

The -1082G/G genotype of the IL1082G>A gene corresponds to a high level, the -1082G/A genotype of the IL10-1082G>A gene corresponds to an average level, and the -1082A/A genotype of the IL10-1082G>A gene corresponds to a low level of IL-10 production by peripheral blood mononuclear cells [61]. A high level of IL-10 production is associated with ineffective clearance of HCV infection, a high risk of chronic infection, and its progression to cirrhosis. Spontaneous clearance of infection is associated with the -1082G/A genotype in the populations of the USA [62], Europe [63], and Argentina [60]. The 1082A/A genotype of the IL10-1082G>A gene is associated with protection against acute otitis media after vaccination [64] and the development of gastric cancer in patients with H. pylori-associated atrophic gastritis [51,52]. The -1082G- allele of the IL10-1082G>A gene increases the susceptibility of patients with severe acute pancreatitis to septic shock [61] and is associated with the risk of pneumonia in children with syncytial viral infection [65] and severe meningitis [66].

In patients with hepatitis C, haplotype -592A-/-819T- is associated with reduced production of IL-10 and a better response to interferon-α therapy [67].

On the other hand, the experimental and clinical data point to a protective role of IL-10 in hepatic fibrogenesis. High production of IL-10 inhibits liver fibrosis. Short-term treatment of patients with chronic hepatitis C with recombinant IL-10 led to a decrease in inflammation and liver fibrosis; however, treatment of patients with liver fibrosis with IL-10 for a year led to an increase in the serum level of viral RNA, confirming that IL-10 not only suppresses fibrogenesis but also increases viremia as a result of a decrease in the number of HCV-specific CD4+ and CD8+ IFN-y-secreting T cells and polarization of the immune response towards the Th2 type [68, 69].

The common SNP polymorphism of the IL10-592A>C gene promoter is associated with a reduced risk of tuberculosis manifestation and the course of HIV infection. The -592A allele of the IL10-592A>C gene is associated with increased viral replication and a significant acceleration of AIDS progression. Carriage frequency of the -592C- allele of the IL10-592A>C gene in healthy people is higher than in patients with tuberculosis [70,71].

The TNFα gene is a highly polymorphic region of the genome in which at least eight polymorphic sites are described. Some of the polymorphisms affect the level of TNFα production in vitro. Many studies have shown the association of individual polymorphisms of the TNFα-308G>A gene promoter with various autoimmune and infectious diseases [72].

In the promoter region of the TNFα gene at position -308, a biallelic polymorphism is known - the transition of guanine (TNFG allele) to adenine (TNFA allele). Data on the functional significance of the TNFA-308G>A gene polymorphism in the works of different researchers are ambiguous, which, apparently, is due to the nature of the pathogenesis of the disease, the characteristics of cell lines, stimulants, and other experimental conditions [72, 73].

The TNFα gene polymorphism influences the evolution of the infection and the pathogenesis of the disease. Substitutions -238G/A, -308G/A, and -857C/T in the gene promoter are associated with chronic HBV infection. Genotypes -238A/A of the TNFα-238G>A gene and -857C/C of the TNFα-857C>T gene are independent factors of predisposition to chronic hepatitis B [74, 75].

Studies conducted on multiple populations, the SNP (single nucleotide polymorphism) genotype -308G/A of the TNFα gene is associated with an increased risk of bacterial infections and inflammatory diseases, including postpartum sepsis, malaria, and lethal meningitis [76, 77].

In some studies, the -308A- allele of the TNFα gene and elevated TNFα levels correlate with the severity of meningitis and the risk of death from bacterial sepsis [76-78].

The role of the studied polymorphism in patients with sepsis is also ambiguous. Stuber F. et al. (1996) found no association between TNFα-308G>A polymorphisms and the development of postoperative sepsis in surgical patients [79]. The same data are confirmed by other researchers. Nonetheless, in patients with septic shock, homozygous for the TNFα allele, a high level of TNFα in the blood is determined and the risk of a fatal outcome increases by 3.7 times [80].

The relationship of the TNFα gene polymorphisms with osteonecrosis of the femoral head in patients with SARS has been established - the TNFα-204T>C allele of polymorphism of the TNFα-204T>C gene is associated with a protective effect against complications of SARS, and the -1031C allele of the TNFα-1031T>C gene polymorphism and heterozygosity for the -863A/C genotype of the TNFα gene is associated with a high risk of osteonecrosis of the femoral head. TNFα-1031C/T, TNFα-1031C/C, and TNFα-863A/C genotypes may be risk factors for osteonecrosis of the femoral head in patients with SARS [81].

No association was found between TNFα-308G>A gene polymorphism and predisposition to rheumatoid arthritis, as well as arthritis exacerbations in patients with psoriasis [82]. However, Cvetkovic J.T. et al. found that rheumatoid arthritis is more severe in heterozygotes for the -308 G>A polymorphic locus of the TNFα gene than in homozygotes for the TNFα-308G allele. The combination of genotypes -308G/A of the TNFα gene and -511T/T of the IL-1B gene also contributes to the severe course of rheumatoid arthritis [83]. In patients with idiopathic juvenile arthritis, the -308A- allele of the TNFα gene predisposes to a severe course of the disease, while the -308G- allele of the TNFα gene performs a protective function [84].

Montes A.H. et al. (2010) investigated the polymorphism of metalloproteinase (MMP) in patients with chronic osteomyelitis, which plays an essential role in the bone extracellular matrix. The typing sites were chosen as MMP1 (1607 1G/2G) and MMP13 (77A/G). As a result of the study, it was concluded that increased expression of MMP1 (1607 1G/2G) may contribute to the development of osteomyelitis and regulate IL-1α [85].

According to E. Kuzminova et al. (2013) identified markers of predisposition to the development of sepsis in patients with severe thermal injury and found increased frequencies of the A allele and the G/A TLR2*G753A genotype among burn patients who were diagnosed with sepsis on the 20-30th day after the burn, compared with healthy individuals [86]. The results obtained are consistent with the data presented in the works of foreign researchers. For instance, E. Lorenz et al., in their work, conclude that TLR2*G753A polymorphism may increase the risk of developing severe sepsis caused by gram-positive microorganisms [87].

Thus, despite large-scale studies of the genetic polymorphism of regulatory and adhesive molecules in various diseases, domestic and foreign researchers have hardly touched on the problems of traumatology, in which the pathogenesis of complications has its own characteristics.

Conclusions

Cytokines secreted by various cell types regulate the intensity and duration of the immune response.

These parameters vary in different individuals and correlate with functionally significant polymorphisms of cytokine genes and the severity of infection, i.e. allelic variants of cytokine genes can modify expression or biological function. Various patterns of cytokine gene expression at the RNA and protein levels are associated with pathophysiological processes and have clinical consequences in the form of changes in the intensity of the immune response, up to the syndrome of generalized inflammation and the syndrome of multiple organ failure. The analysis of the literature shows that molecular genetic studies devoted to the search for an association between polymorphic gene variants and the development of chronic traumatic osteomyelitis are not sufficiently reflected in domestic and foreign literature, which confirms the relevance of this work.

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Жарақаттың нәтижесінде болған остеомиелиттің дамуының иммунологиялық және генетикалық аспектілері: әдебиеттік шолу

Холмуродов У.Т. [1], Кобилов Н.Р. [2], Каримов М.Ю. [3]

[1] *Травматология, ортопедия және әскери-далалық хирургия кафедрасының 3 курс базалық докторанты, Ташкент медициналық академиясы, Ташкент, Өзбекстан. E-mail: ukholmurodov@gmail.com*

[2] *Травматология, ортопедия және әскери-далалық хирургия кафедрасының ассистенті, Ташкент медициналық академиясы, Ташкент, Өзбекстан. E-mail: 1202nodir@gmail.com*

[3] *Травматология, ортопедия және әскери-далалық хирургия кафедрасының меңгерушісі, Ташкент медициналық академиясы, Ташкент, Өзбекстан.. E-mail: m.karimov@mail.ru*

Түйіндеме

Бұл әдебиеттік шолуда жарақаттың нәтижесінде дамыған остеомиелиттің ағымының патофизиологиялық ерекшеліктері біріктіріліп сипатталған. Иммунологиялық және генетикалық бейімділігі бар науқастарда жарақаттың салдарынан дамыған остеомиелиттің даму ерекшеліктерінің нұсқалары қарастырылған. Аталмыш аурудың патофизиологиялық ағымы толық тарқатылған.

Жарақаттың салдарынан болған остеомиелиттің дамуы мен гендердің полиморфты нұсқаларының арасындағы байланысты терең зерттеуге бағытталған молекулярлық-генетикалық зерттеулер отандық және шетелдік зерттеулерде толық тарқатылмаған және бұл осы тақырыптың әлі де өзекті екендігін дәлелдейді.

Түйін сөздер: жарақат салдарынан дамыған остеомиелит, патофизиология, бейімділік, молекулярлық-генетикалық зерттеулер.

Некоторые иммунологические и генетические аспекты развития травматического остеомиелита: обзор литературы

Холмуродов У.Т. [1], Кобилов Н.Р. [2], Каримов М.Ю. [3]

[1] *Базовый докторант 3 курса кафедры травматологии, ортопедии и военно-полевой хирургии, Ташкентская медицинская академия, Ташкент, Узбекистан. E-mail: ukholmurodov@gmail.com*

[2] *Ассистент кафедры травматологии, ортопедии и военно-полевой хирургии, Ташкентская медицинская академия, Ташкент, Узбекистан. E-mail: 1202nodir@gmail.com*

[3] *Заведующий кафедрой травматологии, ортопедии и военно-полевой хирургии, Ташкентская медицинская академия, Ташкент, Узбекистан. E-mail: m.karimov@mail.ru*

Резюме

В данном обзоре обобщены особенности патофизиологического течения посттравматического остеомиелита. Рассмотрены варианты развития травматического остеомиелита у пациентов с иммунологическими и генетическими предрасположенностями. Подробно описаны особенности патофизиологического течения этого заболевания.

Молекулярно-генетические исследования, посвященные поиску ассоциации между полиморфными вариантами генов и развитием хронического травматического остеомиелита, недостаточно отображены в отечественной и зарубежной литературе, что подтверждает актуальность данной работы.

Ключевые слова: травматический остеомиелит, патофизиология, предрасположенность, молекулярно-генетические исследования.