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Research Article

Features of Regeneration in the Area of Humerus Fracture on the Background of Osteoporosis

Konev VP, Moskovskij SN, Krivoshein AE, Sorokina VV, Shishkina YuO, Linnik MM, Saydasheva EM and Milto NS*

Omsk State Medical University, Omsk, Russia

***Corresponding Author:** Milto NS, Resident, Omsk State Medical University, Omsk, Russia.

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Abstract

The work is devoted to morphological studies in various types of humerus injury against the background of osteoporosis. Injury to the bone tissue triggers an additional cascade of processes, in which the central zone is dominated by the processes of bone tissue remodeling with the formation of granulation tissue, and the development of chondral callus. With an increase in the terms of mobilization in the fracture zone against the background of osteoporosis, histological signs of intermediary and endosteal callus are preserved. A lamellar bone with a compact organization, with a characteristic osteon structure, with primary strength characteristics in the fracture zone against the background of osteoporosis is no longer formed.In addition, against the background of osteoporosis with uneven calcification of bone and surrounding dense tissues, with inflammatory and degenerative-dystrophic processes, as well as due to prolonged mobilization of bones and joints, contractures of large joints are formed in the articular part of the bone and cartilage of the joint itself, accompanied by persistent restriction of movements, arthrosis and arthritis.

Keywords: Osteoporosis; Regeneration; Humerus; Fracture; Bone

Introduction

More than 150 years have passed since the time when pathological processes in bone tissue were first recorded, X-ray changes in bones with “transparency of the bone pattern” were revealed. For a period of about 100 years, clinical and instrumental criteria for osteoporotic changes in bone tissue have been established. Almost 40 years have passed since William Albright outlined the modern theories of osteoporosis. To date, new technological techniques for diagnosis and treatment are being developed and put into practice. It is known that fractures on the background of osteoporosis require a longer period of immobilization. This is due to the fact that, against the background of reparative processes, destructive activity in the bone tissue is noted. The inclusion of regenerative compensatory mechanisms leads to an increase in anabolic processes both in bone tissue and in dense and soft tissues in the fracture zone. In this regard, against the background of osteoporosis, with prolonged mobilization of bones in the articular part of the bone and cartilage of the joint itself, contractures are formed, accompanied by persistent restriction of movements, arthrosis and arthritis. However, the reparative processes, regeneration mechanisms, as well as the recovery time in the fracture zone in osteoporosis have not been sufficiently studied [1,2].

The solution of this problem is not only of theoretical importance, but can also create prerequisites for practical use, namely, the prevention of possible complications in the form of pathological or prolonged course of the processes of callosity formation during the healing of fractures [3,5,6].

New technological methods for the treatment of bone fractures and their complications (which are based on the stimulation of osteoreparation with simultaneous treatment of osteoporosis), additional clarifying diagnostic methods, preventive measures will help to reduce the duration of stay of patients in hospital, the duration of disability [7], associated with complications, and most importantly – to prevent the risks of the formation of a pathological fracture, instability of bone fragments in fracture zone, pathological processes in the joints near the fracture.

The purpose of the study - to establish the features and mechanism of the humerus regeneration against the background of osteoporosis.

Materials and Methods

A prospective study was conducted from January 2019 to January 2020 in the clinic of BUZOO “KMHC MZOO” (Omsk, Russia), on the basis of the Department of Traumatology No. 1. The study included 82 patients aged 20 to 59 years with a fractured humerus. The diagnosis of osteoporosis was established according to the diagnostic criteria adopted in clinical practice; the obtained clinical and morphological parallels were investigated on the surgical material obtained in the clinic during traumatic orthopedic operations. The control group included 37 patients aged 20-38 years without radiological signs of osteoporosis. For morphological examination, material was taken in the fracture zone in the presence of clinical indications from the humerus. Some blocks were taken from the metaphysis, others from the diaphysis (injury zone). The material was taken in the presence of clinical indications at various times of observation of the patient (injured). The taken material was fixed in 10% neutral formalin and decalcified in 0.1% hydrochloric acid solution. The prepared micro-preparations were stained with hematoxylin and eosin. Individual sections were stained using the Van Gieson method.

Statistical processing of the obtained data was carried out by methods of variational statistics using standard packages of Microsoft Excel 2010, Statistica 12.0, Biostat. When creating the database, the MS Excel spreadsheet editor was used.

Results and Discussion

In the early stages, in the phase of inflammation, both in the study group and in the control group, damage to the vascular wall with hemorrhage into the surrounding soft tissues, into the cortical plate area, and the periosteum were detected. The features of the traumatic inflammation phase – migration in the lesion of leukocytes and monocytes, hematoma organization, proliferation of fibroblastic–like elements and endotheliocytes - were not revealed. The phase of inflammation during histological examination proceeds the same way and the background pathology does not affect the course of the injury. Based on this, the results of microscopic examination were evaluated and analyzed on the 14th-15th day after the injury (two weeks), on the 21st-22nd day after the injury (three weeks) and within 30 days after the injury (approximately 5 weeks after the injury).

In the control group, in the second week after the injury, differentiation of granulation tissue in the fracture zone into osteoblasts and chondroblasts was noted. Along with that, the primary callus appears to be coarse-fibrous connective tissue and fibrous tissue that fills the gap between the ends of the damaged bone.

Morphological examination of bone tissue 2 weeks after the injury on the background of osteoporosis showed that during this period there was resorption of compact bone, which manifested itself in thinning of bone plates, with uneven resorption of the endost and periosteum. At the same time, the thinned bone tissue was compacted. Connective tissue in the periosteum area proliferated in the area of the fracture itself, the formation of chondral bone callus was observed, while in addition to hyaline cartilage, connective tissue proliferation was also noted.

On day 14, a significant compaction of the compact bone was observed due to the neoplasm of fibrocytic cell mass [4]. At the same time, the transformation of fibroblasts and fibrocytes into osteoblasts was observed, which, unlike the preceding cells, were more intensively stained with eosin, the cell nuclei were larger and hyperchromic. Bone mass neoplasm was observed [4]. The periosteum tissue remained thickened.

The bone plates became uneven in thickness, basophilic. Chondromatous degeneration of bone fragments was noted in the periosteum (Figure 1), and an enlightened cell-free stripe appeared in the endosteum. The bone marrow has become edematous, few-cell with a predominance of fat cells. The Haversian canals were unevenly expanded and filled with lipocytes, in other areas with granulation tissue with inflammatory cells of both polynuclear and mononuclear origin [4].

The spongy bone had thinned bone septums, in some areas they were accompanied by small growths of hyaline cartilage. Slowing down the regeneration of a humerus fracture is associated with the presence of osteoporosis. At the same time, no changes were detected in the bone tissue itself (Table 1).

Terms Micromorpho-metricindicators	14-15 days after injury (two weeks)	14-15 day after injury (two weeks) withosteoporosis	21-22 days after injury (three weeks)	21-22 day after injury (three weeks) with osteoporosis
Thickness of the bone septum on the side of the endost	12,1 ± 0,8	10,8 ± 1,1	17,5 ± 2,4	14,3 ± 1,8
Thickness of the bone septum on the side of the periosteum (9-34 microns)	14,3 ± 2,5	11 ± 1,0	18,1 ± 2,8	15,8 ± 1,7
Width of the Haversian canals (5-36 microns)	4,6 ± 0,5	8,3 ± 1,7	9,1 ±2,7	14 ± 3,6
Number of vessels in the field of view: Periosteum	18,0 ± 1,1	21,1 ± 1,8	15,8 ± 1,4	18,2 ± 1,8
Number of vessels in the field of view: Corticallayer	14 ± 0,9	16 ± 1,2	15,4 ± 1,3	15,7 ± 1,6
Number of vessels in the field of view: Spongylayer	21 ± 1,4	19,7 ± 1,6	18 ± 2,1	17,4 ± 0,9
The number of micro-fractures in the field of view	1,8 ± 0,1	1,7 ± 0,2	3,6 ± 0,5	5,1 ± 0,8
Number of osteons in the field of view	8 ± 0,9	7 ± 1,1	6 ± 2,1	7 ± 0,9
Thickness of the periosteum (950 microns ± 10 microns)	757,2 ± 13,1	749 ± 11,3	857 ± 14,9	789 ± 17

Table 1: Morphometric characteristics of bone in normal condition and with osteoporosis in the early stages after injury.

Note: $p < 0.05$.

It can be stated that osteoporosis along the periphery of the fracture zone increased in some degree. It was the presence of complications that made it possible to conduct a morphological study of this material.

Figure 1: Thinning of bone fragments, enrichment with bone marrow lipocytes [6]. Chondromatous degeneration. Staining: hematoxylin and eosin. Magnification: 10. Lens 40.

By the end of three weeks after the injury, in the control group was noted the development of a chondral-type callus, followed by its transition into the formation of osteoid and delicate bone beams, followed by ossification.

In cases of osteoporosis, 21 days after the injury, precipitation of calcium salts and parts of destroyed bone fragments appeared on the border of bone beams and soft-tissue layers. Fibrous and newly formed bone areas around the resorption zone were combined into a common complex. Bone structures adjacent to the regenerative complex were integrated into the restructuring reaction with the appearance of spongy bone sections and the formation of osteoid and coarse-fibrous bone fields (Table 2).

The bone beams became even more deformed and uneven. With insufficient mineralization of bone tissue, intraosseous fractures

Terms Micromorpho-metricindicators		Within 30 days after injury (approximately 4 weeks after injury)	Within 30 days after injury (approximately 4 weeks after injury) with osteoporosis
Thickness of the bone septum on the side of the endost		19,3 ± 1,5	17,2 ± 1,6
Thickness of the bone septum on the side of periosteum (9-34 microns)		21,4 ± 2,8	16,2 ± 1,3
Width of the Haversian canals (5-36 microns)		4,6 ± 0,5	12,3 ± 2,7
Number of vessels in the field of view	Periosteum	18,0 ± 1,1	18,2 ± 1,8
	Corticallayer	14,3 ± 0,9	14,7 ± 1,6
	Spongylayer	22 ± 1,1	18,4 ± 0,9
The number of micro-fractures in the field of view		1,8 ± 0,1	2,9 ± 0,2
Number of osteons in the field of view		8 ± 0,9	7 ± 1,1
Thickness of the periosteum (950 microns ± 10 microns)		817,2 ± 13,1	781 ± 5,3

Table 2: Morphometric characteristics of bone in normal condition and in cases of osteoporosis in the late stages after injury.

Note: $p < 0.05$.

are noted due to thinning and replacement of bone plates. Foci of basophilic staining due to calcium redistribution, as well as chondromatous degeneration are observed in the thickness of osteones [4]. On the periphery of the bone beams, osteoclasts prevailed over osteoblasts. Osteoclasts were located along the bone beams with signs of resorption of the latter. At the same time, they became larger. The Haversian canals became significantly expanded, layers of fat cells, granulation tissue and inflammatory elements appeared in their lumen (Figure 2). Among the latter, lymphoid cells and macrophages of both monocytic and osteoclastic origin prevailed. The appearance of lipomatosis in the bone tissue, in particular in the expanded Haversian canals, or single lipocytes, entailed a decrease in the quality of bone tissue.

Figure 2: Osteoporosis deformity of bone structures, lipomatosis, expansion of the Haversian canals, proliferation of granulation tissue, inflammatory infiltration. Staining: hematoxylin and eosin. Magnification: eyepiece 10, lens 40 [6].

When the sections were stained with the Masson trichromic method, mainly fields of immature coarse-fibrous bone with non-mineralized fields of the chondroosteoid type with high cellularity were observed. In mineralized fields of red color, the density of cellular elements was lower, and in some areas fields with the arrangement of lamellar bone were observed (Figure 3).

Figure 3: The field of coarse-fibrous bone bordering the fibrous tissue (right) and a fragment of the cortical plate (left). The inter-debris zone. Magnification: lens 10, eyepiece 12,5 (x125). Stained with hematoxylin and eosin.

Subsequently, after 30 days at the microscopic level, there is an increase in osteoclasts with the resorption of excessive trabecular coarse-fibrous primary callus. During the same period, osteogenic cells form new trabeculae. The coarse-fibrous bone of the primary callus is gradually removed and replaced by a lamellar bone. At the same time, we observe smooth Haversian canals. The cartilaginous callus undergoes enchondral ossification and is replaced by coarse-fibrous bone trabeculae (Figure 4).

Figure 4: The fracture area is normal (intermediate callus), day 44. Hematoxylin-eosin staining. Magnification: lens x150.

Against the background of osteoporosis, atrophic and destructive changes in the bone were observed by the end of the fifth week after the injury. At the same time, three patients with the most pronounced osteoporosis were presented in the selected array of observations. Dystrophic and atrophic changes spread from the proximal parts of the bone in the distal direction [3,7]. Compact bone plates were unevenly calcified, especially in the edge zones [3,8]. There were beams with layers of osteoid, as well as areas filled with loose fibrous tissue [3,9]. Foci of cell-free enlightenment appeared along the periphery of the bone plates (Figure 5), with the presence of bone fragments and calcinates [3,10].

Loose fibrous connective tissue was observed between the compact bone plates. The Haversian canals remained thin and curved. In the dynamics of observation of patients at various times by the end, a decrease in the infiltrates of cellular elements was noted [3]. Chondroblasts or macrophages, as well as fibrous structures, were intertwined and formed into fibrous bundles [3,11].

Figure 5: Deformed bone beams, preservation of the inflammatory reaction in the Haversian canals. Staining: hematoxylin and eosin. Magnification: eyepiece 10, lens 40.

The basis of pathological processes in bone tissue in cases of osteoporosis is primarily a violation of the structure of collagen fibers with an increase in the gap between collagen fibrils, which leads to a violation of the spatial organization of the organic matrix. This leads to a violation of mineralization, loss of calcium ions, which in its turn affects the charge of bone tissue and the electrostatic forces holding the ionic lattice of hydroxyapatites, and leads to the activation of osteoclasts. At the same time, there is an increase in the processes of destruction and a decrease in the reparative properties of bone tissue. This is exactly what we observe during histological examination [5,6].

The results of morphological examination of bone tissue, at various times after injury on the background of osteoporosis, showed the development of dystrophic and destructive changes in the fracture zone [4,12]. At the same time, they started from the proximal part of the tubular bone and spread along the distal part, mainly along the diaphyseal part [4]. In the initial periods of observation, rapid resorption of bone plates, expansion of the Haversian canals with the development of granulation tissue in them and the appearance of inflammatory infiltration were noted [4]. In subsequent periods, chondromatous degeneration and uneven calcification were noted on the part of the bone plates [4,8,13]. All this is confirmed by morphometric and statistical indicators of bone tissue (Table 1, 2). The compact bone tissue was tightened and stained with eosin more intensively. In the surrounding area of the compact bone, the periosteum was significantly thickened due to the proliferation of fibroblasts and fibrocytes [4,14]. These connective tissue cellular elements, in terms of colorability and size, more actively formed a dense cellular infiltrate around compact bone tissue. From the outside, this infiltrate is in close contact with the layers of the periosteum. The latter looks with foci of lymphohistiocytic infiltration.

A significant compaction of osteoid cellular elements of the osteoid mass was observed in the compact bone tissue [4]. At the same time, the pre-formed bone tissue differed in tinctorial properties and density from the newly formed bone tissue [4]. If the foci of ossification and petrification prevailed in the composition of the pre-formed bone tissue, in the composition of the newly formed bone tissue there was a lot of fibrous osteoid mass, the cellular elements were large and active. The Haversian canals were expanded, osteoblasts and osteoclasts were preserved in them [2,4,5,12].

Thus, with osteoporosis, an inflammatory reaction persists in the bone fracture zone against the background of active regenerative processes, which preserves the productive formation of coarse-fibrous tissue in the fracture zone. The activity of osteoblasts and osteoclasts leads to uneven ossification of not only dense, but also surrounding soft tissues in the fracture zone. Even after 30 days, there are no signs of the formation of a full-fledged secondary callus in the fracture zone.

Conclusion

The results of histological examination of bone tissue in a fracture on the background of osteoporosis allow us to establish a connection between new knowledge obtained by studying bone tissue with the use of scanning electron microscopy, atomic force microscopy and clinical manifestations of osteoporosis in the post-traumatic period. Imperfect osteogenesis with a violation of the spatial organization of collagen fibers leads to an increase in the distance between the latter. Which in its turn affects the mineralization of bone tissue. Violation of electrostatic forces in the mineral lattice is a trigger mechanism in which reparative processes have already been started in the bone tissue against the background of osteoporosis.

Bone tissue injury in the form of a fracture triggers an additional cascade of processes, in which the processes of bone tissue remodeling with the formation of granulation tissue and the development of chondral-type callus prevail in the central zone. As a rule, this is an indication for an increase in the time of bones and joints mobilization in the fracture zone. Even in this case, in the process of remodeling in the fracture zone against the background of osteoporosis, histological signs of intermediate and endosteal bone callus remain. Lamellar bone with a compact organization, with a characteristic osteonic structure, with primary strength characteristics in the fracture zone against the background of osteoporosis is no longer formed. But in addition, against the background of osteoporosis with uneven calcification of bone and surrounding dense tissues, with inflammatory and degenerative-dystrophic processes, as well as due to prolonged mobilization of bones and joints, contractures of large joints are formed in the articular part of the bone and cartilage of the joint itself, accompanied by persistent restriction of movements, arthrosis and arthritis [10,14].

In cases when the rehabilitation periods are lengthened and go beyond the average terms of bone tissue repair, as well as in cases of the formation of arthrosis, contractures, false joints, it is necessary to prescribe additional research methods, including computer multispiral tomography, determination of optical (densitometric) bone density, the condition of the cartilaginous plate of the bone and the cartilage itself. This will allow us to establish not only the true cause of pathological processes, to identify background pathology in the form of osteoporosis, but also to reduce the risks of possible complications in the form of pathological or prolonged course of the processes of corneation during fracture healing.

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