Indicators of the immune system in chronic hematogenous osteomyelitis in children

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Abstract: The article presents the results of a study of a number of immunological parameters in acute and chronic hematogenous osteomyelitis in comparison with the characteristics of the course of the disease. A characteristic feature of acute hematogenous osteomyelitis (AHO) is the high frequency of chronic inflammation, which is due to the development of secondary immunodeficiency. A significant difference to the surgical rehabilitation of patients with bone defects after hematogenous osteomyelitis Chronic osteomyelitis is characterized by the presence of a focus of infection or non-purulent inflammation of the bone tissue, a recurrent course and is considered an incurable disease.

Keywords: hematogenous osteomyelitis, lymphocyte subpopulations, phagocytosis, oxygen, chronic osteomyelitis

Introduction

Chronic osteomyelitis is characterized by the presence of a focus of infection or non-purulent inflammation of bone tissue, a recurrent course and is considered an incurable disease (P. Miettunen et al., 2009).

Unfavorable treatment results (relapses, amputations, functional disability of the limbs) even in our time reach 20-30%, which leads to disability of the child (Mader J.T. et al., 2013; Verhelle N. et al., 2003; Gonsalez M.H. et al. , 2005; Cierny G. et al., 2016).

The transition of osteomyelitis into a chronic form is due to a number of reasons, the main ones being late treatment, insufficiently radical surgery, and errors in antibiotic therapy (Grinev M.V., 1977, Gostishchev V.K., 2007).

Mostly in children, atypical forms of osteomyelitis occur, which immediately acquire a sluggish, chronic course, without an acute phase (Mikhailov M.K. et al., 1985; Akzhigitov G.N. et al., 1986; Cierny G. et al., 2006 ; Hofmann S.R. et al., 2012). The reasons for the development of a chronic process immediately, bypassing the acute stage, were seen differently by different authors.

LITERATURE ANALYSIS

The most untenable are the theories of the development of chronic osteomyelitis with prolonged unjustified use of antibiotics, the so-called “antibiotic” osteomyelitis, in which the virulence of microorganisms supposedly decreases, resulting in the

development of erased, atypical forms (Akzhigitov G.N. et al.; Prokopova L V. et al., 1984; Harris N.H. and Kirkaldy-Willis W.H.; Kozlovski K., 1983). Another unconfirmed theory attaches too much importance to endo- and exogenous technogenic environmental factors (Chirkin V.V., 1991).

The frequency of unsatisfactory results after surgical treatment methods and relapses of chronic osteomyelitis still remains high from 9% to 56% (Nikitin G.D. et al., 1990; Eremin A.V., 2006; Linnik S.A., 2012; Shtofin S.G., 2009). In this regard, patients often undergo surgical interventions 5-10 or more times, and remain uncured for decades (Goryunov S.V., Romashov D.V., Butivshchenko I.A., 2004; Usik S.F., Fedoseev M.M. ., Bratiychuk A.N., 2007; Bhavan, K.P., 2009; J. Kumar et al., 2010). At the present stage, the organization of medical care for patients with this serious disease remains imperfect. Late hospitalization of patients is noted, which can reach from 77% to 86.2%. The level of timely prehospital diagnosis remains low and there is a misunderstanding of the urgency of providing emergency care in this case serious illness. Diagnostic errors during the initial examination of a patient by a surgeon are observed in 25.1-58.3%. In a number of regions of the country, this disease has a mortality rate of 0.5% to 3.7% (Bordian S.G., 2006).

K.S.Ternova and co-authors, I.S.Vengerovsky attach great importance to the body's defenses in the development of primary chronic forms of osteomyelitis. They believe that the reactivity of the body and tissue resistance play an important role in the clinical course of hematogenous osteomyelitis. Constant exposure to a microbial agent in some cases can cause a decrease in the defenses of the macroorganism and lead to the development of acute osteomyelitis (Vengerovsky I.S., 1965; Grinev M.V., 1977). In other cases, on the contrary, the protective properties of the macroorganism improve, immunity and resistance to the causative agent of the disease are developed, so inflammation either does not develop at all, or the disease takes a subacute or chronic course (Harris N.H., 1965; Udeka K., 1975).

Isolated exposure only to a polluted environment or only incorrect antibiotic therapy cannot lead to the development of chronic atypical osteomyelitis, since many forms of this disease were described back in the 19th century, before the discovery of antibacterial drugs and severe technogenic environmental pollution. Chronic osteomyelitis is a widespread disease, affecting up to 10% of all inpatients with purulent pathology and occupying up to 6% in the structure of pathology of the musculoskeletal system (Nikitin G.D. et al., 2002; Leshchenko I.G. et al., 2003; Fedorov V.D. et al., 2003; Linnik S.A., 2012; Shtofin S.G., 2009; Malcius D. et al., 2009). The number of patients with hematogenous osteomyelitis does not tend to decrease (Bordian S.G., 2006). In Russia and the CIS countries, a high level of transition from the acute to the chronic stage remains - 3.1%-30% of cases (Barskaya M.A. et al., 2000; Abaev Yu.K. et al., 2004; Ferreira G.F. et al. ., 2012). In 1832,

Benjamin Brodie first described a picture of a localized abscess of the tibia of an amputated limb of a patient who suffered severe pain in the affected limb, which was not a manifestation of a systemic process, occurred without an acute illness and had no previous infections (Stephens M.M. et al., 1988). Garré described sclerosing "non-purulent" osteomyelitis in 1893 (Harris N.H., 1965). In our country, cases of various forms of primary chronic osteomyelitis were described before the introduction of antibiotics into medical practice (Vengerovsky I.S., 1969; Gurevich I.B., 1939; Diterichs M.M., 1932; Rosenfeld V.E., 1941; Rosenzvit A.I. 1936; Sviridov S.A., 1946).

In 1889 A.A. Bobrov at the III Congress of Russian Doctors and in 1894 E. Lexer proposed the embolic theory, according to which a bacterial embolus, with slow bone blood flow, settles in one of the terminal vessels of the bone (epiphyseal, metaphyseal, diaphyseal). The settling of the embolus is facilitated by the narrowness of the terminal arteries and the slowing of blood flow in them. The settled microorganisms cause swelling of the surrounding tissues, and complete blockage of the lumen of the intraosseous vessel occurs, which causes hypoxia and, subsequently, bone necrosis. The authors believe that in early childhood, the vessels of the metaphysis end blindly and this explains the onset of the inflammatory process, more often in the metaphysis (Grinev M.V., Mikhailov M.K. et al., 1985).

METHODOLOGY

A significant contribution to the development of the theory of the pathogenesis of osteomyelitis was the experiments of the Smolensk pathologist Professor S.M. Derizhanov in 1837-1840. The author induced sensitization of rabbits with horse serum. Then, by introducing a resolving dose of serum into the bone marrow cavity, he received aseptic allergic osteomyelitis. Based on these experiments, S.M. Derizhanov believed that bacterial emboli do not play any role in the pathogenesis of osteomyelitis. The disease develops only due to sensitization of the body and the occurrence of aseptic inflammation in the bone, which occurs from a variety of reasons. In an osteomyelitic lesion, proliferative changes in the periosteum and Haversian canals compress the vessels from the outside, and swelling of the walls of the vessels themselves reduces their lumen from the inside. All this complicates and disrupts blood circulation in the bone, contributing to the occurrence of osteomyelitis (Derizhanov S.M.). Indirect signs of autoallergic inflammation against the background of previous sensitization were revealed in their studies by A.A. Gorevoy et al., namely, an increase in leukocytes, ESR, a shift in the leukocyte formula to the left, an increase in the number of eosinophils, signs of hypercoagulation, an increased number of circulating antibodies with a decrease in phagocytosis rates, characteristic changes in the protein composition and physicochemical properties of blood plasma. (Gorevoy A.A. et al., 2002).

The biofilm population is thus a constant source of virulent pathogens. (Ciemy G., 2011; Walter G., 2012).

Currently, a number of foreign authors classify chronic nonbacterial osteomyelitis (CNO) as an autoinflammatory disease (McGonagle D. and McDermott M. F., 2006;

Hofmann S.R. et al., 2012; Miettunen P. et al., 2009). Autoinflammatory diseases are rare disorders characterized by repeated episodes of fever and inflammation in the absence of high titers of autoantibodies, autoreactive T lymphocytes and underlying infection. The relationship with other autoimmune and autoinflammatory diseases such as palmoplantar pustulosis, chronic inflammatory bowel disease, psoriasis, c-ANCA positive vasculitis, Takayasu arteritis, and IL-1 receptor antagonist deficiency is debated. (Hamel J. et al., 2011; Iyer R.S. et al., 2011; Aksentijevich I. et al., 2009). The basis of the autoinflammatory mechanism is believed to be cytokine dysregulation, which can occur at different levels: transcriptional disruption (as a result of gene variability) and epigenetic modifications. Cytokine imbalances can cause disruption of immune homeostasis by increasing or decreasing inflammatory responses, which in turn may cause susceptibility to infection or autoimmune disorder.

A theory of the occurrence of bone tissue necrosis during relapses of CRHO, based on the occurrence of thrombosis and embolism in the microcircular bed, resulting from disturbances in the coagulation and fibrinolytic systems of the blood, has been proposed. They published the results of surgical treatment of 69 patients with CRHO of various locations in combination with heparin and streptokinase. According to the authors, the proposed method gives positive results and reduces the frequency of relapses of CRHO.

In order to correct increased blood viscosity, hypercoagulation phenomena, accompanied by disruption of microcirculatory processes during chronic hose, it is recommended to administer hyperosmotic solutions, as well as forced diuresis in the postoperative period.

However, these attempts are not systemic in nature and do not affect all links in the chain of pathogenesis of relapse of CRHO. In the literature available to us, we have not found any works describing, much less indicating, correction of the LPO-antioxidant system in the treatment of CRHO. There is no information about such a systemic treatment of CRHO, in which a complex and consistent effect on all parts of the pathological process associated with the formation of bone necrosis would be noted.

The school has a significant difference in the surgical rehabilitation of patients with bone tissue defects after hematogenous osteomyelitis. Ilizarov [1,2,3,4].

He gave a quantitative description of RVG depending on the duration of the disease. The author showed that in patients admitted in the first 3 days of the disease, there was a shift in the quantitative indicators of RVH. These data allowed the author

to conclude that in the early stages of development In the case of CHO, there were functional circulatory disorders, which later developed into organic ones with the formation of avascular zones and foci of necrosis.

He indicated pronounced circulatory disorders in paraosseous tissues (vasospasm, their hypertonicity, increased volumetric pulse, etc.) in the affected limb, which occur much later than intraosseous ones [12].

In case of acute respiratory syndrome, the greatest changes in the coagulogram are observed in patients 6-12 days from the onset of the disease and are manifested in a shortening of whole blood coagulability [13]. Plasma tolerance to heparin and thromboplastin activity increase with inhibition of heparin content and fibrinolytic activity of the blood.

Disturbances in the hemostatic system in patients with acute respiratory syndrome in the form of hypercoagulation were discovered [14].

Scientific research and experimental work of a number of authors have shown that bone necrosis in osteomyelitis is the result of damage to the intraosseous circulation, resulting from disturbances in the coagulation and fibrinolytic systems of the blood.

ANALYSIS RESULTS

According to some authors, clinical and experimental data showed an increase in the overall activity of the blood coagulation system in the septicopyemic form of CSO; in the local form of the disease, disturbances in the coagulation system were insignificant. Other authors point to the possibility of developing disseminated intravascular coagulation in patients with acute respiratory syndrome and even suggest that this syndrome occurs in one anatomical space without the manifestation of pronounced changes in the coagulation and fibrinolytic systems of the blood [13,14,15].

Many authors associate relapses of chronic osteomyelitis and unsuccessful outcomes in the treatment of chronic osteomyelitis with the fact that bone, consisting of 70% inorganic substance and equipped with specific microcirculation, is not able to provide collateral microcirculation. This contributes to the formation of thrombosis and embolism, which, by complicating the blood supply to various areas of bone tissue, is the cause of bone necrosis [15.16.17].

Disturbances in the microcirculatory system lead to a decrease in oxygen saturation of tissues, disrupt its normal metabolism, which in turn leads to inhibition of all other metabolic processes in ischemic tissues, which is a fundamental point in the occurrence of the pathological process Metabolism of oxygen in purulent tissue previously studied in more detail due to more favorable methodological possibilities. On the other hand, the pathogenesis of osteomyelitis and purulent wounds of soft tissues has many common mechanisms, since their biological essence is the same - the process of inflammation, which occurs with excessive migration of macrophages and

leukocytes to the area of tissue damage. Naturally, clinical and biochemical changes in the body during osteomyelitis are qualitatively similar to other processes occurring with an inflammatory component [17].

The importance of the required amount of oxygen for the healing of a clean wound has been shown in experimental works and others. At the same time, it was discovered that a significant part of the damaged tissue is in non-optimal conditions of low oxygen pressure and the wound healing process occurs under hypoxic conditions.

In conditions of an infected wound, hypoxia is further aggravated and reaches anoxia. This conclusion was made by discovering the absence of oxygen in the dead space of infected wounds, starting from the 10th day. A decrease in critical oxygen pressure, which is different for different types of cells, causes a deterioration in tissue metabolism.

Thus, based on experimental data, it was shown that there is a hypoxic gradient in wounds with incomplete blood circulation - i.e. the center of the lesion relative to the edges of the wound and surrounding tissues is hypoxic. The edges of the wound and surrounding tissue show abnormally high oxygen pressure, approaching in many places the pressure measured in the arteries. Based on this, it has been suggested that low oxygen pressure in the center of a purulent wound may be biologically beneficial to the wound [18.19.20]. As for the metabolism of oxygen in bone tissue, it has been shown that with low oxygen pressure in the atmospheric air, healing of fractures occurs more slowly. Studies have shown that acute tissue hypoxia slows down bone regeneration, reducing both the synthesis of collagen intercellular tissue substance and mineralization. Hyperbaric oxygen saturation has been found to stimulate fracture healing. Low oxygen pressure in bone tissue was discovered in osteomyelitis. They also showed that a decrease in the partial pressure of oxygen in the tibia during osteomyelitis can be caused by three reasons: microorganisms use oxygen in the process of their vital activity, infection intensifies the inflammatory process, as a result of which oxygen consumption increases and microorganisms, penetrating into the microcirculation system, reduce oxygen supply. [17,18,20].

Conclusion

Most cases of osteomyelitis are caused by the spread infections from adjacent areas or open wounds, and the infection is often polymicrobial and/or includes S. aureus. Osteomyelitis should be considered in patients who complain of local pain in the peripheral bones, fever, malaise, as well as local, resistant spinal pain and weakness, especially in the presence of risk factors for recent bacteremia. CT or MRI should be obtained because in osteomyelitis, radiographic findings may be unrevealing for > 2 weeks after onset. Initial therapy should include broad-spectrum antibiotics. For best results, treatment should be based on bone culture results.

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