South Russian Journal of Cancer 2020, v.1, №4, p. 6-14
https://doi.org/10.37748/2687-0533-2020-1-4-1

ORIGINAL ARTICLE

THE FIRST RESULTS OF COMBINED TREATMENT OF GIANT CELL TUMOR OF BONE

A.A.Barashev, V.V.Mozulyaka, T.V.Ausheva*, Yu.R.Vinnik, L.N.Vashchenko, E.M.Nepomnyashchaya, P.V.Chernogorov

National Medical Research Centre for Oncology of the Ministry of Health of Russia,
63 14 line str., Rostov-on-Don 344037, Russian Federation

ABSTRACT

Purpose of the study. To evaluate the effectiveness and possibility of wide clinical use of denosumab in neoadjuvant mode in patients with giant-cell bone tumors to simplify the operation by reducing the size of the tumor, consolidating pathological fractures, improving the quality of life, restoring the function of adjacent joints, by conducting 2 courses of denosumab as neoadjuvant targeted therapy for patients with giant-cell bone tumors, as well as evaluating morphological changes in tumor.

Materials and methods. Considering the data on the efficacy of denosumab, all 10 patients underwent 2 courses of Denosumab 120 mg subcutaneously 1 time per month, as a neoadjuvant targeted therapy for a giant cell bone before performing a surgical treatment. The morphological picture was analyzed before and after the start of treatment, and the clinical and radiological results were evaluated.

Results. A similar clinical picture was observed in all 10 cases involving pain relief and restoration of support ability of the bone. X-ray changes demonstrated the development of sclerotic processes in the foci of lytic destruction. Consolidation of pathological fractures was observed.

The main changes determining the clinical and radiological characteristics were associated with the morphological processes occurring in the tumor under the influence of denosumab.

The morphological picture in the surgically removed bone samples was associated with the development of fibrosclerotic processes leading to the consolidation of pathological fractures.

The histological changes were assessed at the light-optical level. Tumor cells (osteoblasts and osteoclasts) were replaced with fibrous tissue of varying maturity. That is, a response to the therapy (pathomorphosis in the tumor) was observed under the action of denosumab.

Conclusions. Denosumab in neoadjuvant targeted therapy for patients with giant cell bone tumors prior to surgical treatment allows reduction in tumor sizes and consolidation of pathological fractures. The functions of adjacent joints were restored during Denosumab treatment. Improvements in the quality of life of patients were registered. The clinical and radiological effect of the therapy corresponded to the morphological changes occurring in the tumor. All of the above made it easier to perform surgery.

Keywords:
giant cell tumor of bone, denosumab, targeted therapy, therapeutic pathomorphosis, tumor sclerosis, a monoclonal human antibody.

For correspondence:
Tatyana V. Ausheva – Cand. Sci. (Med.), oncologist at the Department of bone, skin, soft tissue and breast tumors № 1, National Medical Research Centre for Oncology of the Ministry of Health of Russia, Rostov-on-Don, Russian Federation.
Address: 63 14 line str., Rostov-on-Don 344037, Russian Federation
E-mail: tatanaauseva@gmail.com
ORCID: https://orcid.org/0000-0002-7073-9463
SPIN: 5069-4010, AuthorID: 264138
Researcher ID: AAQ-9943-2020

Information about funding: no funding of this work has been held.
Conflict of interest: authors report no conflict of interest.

For citation:
Barashev A.A., Mozulyaka V.V., Ausheva T.V., Vinnik Yu.R., Vashchenko L.N., Nepomnyashchaya E.M., Chernogorov P.V. The first results of combined treatment of giant cell tumor of bone. South Russian Journal of Cancer. 2020; 1(4): 6-14. https://doi.org/10.37748/2687-0533-2020-1-4-1

Received 21.01.2020, Review (1) 02.07.2020, Review (2) 07.07.2020, Accepted 01.12.2020

Южно-российский онкологический журнал 2020, т.3, №4, с. 6-14
https://doi.org/10.37748/2687-0533-2020-1-4-1
ОРИГИНАЛЬНАЯ СТАТЬЯ

ПЕРВЫЕ РЕЗУЛЬТАТЫ КОМБИНИРОВАННОГО ЛЕЧЕНИЯ ГИГАНТОКЛЕТОЧНОЙ ОПУХОЛИ КОСТИ

А.А.Барашев, В.В.Мозуляка, Т.В.Аушева*, Ю.Р.Винник, Л.Н.Ващенко, Е.М.Непомнящая, П.В.Черногоров

ФГБУ «НМИЦ онкологии» Минздрава России,
344037, Российская Федерация, г. Ростов-на-Дону, ул. 14-я линия, д. 63

РЕЗЮМЕ

Цель исследования. Оценить эффективность и возможность широкого клинического использования препарата деносумаб в неоадъювантном режиме у больных с гигантоклеточной опухолью костей для упрощения выполнения операции за счёт уменьшения размеров опухоли, консолидации патологических переломов, улучшения качества жизни, восстановления функции смежных суставов, путём проведения 2-х курсов деносумаба в качестве неоадъювантной таргетной терапии больным с гигантоклеточными опухолями костей, а также оценки морфологических изменений в опухоли.

Материалы и методы. Учитывая данные об эффективности деносумаба, всем 10 пациентам было проведено 2 курса деносумаба 120 мг подкожно 1 раз в месяц в качестве неоадъювантной таргетной терапии по поводу гигантоклеточной опухоли кости перед проведением хирургического лечения. Осуществлено изучение морфологической картины до и после лечения, а также оценены клинико-рентгенологические результаты.

Результаты. Во всех 10 наблюдениях была отмечена однотипная клиническая картина, выражавшаяся в уменьшении болевого синдрома, восстановлении функции конечности.

Рентгенологические изменения позволили констатировать развитие склеротических процессов в очагах литической деструкции. В местах патологических переломов наблюдали их консолидацию. Основные изменения, обусловливающие клинико-рентгенологические характеристики были связаны с морфологическими процессами, происходящими в опухоли под действием деносумаба. Морфологическая картина в удаленных операционных препаратах костей была связана с развитием фиброзносклеротических процессов, приводящих к консолидации патологических переломов. Гистологические изменения были оценены на светооптическом уровне. При этом происходило замещение опухолевых клеток (остеобластов и остеокластов) фиброзной тканью разной степени зрелости. То есть под действием деносумаба наблюдался ответ от проводимой терапии (патоморфоз в опухоли).

Заключение. Данный способ применения деносумаба в качестве неоадъювантной таргетной терапии больных с гигантоклеточными опухолями костей перед проведением хирургического лечения позволяет добиться уменьшения размеров опухоли, консолидации патологических переломов. Под действием препарата в ходе лечения происходило восстановление функции смежных суставов. Было отмечено улучшение качества жизни пациентов. Доказательством клинико-рентгенологического эффекта проводимой терапии являлись морфологические изменения, происходящие в опухоли.

Всё вышеизложенное давало возможность выполнения оперативного вмешательства.

Ключевые слова:
гигантоклеточная опухоль кости, деносумаб, таргетная терапия, терапевтический патоморфоз, склероз опухоли, моноклональное человеческое антитело.

Для корреспонденции:
Аушева Татьяна Валерьевна – к.м.н., врач-онколог отделения опухолей костей, кожи, мягких тканей и молочной железы № 1, ФГБУ «НМИЦ онкологии» Минздрава России, г. Ростов-на-Дону, Российская Федерация.
Адрес: 344037, Российская Федерация, г. Ростов-на-Дону, ул. 14-я линия, д. 63
E-mail: tatanaauseva@gmail.com
ORCID: https://orcid.org/0000-0002-7073-9463
SPIN: 5069-4010, AuthorID: 264138
Researcher ID: AAQ-9943-2020

Информация о финансировании: финансирование данной работы не проводилось.
Конфликт интересов: авторы заявляют об отсутствии конфликта интересов.

Для цитирования:
Барашев А.А., Мозуляка В.В., Аушева Т.В., Винник Ю.Р., Ващенко Л.Н., Непомнящая Е.М., Черногоров П.В. Первые результаты комбинированного лечения гигантоклеточной опухоли кости. Южно-российский онкологический журнал. 2020; 1(4): 6-14.
https://doi.org/10.37748/2687-0533-2020-1-4-1

Получено 21.01.2020, Рецензия (1) 02.07.2020, Рецензия (2) 07.07.2020, Принята к печати 01.12.2020

INTRODUCTION

Bone tumors are one of the most difficult sections in the diagnostic aspect, so they occupy a special place in human pathology.

Giant cell tumor of bone (GCT) — a tumor of the skeleton that are related to tumors with uncertain potential of malignancy. In the mid-20th century, J.C. Bloodgood considered this tumor to be absolutely benign, but now this view is revised, since according to a number of authors, primary malignant variants (up to 5% of cases) and the ability of this tumor to malignancy (in 1.5–13% of cases) are described [1]. The peak incidence of GCT is detected in the age group from 18 to 40 years, in children under 12 years of age practically does not occur. Currently, due to the use of immunohistochemical (IHC) research methods, it is possible to isolate malignant fibrous histiocytes from the group of malignant giant cell tumors, which have a similar microscopic picture, and formed a group of malignant giant cell tumors. The most frequent localization of a giant cell tumor is the epimetaphysis of long tubular bones, somewhat less often-the pelvic bones, spine, scapula, and ribs [2].

Clinical manifestations in giant cell tumors are non-specific. The disease manifests itself in discomfort and moderate pain at rest. Patients go to the clinic, in the absence of sufficient examination, they are prescribed non-steroidal anti-inflammatory drugs, physiotherapy, blockades, at the initial stages with a positive clinical effect. In the absence of adequate treatment, the clinical symptoms progress, the pain syndrome becomes persistent. It is also possible to establish a diagnosis of a giant cell bone tumor when contacting a doctor after a previous injury, where an x-ray examination diagnoses a pathological fracture against the background of a giant cell tumor [1].

The x-ray picture of a giant cell tumor is characterized by an eccentrically located focus of destruction of a rounded shape, bone swelling is characteristic, the cortical layer is thinned, and in some places it may not be traced at all. In half of the patients, the lesion is clearly separated from the healthy bone, which takes the form of a sclerotic rim. When the tumor is located in the pelvic bones, ribs, spine, sternum, and scapula, the contours are usually indistinct [1, 3–6].

To date, the method of choice in the treatment of giant cell tumors has been surgical, but with the deepening of knowledge about the pathogenesis of development and molecular genetic features of giant cell tumors, it has been proposed to use in its treatment a targeted effect on RANKL of an inhibitory monoclonal antibody — denosumab. Most of the cases described in the available literature indicate the use of denosumab in the treatment of giant cell cancerous bone tumors as the only treatment method that does not involve surgical removal of the tumor at one stage due to its unresectability [1, 7].

Molecular pathophysiological aspects of a giant cell tumor are characterized by proliferation of mesenchymal stromal cells-bone progenitors that serve as a trigger and support osteoclastogenesis instead of differentiation into osteoblasts and osteocytes. It follows that the main component of the tumor is stromal cells. Resorbing giant cells are the product of interaction between stromal cells and attracted monocytes, which are transformed into tumor cells. Cell markers give a positive reaction with CD45 in multicore giant cells, which indicates that they belong to monocytes. In addition, overexpression of receptors to the ligand of nuclear factor-b activators (RANKL) and stromal factor SDF-1 is detected. Stromal cells produce chemoattractants that can attract monocytes and transform them into resorbing giant cells. Stromal cells also secrete various chemokines, monocyte chemoattractant proteins, and SDF-1 factor, which attract monocytes from the bloodstream and promote their migration to the tumor tissue. These monocytes eventually turn into osteoclast-like multinucleated giant cells. Monocytes Express RANK, which is necessary for differentiation of Mature osteoclasts and their activation in the presence of co-factor, macrophage colony-stimulating factor M–CSF. These osteoclast-like giant multinucleated cells resorb bone tissue leading to osteolysis [8].

Denosumab is a fully human monoclonal antibody (IgG2) that has a high affinity and speci-

ficity for the ligand of the nuclear factor activator receptor APPA B (RANKL) and prevents the activation of the only RANKL receptor — the nuclear factor activator kB (RANK) located on the surface of osteoclasts and their precursors. The RANK ligand is a protein present in the body as a membrane-bound and soluble form. RANKL is the main mediator of the metabolic pathway necessary for the formation, functioning, and survival of osteoclasts, the only cell type responsible for bone resorption. Increased osteoclast activity induced by RANKL is the main cause of bone destruction in metastases of solid tumors to bone tissue and in multiple myeloma. Preventing the RANKL/RANK interaction inhibits the formation, activation, and survival of osteoclasts. As a result, denosumab reduces bone resorption and destruction of bone tissue caused by malignant neoplasms [9–11].

The purpose of the study: to evaluate the effectiveness and possibility of wide clinical use of the drug denosumab in neoadjtuvant mode in patients with giant cell bone tumors to perform surgery by reducing the size of the tumor, consolidating pathological fractures, restoring the function of adjacent joints, and morphological changes occurring in the tumor tissue by conducting 2 courses of denosumab as a neoadjuvant targeted therapy for patients with giant cell bone tumors.

MATERIALS AND METHODS

The authors ' research has shown that 2 courses of denosumab as a neoadjuvant targeted therapy for patients with a giant cell bone tumor before surgical treatment reduces the size of the tumor (Fig. 1A, B), promotes the fusion of pathological fractures, helps restore the function of adjacent joints, and causes sclerotic processes in the tumor tissue (Fig. 2 A-D) [12].

All patients underwent a comprehensive examination, including anamnesis, physical examination, General clinical analysis of blood and urine, biochemical blood analysis, coagulogram, EKG, radiation diagnostic methods (radiography, spiral computed tomography).

In the biopsy material, the tumors had the usual histological structure characteristic of a giant cell tumor with destruction of bone beams, focal hemorrhages, and the presence of osteoblasts and osteoclasts (Fig. 2A). After treatment, all observations showed marked signs of therapeutic pathomorphosis. Between the preserved bone beams, the tumor tissue underwent pronounced dystrophic changes with edema, the disappearance of giant multinucleated cells, and the formation of connective tissue. There were areas of hemorrhage, but a much larger area was occupied by foci of fibrosis, sometimes with the presence of hemosiderin

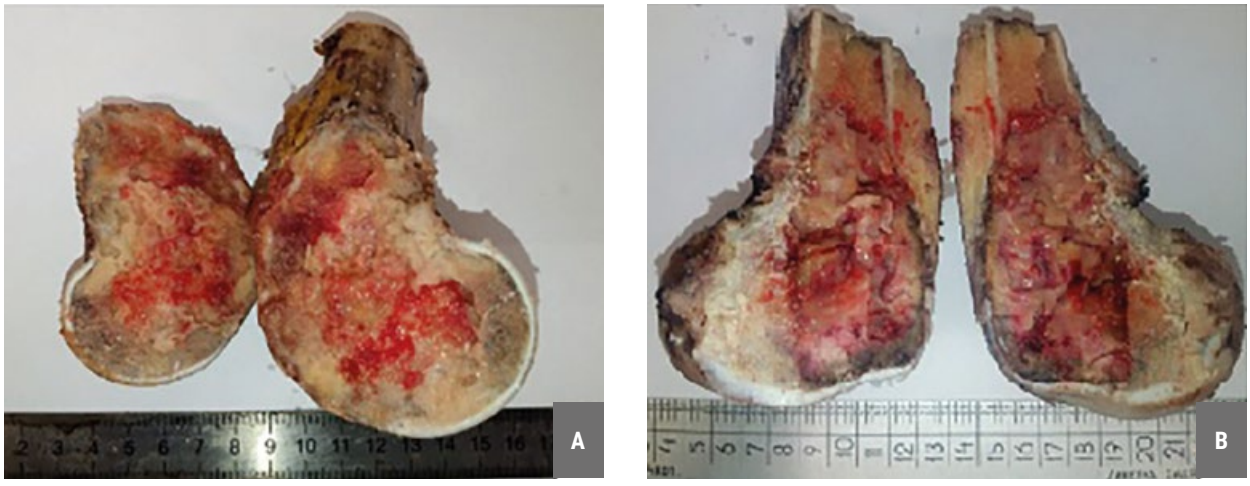

Fig. 1. Type of macroslides on the cut after neoadjuvant targeted therapy with denosumab and in the absence of treatment. A – the lower third of the femur after 2 courses of neoadjuvant targeted therapy with denosumab, a significant reduction in the size of the tumor, and sclerosis of the tumor tissue. B – the lower third of the femur with a tumor before neoadjuvant targeted therapy with denosumab, a large tumor, liquid.

(Fig. 2B, C). In some cases, the tumor tissue was completely absent and was represented by loose and dense fibrous connective tissue with a small number of osteoblasts (Fig. 2G).

Using this method, we treated 10 patients with giant cell bone tumors of various localization.

Clinical, radiological and morphological dynamics were evaluated after 2 courses of denosumab treatment.

In the course of our study, all patients showed a clinical effect of the treatment.

By gender, the patients are distributed equally: 5 men and 5 women.

The median age was 36±3.14 years. The localization of tumors was as follows: the upper third of the tibia-3, the lower third of the tibia-3, the Ilium, the heel bone, the lower third of the femur and the lower third of the humerus according to one observation. Operations performed after neoadjuvant therapy were as follows: bone defect reconstruction using bone grafting for marginal resections and endoprosthetics for segmental resections.

Before starting treatment and including patients for treatment, all patients signed an informed consent.

Here are clinical examples of the use of this method of treatment.

1. Patient A. 51 years old. In June 2017, he was injured at home and received conservative treatment with a temporary positive effect. At the place of residence, he was examined by radiation diagnostic methods: R-gr from 11.12.2017-signs of osteolytic formation of the proximal part of the right femur, pathological fracture (Fig. 3A). Independently asked NMRCO surveyed. A trepan biopsy was performed. The trepan biopsy contains

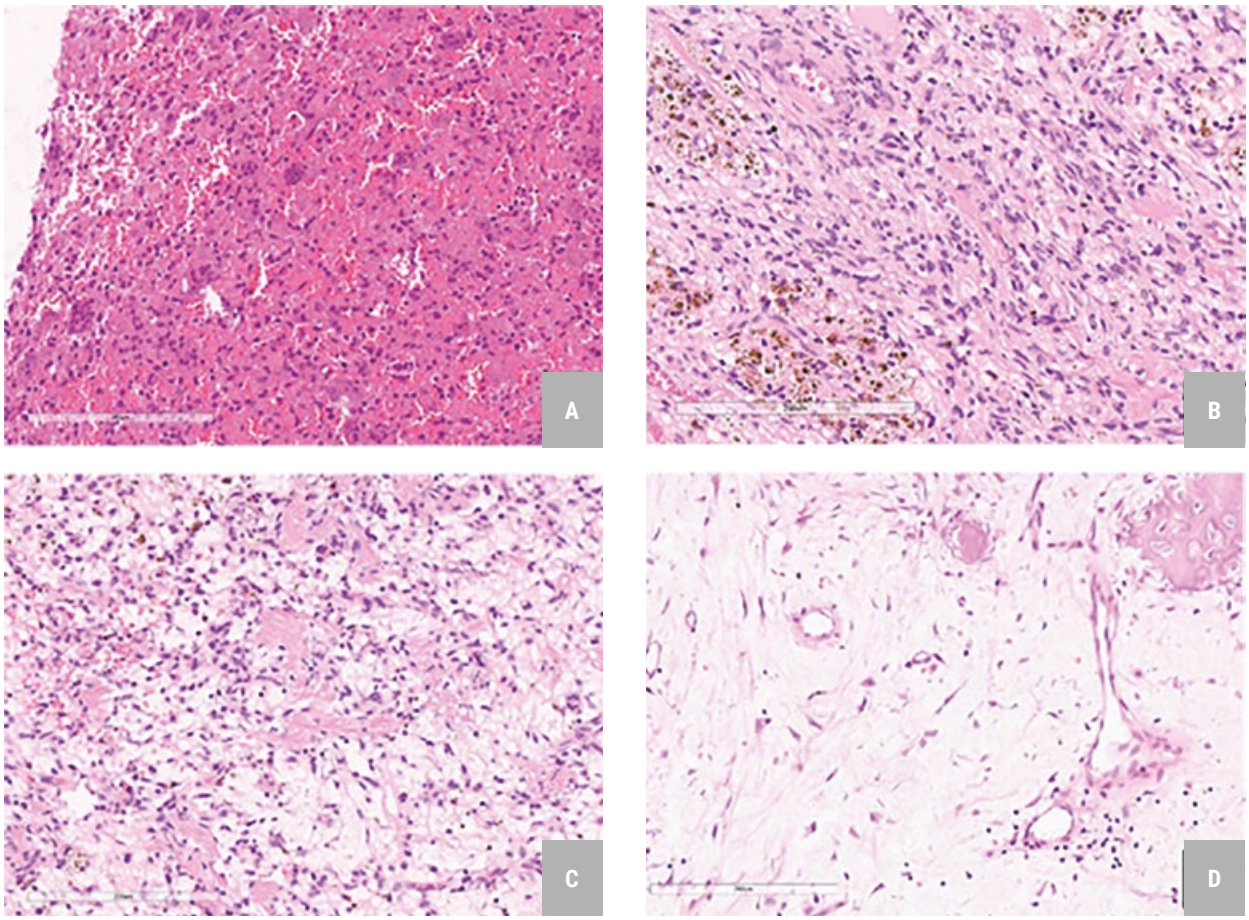

Fig. 2. Morphological changes in giant cell tumors before and after treatment. A – giant cell tumor with hemorrhages-biopsy. B, C – fibrotic tumor tissue with focal hemorrhages, hemosiderin deposition. D – pronounced fibrosis of the tumor between the preserved bone beams. Color: G-E. Magnification: X200

extensive layers of giant cell tumor with hemosiderin deposition and destruction of bone beams. Diagnosis: giant Cell tumor of the upper third of the right femur. Three courses of neoadjuvant therapy with denosumab (120 mg once a month) were performed. After that, the patient had a decrease in pain, he completely refused painkillers, and partially restored his ability to support himself. Radiologically, we observed sclerosis of the focus of lytic destruction, signs of consolidation of the pathological fracture (Fig. 3B). Then the operation was performed in the following volume: segmental resection of the upper third of the right femur with a tumor, replacement of the defect with a hip replacement (Fig. 3B). When examining the surgical material, macroscopically complete consolidation of the pathological fracture of the upper third of the femur. On the cut, the pathological focus is filled with a dense whitish tissue. Histological examination of the surgical material between the bone beams shows fibrous tissue with hemorrhages and foci of myxomatosis.Significant response to the therapy is admitted.

2. Female patient G., aged 45 years. Since October 2016, I have been concerned about pain in my left elbow joint. The pain syndrome gradually increased, there was a restriction of extension. She was observed by an orthopedist at the place of residence, received conservative therapy without effect. In may 2017, she applied to the NMRCO and was examined. SCT of the chest, abdominal cavity, and pelvic organs was performed, but no pathology was detected. On the radiograph of the left elbow joint, there is a focus of lytic destruction in the distal metaepiphysis of the humerus (Fig. 4A). A trepan biopsy was performed. In the biopsy among the blood bundles, single bone beams layers of giant cell tumor. Diagnosis: giant Cell tumor of the lower third of the left humerus. Two courses of neoadjuvant targeted therapy with denosumab (120 mg once a month) were performed. Repeated radiography of the left elbow joint was performed, where sclerosis of the focus of lytic destruction was observed (Fig. 4B). The patient experienced relief of pain, restoration of full range of motion in the left elbow joint. After that, the operation was performed in the following volume: segmental resection of the lower third of the left humerus with a tumor, replacement of the defect with an endoprosthesis of the elbow

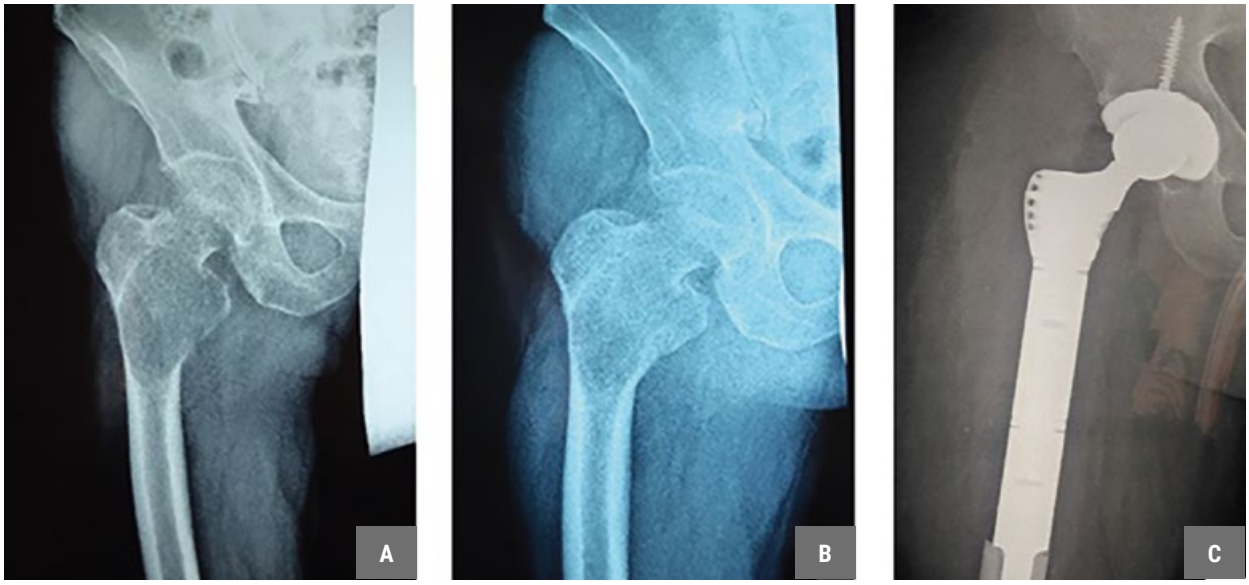

Fig. 3. x-Ray images of the patient. A – before the start of neoadjuvant therapy with denosumab, signs of osteolytic formation of the proximal part of the right femur, pathological fracture. B – after completion of neoadjuvant therapy with denosumab, sclerosis of the focus of lytic destruction, signs of consolidation of the pathological fracture. C – condition after segmental resection of the upper third of the right femur with a tumor, replacement of the defect with a hip replacement.

joint (Fig. 4 C, D). In macroscopic assessment of the surgical material, the lower third of the left humerus with a lumpy bone density tumor in the condyle region, the pathological focus is filled with dense whitish tissue on the cut. When histological examination of the surgical material in the preparations after treatment, there are extensive fields of fibrous tissue with few cellular elements, which can be regarded as a response to the therapy (therapeutic pathomorphosis).

3. Patient K., 68 years old. Pain in the right wrist joint is noted for 6 months. He received conservative treatment with a temporary effect. Radiography was performed at the place of residence, and the volume formation of the distal third of the radius on the right was revealed (Fig. 5A). Asked for a consultation in NMRCO. A trepan biopsy ofthe lower third of the right radius was performed. In the trepan biopsy, there are extensive fields of giant cell tumor among the blood clots. SCT of the forearm and hand bones most likely show signs of the cellular-trabecular phase of a giant cell tumor. SCT of the chest cavity, abdominal cavity and small pelvis from 20.10.2018 year-without a pathology. Diagnosis: giant Cell tumor of the distal third of the right radius. Three courses of neoadjuvant targeted therapy with denosumab (120 mg once a month) were performed. After that, the patient had a decrease in pain, which allowed more than twice to reduce the dose of analgesics taken. X-ray sclerosis of the destruction site (Fig. 5B). Then the operation was performed in volume: segmental resection

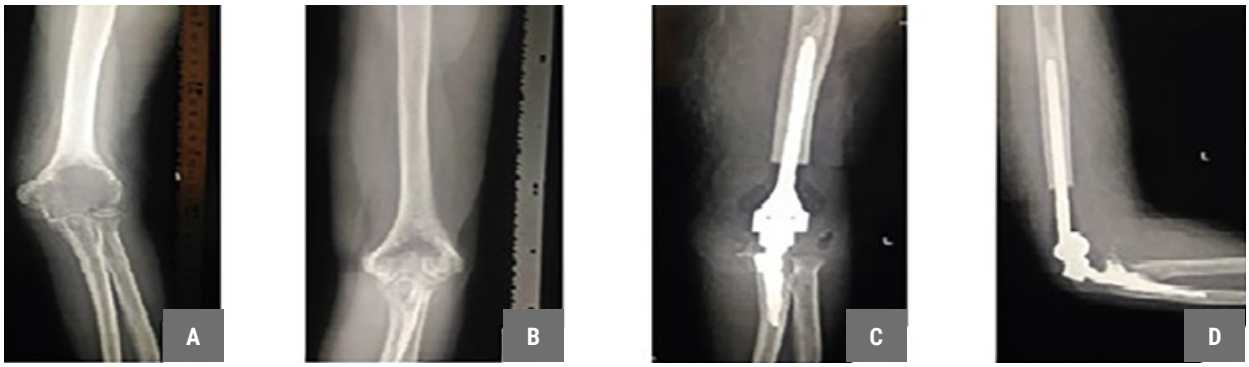

Fig. 4. x-Ray images of the patient. A – before starting neoadjuvant targeted therapy with denosumab, the image shows the presence of a focus of lytic destruction. B – after completing the course of neoadjuvant targeted therapy with denosumab, reducing the size and sclerosing the focus of lytic destruction. C, D – show condition after segmental resection of the lower third of the left humerus with a tumor, replacement of the defect with an elbow joint endoprosthesis in direct and lateral projections.

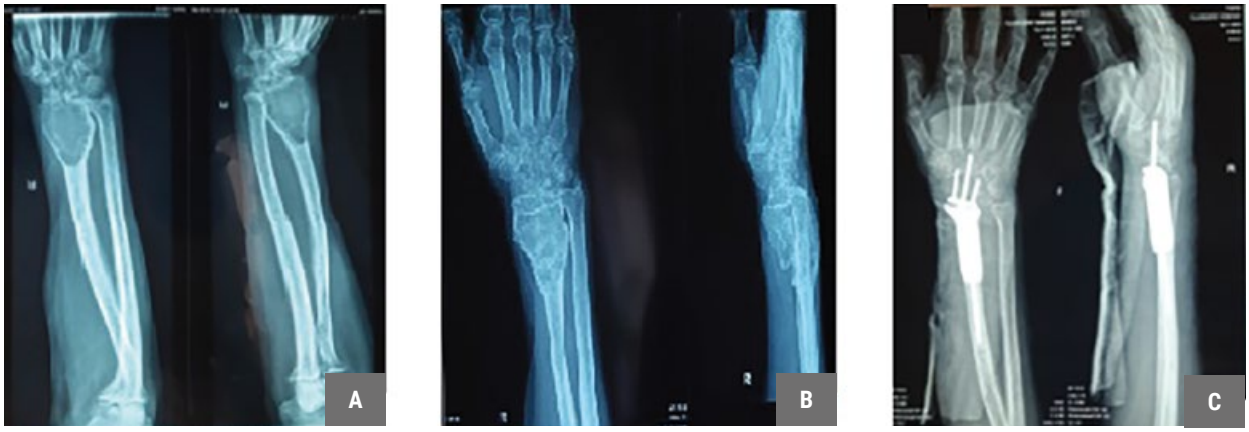

Fig. 5. X-Ray images of the patient. A – before the start of neoadjuvant targeted therapy with denosumab, volume formation of the distal third of the radius on the right. B – after completion of neoadjuvant targeted therapy with denosumab, sclerosis of the focus of lytic destruction is determined. C – condition after segmental resection of the lower third of the right radius with a tumor, replacement of the defect with a wrist joint endoprosthesis.

of the lower third of the right radius with a tumor, replacement of the defect with an endoprosthesis of the wrist joint (Fig. 5B). In macroscopic assessment of the surgical material, the lower third of the right radius is uneven, bumpy, and the pathological focus is filled with dense whitish tissue on the cut. Histological examination of the surgical material in the tumor has extensive fields represented by fibrous tissue. There are tumor fields consisting of loose fibrous connective tissue with multiple myxomatosis, a small number of cellular elements. Histological picture of a giant cell tumor with pronounced therapeutic pathomorphosis.

CONCLUSION

This method of using denosumab as a neoadjuvant targeted therapy for patients with giant cell bone tumors before surgical treatment allows to reduce the size of the tumor and consolidate pathological fractures. Under the influence of the drug during treatment, the function of adjacent joints was restored. There was an improvement in the quality of life of patients. The clinical and morphological effect of the therapy corresponded to the morphological changes occurring in the tumor.

The duration and number of courses are discussed in the literature. However, there is no clear opinion on this issue. In this regard, the observed clinical and radiological data that occur during 2 courses allowed us to implement this technique. At the same time, the result was similar for 2-course therapy. Our results are consistent with the literature data on morphological changes that occur when using denosumab.

Authors contribution:
Barashev A.A. – collection, analysis and interpretation of data, perform operations, the preparation of this article.
Mozulyaka V.V. – concept and design of study,the text writing , processing of the material..
Ausheva T.V. – technical editing, design of the bibliography, preparation of figures.
Vinnik Yu.R. – assistance on surgeries, preparation of an article.
Vashchenko L.N. – scientific editing.
Nepomnyashchaya E.M. – morphological research, scientific editing.
Chernogorov P.V. – scientific editing.

References

1. Zatsepin ST. Bone pathology of adults: a guide for doctors. Moscow: Medicine, 2001, 640 p. (In Russian).
2. Snetkov AI, Frantov AR, Morozov AK, Berchenko GN, Bratkov SYu, Anisimov MA. Diagnosis and treatment of benign tumors and tumor-like diseases in children. Ed. by S.P. Mironov. Moscow: GEOTAR-Media, 2017. (In Russian).
3. Ward WG, Li G. Customized treatment algorithm for giant cell tumor of bone: report of a series. Clin Orthop Relat Res. 2002 Apr;(397):259–270.
https://doi.org/10.1097/00003086-200204000-00030
4. Soloviev YuN. Bone tumor pathology: Practical guidance. Moscow: Practical medicine, 2019, 272 p. (In Russian).
5. Neyshtadt EL, Markochev AB. Tumors and tumor-like bone lesions]. St. Petersburg: Foliant, 2007, 344 p. (In Russian).
6. Berchenko GN, Morozov AK, Semenova LA, Frantov AR. Diagnosis of giant cell reparative granuloma of bones of hands and feet. Bulletin of traumatology and orthopedics named After N.N.Priorov. 2001;2:87–92. (In Russian).
7. Mahson AN, Schupak MU, Bondarev AV. Denosumab. Experience of conservative treatment giant cell bone tumor. Sarcomas of bones, soft tissues, and skin tumors. 2014;(2):24–28. (In Russian).
8. Vladimirova LYu, Abramova NA, Lyanova AA, Storozhakova AE, Popova IL, Tikhanovskaya NM, et al. Denosumab in treatment of bone metastases from solid tumors. Farmateka. 2018;7(360):76-81. (In Russian).
9. VIDAL reference book. Pharmaceuticals in Russia, 2017. (In Russian).
10. Barkowska A, Goryń T, Pieńkowski A, Wągrodzki M, Jagiełło-Wieczorek E, Rogala P, et al. Denosumab treatment

of inoperable or locally advanced giant cell tumor of bone. Oncol Lett. 2016 Dec;12(6):4312–4318.
https://doi.org/10.3892/ol.2016.5246

11. Traub F, Singh J, Dickson BC, Leung S, Mohankumar R, Blackstein ME, et al. Efficacy of denosumab in joint preservation for patients with giant cell tumour of the bone. Eur J Cancer. 2016;59:1–12.
https://doi.org/10.1016/j.ejca.2016.01.006

12. Kit OI, Barashev AA, Mozulyaka VV, Nepomnyashchaya EM, Vashchenko LN, Ausheva TV, et al. Method of combined treatment of giant-cell bone tumor. Patent RU 2696097 C1, IPC A61K; A61R; patent Holders: Federal state budgetary institution "Rostov research oncological Institute" of the Ministry of health of the Russian Federation (RU). Application: no. 2018127819 dated 27.07.2018, published 31.07.2019. Byul. No. 22. (In Russian).

Information about author:

Artem A. Barashev – Cand. Sci. (Med.), traumatologist-orthopedist, Department of bone, skin, soft tissue and breast tumors № 1, National Medical Research Centre for Oncology of the Ministry of Health of Russia, Rostov-on-Don, Russian Federation. ORCID: https://orcid.org/0000-0002-7242-6938, SPIN: 4590-5745, AuthorID: 697517

Viktoriya V. Mozulyaka – resident pediatric oncologist, Department of bone, skin, soft tissue and breast tumors №1, National Medical Research Centre for Oncology of the Ministry of Health of Russia, Rostov-on-Don, Russian Federation.

Tatyana V. Ausheva* – Cand. Sci. (Med.), oncologist, Department of bone, skin, soft tissue and breast tumors №1, National Medical Research Centre for Oncology of the Ministry of Health of Russia, Rostov-on-Don, Russian Federation. ORCID: https://orcid.org/0000-0002-7073-9463, SPIN: 5069-4010, AuthorID: 264138, Researcher ID: AAQ-9943-2020

Yuliya R. Vinnik – resident pediatric oncologist, Department of bone, skin, soft tissue and breast tumors №1, National Medical Research Centre for Oncology of the Ministry of Health of Russia, Rostov-on-Don, Russian Federation.

Larisa N. Vashchenko – Dr. Sci. (Med.), professor, head of the Department of bone, skin, soft tissue and breast tumors №1, National Medical Research Centre for Oncology of the Ministry of Health of Russia, Rostov-on-Don, Russian Federation. ORCID: https://orcid.org/0000-0002-7302-7031, SPIN: 5573-4396, AuthorID: 286598

Evgeniya M. Nepomnyashchaya – Dr. Sci. (Med.), professor, pathologist at the pathology Department, National Medical Research Centre for Oncology of the Ministry of Health of Russia, Rostov-on-Don, Russian Federation. ORCID: https://orcid.org/0000-0003-0521-8837, SPIN: 8930-9580, AuthorID: 519969

Pavel V. Chernogorov – traumatologist-orthopedist, Department of bone, skin, soft tissue and breast tumors №1, National Medical Research Centre for Oncology of the Ministry of Health of Russia, Rostov-on-Don, Russian Federation. SPIN: 4643-4485, AuthorID: 922419