GEORGIAN MEDICAL NEWS

ISSN 1512-0112

No 4 (313) Апрель 2021

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board and The International Academy of Sciences, Education, Industry and Arts (U.S.A.) since 1994. **GMN** carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией и Международной академией наук, образования, искусств и естествознания (IASEIA) США с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения.

Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

GEORGIAN MEDICAL NEWS
Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press; International Academy of Sciences, Education, Industry and Arts (USA).
Published since 1994. Distributed in NIS, EU and USA.

EDITOR IN CHIEF
Nicholas Pirtskhalaishvili

SCIENTIFIC EDITOR
Elene Giorgadze

DEPUTY CHIEF EDITOR
Nino Mikaberidze

SCIENTIFIC EDITORIAL COUNCIL
Zurab Vadachkoria - Head of Editorial council
Michael Bakhmutsky (USA), Alexander Gënning (Germany),
Amiran Gamkrelidze (Georgia), David Elua (USA),
Konstantin Kipiani (Georgia), Giorgi Kamkamidze (Georgia), Paata Kurtanidze (Georgia),
Vakhtang Maskhulia (Georgia), Tengiz Riznis (USA), Revaz Sepiashvili (Georgia)

SCIENTIFIC EDITORIAL BOARD
Konstantin Kipiani - Head of Editorial board
Archimandrite Adam - Vakhtang Akhaladze, Amiran Antadze, Nelly Antelava,
Tengiz Asatiani, Gia Beradze, Rima Beriashvili, Leo Bokeria, Kakhaber Chelidze,
Tinatin Chikovani, Archil Chkhotua, Lia Dvaladze, Tamar Doliashvili, Ketevan Ebralidze,
Otar Gerzmava, Liana Gogiashvili, Nodar Gogebashvili, Nicholas Gongadze,
Rudolf Hohenfellner, Zurab Kevanishvili, Ramaz Khetsuriani, Guram Kiknadze,
Dimitri Kordzaia, Irina Kvachadze, Nana Kvirkvelia, Teymuraz Lezhava, Nodar Lomidze, Marina Mamaladze, Gianluigi Melotti, Kharaman Pagava, Mamuka Pirtskhalaishvili,
Anna Rekhviashvili, Maka Sologhashvili, Ramaz Shengelia, Tamar Zerekidze, Manana Zhvania

CONTACT ADDRESS IN TBILISI

GMN Editorial Board
7 Asatiani Street, 4th Floor
Tbilisi, Georgia 0177

Phone: 995 (32) 254-24-91
995 (32) 253-70-58
Fax: 995 (32) 253-70-58

CONTACT ADDRESS IN NEW YORK

NINITEX INTERNATIONAL, INC.
3 PINE DRIVE SOUTH
ROSLYN, NY 11576 U.S.A.

Phone: +1 (917) 327-7732

WEBSITE
www.geomednews.org

რეზიუმე

ეგზოგენური კრეატინის ეფექტი ხანგრძლივი სტრესის პირობებში შეცვლილ Akt/mTOR სასიგნალო გზაზე

მ.შენგელია, გ.ბურჯანაძე, მ.კოშორიძე, ზ.ქუჩუკაშვილი, ნ.კოშორიძე

ივ. ჯავახიშვილის სახ. თბილისის სახელმწიფო უნივერსიტეტი, ზუსტ და საბუნებისმეტყველო მეცნიერებათა ფაკულტეტი, ბიოლოგიის დეპარტამენტი, საქართველო

ცნობილია, რომ ბუნებრივი ცირკადული რიტმის დარღვევას თან სდევს უჯრედული მეტაბოლიზმის ცვლილება და ქრონიკული სტრესის განვითარება, რაც გულისხმობს როგორც უჯრედის ენერგეტიკული სტატუსის დაქვეითებას,ასევე ანაბოლური რეაქციების შემცირებას. ზემოაღნიშნულის გათვალისწინებით, მნიშვნელოვანია ისეთი ნაერთების მოძიება, რომლებსაც შესწევთ უნარი ქრონიკული სტრესის პირობებში მოახდინონ ამ პროცესების პრევენცია.

ექსპერიმენტში ნაჩვენებია, რომ ცირკადული რიტმის ხანგრძლივი დარღვევის პირობებში კრეატინის ინტრაპერიტონიალური შეყვანა ჰიპოკამპის უჯრედებში ააქტივებს სტრესის შედეგად დაქვეითებული მიტოქონდრიალური კრეატინკინაზას აქტივობას. იმის გათვალისწინებით, რომ უჯრედის ენერგეტიკული მეტაბოლიზმის მიმდინარეობის ერთ-ერთ ცენტრალურ რეგულატორად ითვლება mTOR, შესწავლილია მისი რაოდენობრივი ცვლილებები ხანგრძლივი ცირკადული რიტმის დარღვევის პირობებში და ეგზოგენური კრეატინის გავლენა ამ პროცესზე. მიღებულმა შედეგებმა აჩვენა, რომ ორგანიზმში კრეატინის შეყვანა ზრდის როგორც გააქტივებული mTOR-ის, ასევე მისი აქტივატორის Akt რაოდენობას.

აღნიშნულის გათვალისწინებით, შესაძლებელია ვივარაუდოთ, რომ კრეატინის დადებითი ეფექტი ხანგრძლივი ცირკადული რიტმის დარღვევის პირობებში განვითარებული სტრესის დროს ჰიპოკამპის უჯრედების ენერგეტიკულ მეტაბოლიზმზე გამოწვეულია მისი მოდულატორული მოქმედებით PI3K/Akt/mTOR სასიგნალო გზაზე.

FEATURES OF GRANULATION TISSUE MORPHOLOGY AROUND THE NET ALLOTRANSPLANT WHEN APPLYING POSTOPERATIVE RADIATION THERAPY

Morar I., Ivashchuk A., Bodyaka V., Domanchuk T., Antoniv A.

Higher State Educational Institution of Ukraine Bukovinian State Medical University, Chernivtsi, Ukraine

Patients with oncological diseases of the abdominal organs are known to constitute the highest risk group for the postoperative eventration [1]. In order to prevent the development of the postoperative eventration, the majority of surgeons strengthens the anterior abdominal wall with mesh allografts, but the rate of regeneration and the risk of purulent-septic complications' development from the side of the postoperative wound in patients with cancer has certain features stipulated by the presence of tumorous intoxication, phenomenon of the secondary immunodeficiency cachexia, anemia, etc. [2-4]. The use of complex treatment, which includes postoperative radiation therapy, significantly slows down reparative processes in the irradiation area, that also increases the risk of eventration.

The study of the postoperative teleirradiation therapy influences on the morphology of granulation tissue around reticular allograft will allow to determine more optimally the expediency and safety of this type of treatment in strengthening the anterior abdominal wall in patients with abdominal cancer.

The objective of the article to study the peculiarities of the granulation tissue morphology around the elements of the reticular allograft of the muscular-aponeurotic layer of the anterior abdominal wall when using postoperative distant gamma therapy in the experiment.

Material and methods. The experiment was performed on 168 mature nonlinear rats of middle age of both sexes, weighing not less than 180 g, which were implanted with prolene (Prolene) reticular allograft of ETHICON company into the tissues of the muscular-aponeurotic layer of the anterior abdominal wall, according to the method proposed by us (Pat.106161 dated 25.04.2016) [5].

All experimental animals were divided into two groups – the group of comparison (72 rats) and the main one (96 rats). Animals of the main group, from the 13th to the 19th day after implantation of a reticular allograft, received distant gamma therapy on the organs of the abdominal cavity with gamma-therapeutic device AGAT - P1U isotope Co60, 1.25 MeV, by a single irradiating dose of 2 g, total irradiation dose - 14 g.

Taking of biological material was carried out on the 20th, 30th, 40th and 50th day after surgery, by excision of the muscular-aponeurotic layer of the anterior abdominal wall together with a reticular allograft, under general intravenous anesthesia (solution chloral hydrate 200-250 mg/kg).

The surgical procedures were performed in the vivarium of the Higher State Educational Establishment of Ukraine "Bukovinian State Medical University", in accordance with the national requirements of the "General Ethical Principles of Experiments on Animals" (Ukraine, 2011), which are in line with the Council of Europe Convention about protection of the vertebrate animals used for research and other scientific purposes (dated 18.03.1986).

For light optical examination, at histological investigation bioptates of the muscular-skeletal aponeurotic layer of the ante-

rior abdominal wall were fixed in 10% neutral formalin. Paraffin sections were stained with hematoxylin and eosin. To identify collagen fibers and fibrin the method of staining histological sections with aqueous blue - chromotrope 2 V according to N.Z. Slinchenko was used [6].

Comparison of the number of the granulation tissue cells using computer micro-densitometry (computer program ImageJ 1.48 v) was carried out.

The statistical analysis of the results was carried out in accordance with the type of research and the types of numerical data that were obtained. Distribution normality was verified using the Lilliefors and Shapiro-Wilk tests and by the direct visual evaluation of eigenvalues distribution histograms. Quantitative indices having a normal distribution are represented as mean (M)±standard error (S). In the nonparametric distribution the data are presented as median (Me) as a measure of position, upper (Q75) and lower (Q25) quartiles as a measure of dispersion. Discrete indices are presented in the form of absolute and relative frequencies (percentage of observations to the total number of examined). Parametric tests with the assessment of Student's t-test, Fisher's F-test were used to compare the data that had normal distribution. The median test, Mann-Whitney Rank U-test, and Wilcoxon signed-rank test for multiple comparisons (in the case of dependent groups) were used in abnormal distribution. The Pearson correlation analysis was used to estimate the degree of dependence between variables in parametric distribution and the Spearman rank correlation coefficient was used in the case of the indices distribution that significantly differed from the normal one. In order to compare discrete values in independent groups, the criterion $\chi 2$ of maximum probability (log-likelihood) (MP $\chi 2$) was used; to compare the pairs of discrete values, the calculation of the modification of the exact criterion by Fisher (mid-p) was used. Determination of the diagnostic advantage of the method was performed on the basis of assessing the quality of diagnostic procedures using ROC-analysis, with the determination of sensitivity, specificity, diagnostic value, area under the ROC-curve (AUROC), diagnostic odds ratio (DOR). Statistica for Windows version 8.0 (Stat Soft Inc., USA), Microsoft Excel 2007 (Microsoft, USA) software packages were used for statistical and graphical analysis of the obtained results.

Results and discussion. Uneven structure of the granulation tissue, characterized by areas where blood vessels predominate, places of accumulation of fibroblasts or lymphoid cells, as well as foci with edema of the latter one, is marked in the animals of the main group on the 20th day of observation. In animals of the comparison group, in contrast to the main one, edema of the granulation tissue is absent, and lymphoid cells are mainly found on the periphery of the latter (Fig. 1-4).

On the 30th day of the study, the granulation tissue volume in both groups under study was smaller compared to the 20th day of observation. In the animals of the main group, in contrast to the group of comparison, the granulation tissue edema remains, a larger volume of the latter one is observed as well. Collagen fibers in animals of the main group are thickened and straightened.

On the 40th and 50th days of observation, the morphological picture of granulation tissue in animals of the comparison group remains unchanged. In the main group of animals, the swelling of the granulation tissue is preserved, however, its volume decreases. Areas of lipofuscin accumulation, formed because of irradiation, by means of enhanced lipid peroxidation take place in animals of the main group as well (Fig. 5-8).

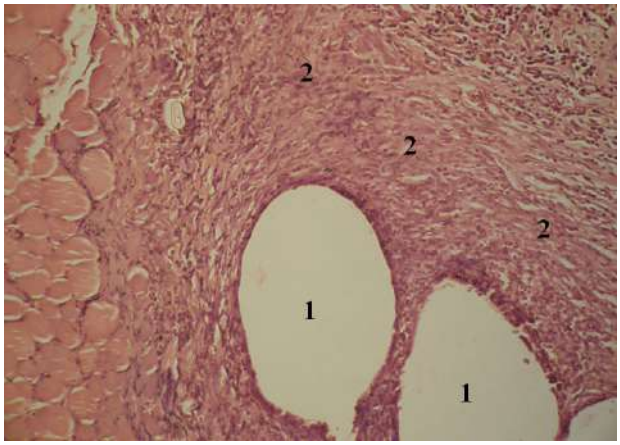

Fig. 1. Photo of micro-preparation of the anterior abdominal wall of the rat of the group of comparison on the 20th day after implantation of the reticular allograft. Elements of the reticular allograft (1). Granulation tissue (2). Hematoxylin and eosin. Vol. 10 ×. Op. 10 ×

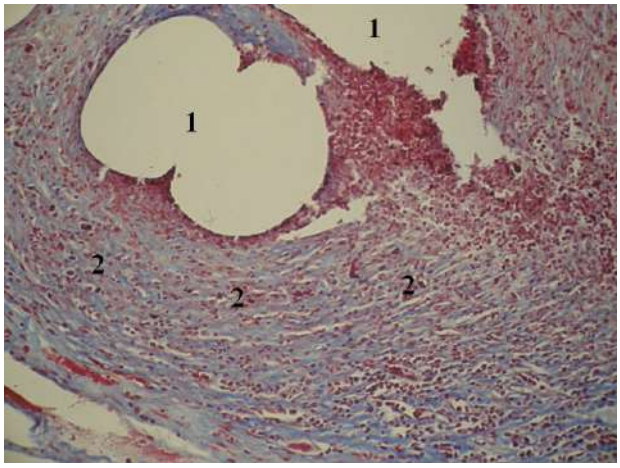

Fig. 2. Photo of micro-preparation of the anterior abdominal wall of the rat of the comparison group on the 20th day after implantation of the net allograft. Elements of the net allograft (1). Granulation tissue (2). Staining with water blue chromotropic 2B. Vol. 10 ×. Op. 10×

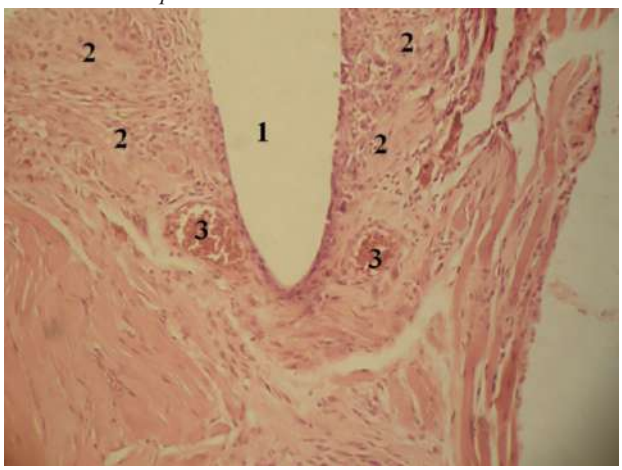

Fig. 3. Photo of the anterior abdominal wall micro-preparation of the rats of the main group on the 20th day after implantation of the reticular allograft. Elements of the reticular allograft (1). Granulation tissue (2). Blood vessels (3). Hematoxylin and eosin. Vol. 10 ×. Op. 10×

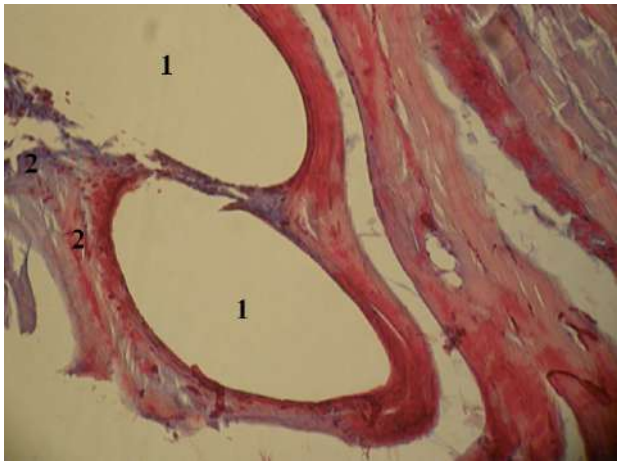

Fig. 4. Photo of micro-preparation of the anterior abdominal wall of the rats of the main group on the 20th day after implantation of the reticular allograft. Elements of the reticular allograft (1). Granulation tissue (2). Staining with water blue chromotropic 2B. Vol. 10 ×. Op. 10×

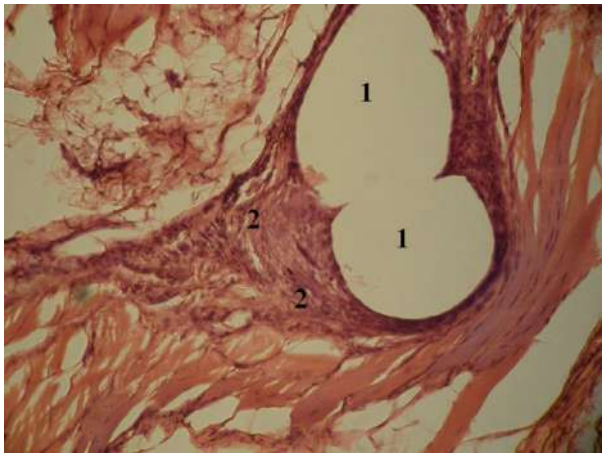

Fig. 5. Photo of the micro-preparation of the anterior abdominal wall of the rat of the comparison group on the 50th day after implantation of the net allograft. Elements of the net allograft (1). Granulation tissue (2). Hematoxylin and eosin. Vol.. 10 ×. Op. 10×

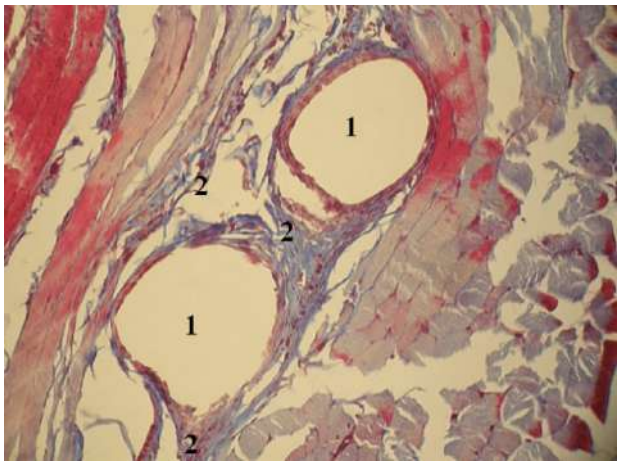

Fig. 6. Photo of the micro-preparation of the anterior abdominal wall of the rat of the group of comparison on the 50th day after implantation of the reticular allograft. Elements of the reticular allograft (1). Granulation tissue (2). Staining with water blue chromotropic 2B. Vol.. 10 ×. Op. 10×

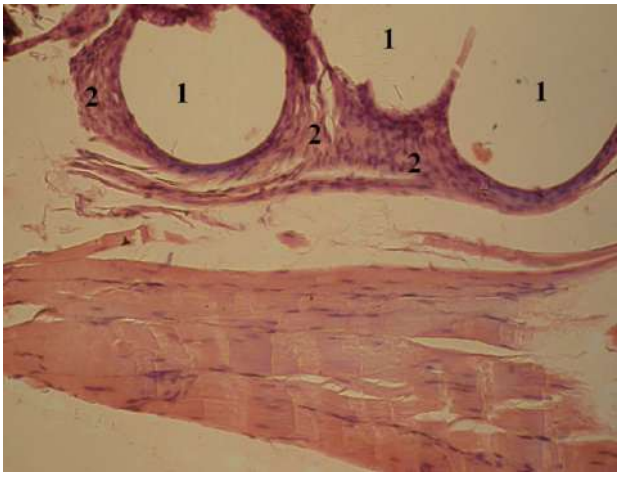

Fig. 7. Photo of the micro-preparation of the anterior abdominal wall of the rat of the main group on the 40th day after implantation of the reticular allograft. Elements of the reticular allograft (1). Granulation tissue (2). Hematoxylin and eosin. Vol. 10 ×. Op. 10×

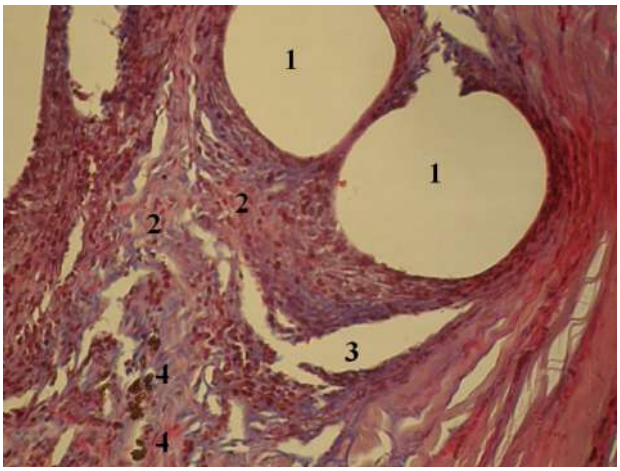

Fig. 8. Photo of the anterior abdominal wall micro-preparation of the main group of rats on the 50th day after implantation of the reticular allograft. Elements of the reticular allograft (1). Granulation tissue (2). The area of edema (3). Lipofuscin accumulation sites (4). Staining with water blue chromotropic 2B. Vol. 10 ×. Op. 10×

For more detailed analysis of the cellular composition of the granulation tissue the indices of the latter one between the animals of both experimental groups, depending on the time following the net allograft implantation were compared by us.

Analyzing the results of the study, presented in Table 1, it should be noted the veritable predominance of the number of fibroblasts on the 30th day of observation in animals of the main group. Throughout the observation period animals of the comparison group showed an increase in the number of fibroblasts, with exception of the 50th day of observation, where this difference against the 40th day is uncertain. An increase in the number of fibroblasts is also marked in the main group of animals throughout the observation period, but on the 40th day there is a probable decrease in their number.

The results of the study, presented in table 2, indicate a probable predominance of the lymphoid cells in animals of the main group throughout the whole period of investigation, with excep-

tion of the 30th day of observation, where on the contrary their number is less. In both groups under study throughout the whole period, a probable decrease in the number of the lymphoid cells is noted on the 40th day of observation, with exception of the main group, where the number of the latter increases.

Evaluating the results, presented in table 3, it should be noted the absence of plasma cells in the group of comparison, starting from the 40th day of observation. Indices of the main group probably prevail only on the 20th day of observation. On the 30th day of observation a decrease in the number of plasma cells is noted in both experimental group, but this difference is uncertain in the comparison group.

Table 1. Granulation tissue fibroblasts around the net allograft in different observation terms after implantation of the latter M±m), %

Terms of observation, day	Group of animals	
	Comparison n=16	**Main n=22**
20-th	72,31±0,746	19,32±0,672 p<0,001
30-th	79,31±0,794 p_1<0,001	90,68±0,815 p<0,001; p_1<0,001
40-th	97,13±0,473 p_1<0,001*	84,05±0,622 p<0,001; p_1<0,001*
50-th	98,06±0,309 p_1<0,001	90,32±0,782 p<0,001; p_1<0,001*

*notes: n - number of observations; p - difference between the two experimental groups; p1 - difference against the indices of the 20th day of observation; * - probable difference against the indices of the previous observation period*

Table 2. Lymphoid cells of granulation tissue around the reticular allograft after implantation of the latter in different times of observation (M±m),%

Terms of observation, day	Group of animals	
	Comparison n=16	**Main n=22**
20-th	23,13±0,865	70,23±0,631 p<0,001
30-th	17,44±0,508 p_1<0,001	7,55±0,473 p<0,001; p_1<0,001
40-th	3,19±0,319 p_1<0,001*	13,27±0,484 p<0,001; p_1<0,001*
50-th	2,13±0,272 p_1<0,001	6,32±0,408 p<0,001; p_1<0,001*

*notes: n - the number of observations; p - difference between the two groups under study; p1 - difference against the indices of the 20th day of observation; * - probable difference against the indices of the previous observation term*

Table 3. Plasma cells of granulation tissue around the net allograft following implantation of the latter in different observation terms (M±m),%

Terms of observation, day	Group of animals	
	Comparison n=16	**Main n=22**
20-th	1,16±0,14	4,27±0,337 p<0,001
30-th	1,11±0,148 p_1>0,05	0,52±0,057 p<0,001; p_1<0,001
40-th	Separate	1,03±0,121 p_1<0,001*
50-th	Separate	1,05±0,12 p_1<0,001

*notes: n - the number of observations; p - the difference between the two experimental groups; p1 - the difference against the indices of the 20th day of observation; * - probable difference against the indices of the previous observation period*

Analyzing the results of the study of the granulation tissue macrophages, which are shown in table 4, the absence of the latter ones in the comparison group, starting from the 40th day of observation, should be noted as well. The number of macrophages in the main group of animals predominates, but this difference on the 30th day of observation is uncertain. In both groups of animals under study, a decrease in the number of macrophages was observed throughout the whole period of observation.

Thus, the use of the distant gamma therapy after reticular allograft implantation leads to uneven maturation of the granulation tissue and its edema, probable decrease in the percentage of fibroblasts, an increase in the lymphoid cells, as well as the appearance of plasma cells and macrophages on the day 40th and 50th day of observation.

When evaluating the results of the research of the specific volume of the collagen fibers per unit area of the granulation tissue, presented in table 5, it should be noted the probable predominance of indices in the animals of the main group throughout the whole period of investigation. In both experimental groups, there is a probable increase in the specific volume of collagen fibers throughout the observation period.

Table 4. Macrophages of granulation tissue around the net allograft after implantation of the latter one at different observation times (M±m),%

Terms of observation, day	Group of animals	
	Comparison n=16	Main n=22
20-th	4,44±0,387	7,23±0,558 p<0,001
30-th	2,19±0,262 p_1<0,001	2,23±0,227 p>0,05; p_1<0,001
40-th	Separate	2,45±0,261 p_1<0,001
50-th	Separate	2,05±0,283 p_1<0,001

notes: n - the number of observations; p - difference between the two experimental groups;
p1 - difference against the indices of the 20th day of observation;
** - probable difference against the indices of the previous observation period*

Table 5. Specific volume of collagen fibers per unit area of granulation tissue, %

Terms of observation, day	Group of animals	
	Comparison =16	Main n=22
20-th	48,31±0,805	52,18±0,591 p<0,001
30-th	50,63±0,547 p_1<0,001	53,27±0,484 p<0,001; p_1>0,05
40-th	52,44±0,701 p_1<0,001*	60,05±0,629 p<0,001; p_1<0,001*
50-th	52,38±0,554 p_1<0,001	54,23±0,603 p<0,001; p_1<0,001*

notes: n - the number of observations; p - difference between two groups under study;
p1 - difference against the indices of the 20th day of observation;
** - probable difference against the indices of the previous observation period*

Table 6. Optical density of the colored collagen fibers with water blue in units of optical density

Terms of observation, day	Group of animals	
	Comparison =18	Main n=24
20-th	0,14±0,002	0,21±0,002 p<0,001
30-th	0,21±0,002 p_1<0,001	0,21±0,002 p>0,05; p_1>0,05
40-th	0,24±0,003 p_1<0,001*	0,24±0,002 p>0,05; p_1<0,001*
50-th	0,25±0,002 p_1<0,001	0,24±0,001 p>0,05; p_1<0,001

notes: n - the number of observations; p - difference between the two experimental groups;
p1 - difference against the indices of the 20th day of observation;
** - probable difference against the indices of the previous observation period*

Table 7. Specific volume of blood vessels in granulation tissue, %

Terms of observation, day	Group of animals	
	Comparison n=18	Main n=24
20-th	7,06±1,879	0,52±0,266 p<0,001
30-th	3,06±1,237 p_1<0,001	3,09±1,151 p>0,05; p_1<0,001
40-th	1,52±0,544 p_1<0,001*	2,18±0,853 p<0,01; p_1<0,001*
50-th	1,53±0,491 p_1<0,001	3,14±0,99 p<0,001; p_1<0,001*

notes: n - the number of observations; p - difference between the two experimental groups;
p1 - difference against the indices of the 20th day of observation;
** - probable difference against the indices of the previous observation period*

The results of the study of the optical density of the colored collagen fibers, presented in table 6, indicate that there is no difference between the two groups, with exception of the 20th day of observation, where a probable predominance of indices in the main group of animals is observed. Throughout the whole period of study a probable increase in the optical density of the colored collagen fibers is marked in both experimental groups of animals.

The results of the study of the specific volume of the blood vessels in the granulation tissue, which are presented in table 7, indicate a probable predominance of indices in the animals of the main group, starting from the 40th day of observation. In the main group of animals, in contrast to the comparison group, a probable increase in the specific volume of the blood vessels in the granulation tissue throughout the whole period of investigation is noted.

In such a manner, the use of the postoperative radiation therapy somewhat distorts the granulation tissue maturation, that is manifested by a probable predominance of the specific volume of the collagen fibers, as well as an increase of the specific volume of the blood vessels, on the 50th day of observation. Therefore, summarizing the results of the study, it should be noted that the postoperative radiation therapy leads to edema of the granulation tissue, even in the remote term after surgery, which remains for a long time. The rise of the granulation tissue edema after radiotherapy is confirmed by the results of other studies.

It is known that irradiation leads to a decrease in the number of fibroblasts in the site of inflammation, which proves a probably smaller number on the 20th day of observation and a sharp increase on the 30th day. Also, irradiation stimulates not only the proliferation but also the maturation of fibroblasts, which proves the probable predominance of the specific volume of collagen fibers throughout the observation period in animals of the main group [7]. Moreover, the degree of their maturity does not change, which proves the incredible difference in the optical density of colored collagen fibers with water blue.

The use of radiation therapy leads to increased migration of lymphoid cells and macrophages, as well as the predominance of specific volume of blood vessels in the longer observation period, indicates inflammation in this area and immaturity of granulation tissue.

This study shows the reaction of almost formed granulation tissue to prolonged, strong irradiation.

Therefore, the use of postoperative radiation therapy, in large doses, leads to increased collagen synthesis and the development of inflammation in the postoperative wound.

Despite the predominance of the specific volume of collagen fibers, this negatively affects the strength of the postoperative scar, because the granulation tissue has not completed the maturation process due to inflammation caused by irradiation.

Conclusions. The use of the postoperative radiation therapy, when performing plastics of the anterior abdominal wall with net allograft, leads to distortion of the maturation processes of the granulation tissue, its edema, which is manifested by a probable decrease in the percentage of fibroblasts, an increase in the lymphoid cells, the appearance of plasma cells and fibers, an increase in the specific volume of the blood vessels.

Prospects for further research. We consider it necessary to study the effect of postoperative remote gamma therapy of the abdominal cavity on the features of the morphology of the granulation tissue of the laparotomy wound, depending on the radiation dose.

REFERENCES

1. Morar I. K, Ivashchuk O. I, Bodyaka V.Yu [ta in.] (2017) Pisliaoperatsiyna eventratsiya. Klinichna ta eksperymentalna patologiia, 16, 1 (59), 177-181.
2. Morar I. K, Ivashchuk O. I, Bodyaka V.Yu., Gushul I.Ya., Unguryan V.P Patent of Ukrainy na korysnu model 106161, IPC A 61 B 17/00. Sposib implantatsii sitchastogo alotransplantata v tkanyny m'yazovo-aponevrotychnogo sharu perednyoi cherevnoi stinky laboratornogo shchura; zayavnyk ta patentovlasnyk Vyshchyi derzhavnyi navchalnyi zaklad "Bukovynskyi derzhavnyi medychnyi universytet" MOZ Ukrainy. № u 2015 06913 zayavl.13.07.15; opubl. 25.04.16, Biul. № 8.
3. Kenchadze G., Pipia I., Demetrashvili Z. Component separation technique in large incisional abdominal hernia repair: our experience. 154 Hernia. Abstract book. 1st World conference on abdominal wall hernia surgery. Milan, Italy. 2015. V.19 (Suppl 1). S. 187.
4. Fei Long, Loubin Si, Xiao Long, Bob Yang, Xiaojun Wang, Fuquan Zhan. 2ME2 increase radiation-induced apoptosis of keloid fibroblasts by targeting HIF-1α in vitro. Australas J Dermatol. 2016 May;57(2):e32-8. doi: 10.1111/ajd.12340.
5. Hong Zhao, Huangang Jiang, Zheng Li, Yafei Zhuang, Yinyin Liu, Shuliang Zhou, Youde Xiao, Conghua Xie, Fuxiang Zhou, Yunfeng Zhou, 2-Methoxyestradiol enhances radiosensitivity in radioresistant melanoma MDA-MB-435R cells by regulating glycolysis via HIF-1α/PDK1 axis, International Journal of Oncology, 10.3892/ijo.2017.3924, 50, 5, (1531-1540).

6. Marcello Pozzi, Giovanni Zoccali, Maria C Drago, Maria A Mirri, Maurizio Costantini, Roy DE Vita. Radiotherapy following surgery in keloid treatment: our protocol. G Ital Dermatol Venereol. 2016 Oct;151(5):492-8.
7. Shirley Genah, Francesca Cialdai, Valerio Ciccone, Elettra Sereni, Lucia Morbidelli, Monica Monici. Effect of NIR Laser Therapy by MLS-MiS Source on Fibroblast Activation by Inflammatory Cytokines in Relation to Wound Healing. Biomedicines. 2021 Mar 16;9(3):307. doi: 10.3390/biomedicines9030307.
8. Qingwu Liu, Ping Li, Zhishan Yang, Baoquan Qu, Chunfang Qin, Shengnan Meng, Huijuan Fang, Ruiying Wu, Tiantian Cheng, Dingquan Yang. Multi-stage surgery combined with radiotherapy for treatment of giant anterior chest wall keloid: A case report. Medicine (Baltimore). 2020 Jan;99(4):e18886. doi: 10.1097/MD.0000000000018886.
9. Li Yan, Lian-Zhao Wang, Ran Xiao, Rui Cao, Bo Pan, Xiao-Yan Lv, Hu Jiao, Qiang Zhuang, Xue-Jian Sun, Yuan-Bo Liu. Inhibition of microRNA-21-5p reduces keloid fibroblast autophagy and migration by targeting PTEN after electron beam irradiation. Lab Invest. 2020 Mar;100(3):387-399. doi: 10.1038/s41374-019-0323-9.
10. Yuan Chen, Yue Chen, Yong Liu. Abnormal Presentation of Aggressive Fibromatosis After Radiotherapy for Keloids: Case Report and Brief Literature Review. Ann Plast Surg. 2019 Jul;83(1):104-107. doi: 10.1097/SAP.0000000000001675.

SUMMARY

FEATURES OF GRANULATION TISSUE MORPHOLOGY AROUND THE NET ALLOTRANSPLANT WHEN APPLYING POSTOPERATIVE RADIATION THERAPY

Morar I., Ivashchuk A., Bodyaka V., Domanchuk T., Antoniv A.

Higher State Educational Institution of Ukraine Bukovinian State Medical University, Chernivtsi, Ukraine

The aim of the research was to study experimentally the morphologic peculiarities of the granular tissue around the elements of the reticular allotransplant of the muscular aponeurotic layer of the anterior abdominal wall when using postoperative distant gamma therapy.

The experiment has been done on 168 laboratory rats which were implanted with a prolenic mesh allograft into the tissues of muscular aponeurotic layer of the anterior abdominal wall. From the 13th to 19th day after the implantation of the reticular allograft, animals from the main group (96 rats) received irradiation of the site of the last one. Taking of the biological material was carried out on the 20th, 30th, 40th and 50th day after surgery. For optical research at histological examination the samples of biopsy were fixed in 10% neutral formalin. Paraffin sections were stained with hemotoxylin and eosin. To identify collagen fibres the method of histological sections' coloring was applied. The results of the research indicate that the use of distant gamma therapy after reticular allotransplant implantation leads to uneven maturation of the granulation tissue, its edema, probable decrease in the percentage of fibroblasts, increase of lymphoid cells as well as the appearance of plasma cells and macrophages on the 40th and 50th days of observation. At the histologic sections coloring with aquious blue-chromotrope B2, there is a predominance of the specific volume of collagen fibers and an increase in the specific volume of blood vessels on the 50th day of observation. Thus, the use of the postoperative radiotherapy at the plasty of the anterior abdominal wall with a reticular allograft leads to the distortion of the maturation process of the granular tissue, its edema, which shows itself in the probable reduction in the percentage of fibroblasts, increase in lymphoid cells, appearance of plasma cells and macrophages as well as prevalence of specific volume of collagen fibres, increase in the specific volume of vessels.

Keywords: granular tissue, gamma teletherapy, reticular allograft / allotransplant, muscular aponeurotic layer.

РЕЗЮМЕ

ОСОБЕННОСТИ МОРФОЛОГИИ ГРАНУЛЯЦИОННОЙ ТКАНИ ВОКРУГ СЕТЧАТОГО АЛЛОТРАНСПЛАНТАТА ПРИ ПРИМЕНЕНИИ ПОСЛЕОПЕРАЦИОННОЙ ЛУЧЕВОЙ ТЕРАПИИ

Морар И.К., Иващук А.И., Бодяка В.Ю., Доманчук Т.И., Антонив А.А.

Высшее государственное образовательное учреждение Украины Буковинский государственный медицинский университет, Черновцы, Украина

Целью исследования явилось определение особенности морфологии грануляционной ткани вокруг элементов сетчатого аллотрансплантата мышечно-апоневротического слоя передней брюшной стенки при применении послеоперационной дистанционной гамма-терапии в эксперименте.

Эксперимент выполнен на 168 лабораторных крысах, которым имплантирован проленовый сетчатый аллотрансплантат в ткани мышечно-апоневротического слоя передней брюшной стенки.

Животные основной группы (n=96) с 13 по 19 сутки после имплантации сетчатого аллотрансплантата получали облучение участка расположения последнего гамма-терапевтическим аппаратом АГАТ Р1-У, ("Балтиец", Эстония). Забор биологического материала проводили на 20, 30, 40 и 50 сутки после оперативного вмешательства. Для свето-оптического исследования при гистологическом исследовании биоптаты фиксировали в 10% нейтральном формалине. Парафиновые срезы окрашивали гематоксилином и эозином. Для идентификации коллагеновых волокон использовали методику окраски гистологических срезов водным голубым - хромотропом 2В.

Для морфометрического исследования сначала получали цветные цифровые копии оптических изображений (цифровое разрешение - 1600х1200) с помощью микроскопа Delta Optical Evolution 100, Польша (планахроматические объективы - 20х и 40х в зависимости от целей исследования) и цифровой камеры Olympus SP-550UZ (Япония). На цифровых клопиях оптических изображений в среде и инструментами компьютерной программы Image J (1.48, W. Rasband, National Institutes of Health, USA) производили безповторный подсчет числа клеток разных типов (скор-тест) с последующим представлением их числа в процентном виде и определение удельного обьема коллагеновых волокон и кровеносных сосудов путем их выделения и автоматического подсчета числа приходящихся на них пикселей с последующим переводом данных в %.

Полученные результаты исследования свидетельствуют, что применение дистанционной гамма-терапии после имплантации сетчатого аллотрансплантата приводит к неравномерному созреванию грануляционной ткани, ее отеку, достоверному уменьшению процента фибробластов, увеличению лимфоидных клеток и появлению плазматических клеток и макрофагов на 40 и 50 сутки наблюдения. При окраске гистологических срезов водным голубым - хромотропом 2В отмечается достоверный рост удельного объема коллагеновых волокон и сосудов на 50 сутки наблюдения.

რეზიუმე

გრანულაციური ქსოვილის მორფოლოგიის თავისებურებანი ბადებრივი ალოტრანსპლანტატის ირგვლივ ოპერაციისშემდგომი სხივური თერაპიის გამოყენების პირობებში

ი.მორარი, ა.ივაშჩუკი, ვ.ბოდიაკა, ტ.დომანჩუკი, ა.ანტონივი

ბუკოვინის სახელმწიფო სამედიცინო უნივერსიტეტი, ჩერნოვცი, უკრაინა

კვლევის მიზანს წარმოადგენდა გრანულაციური ქსოვილის მორფოლოგიის თავისებურებათა განსაზღვრა მუცლის წინა კედლის კუნთოვან-აპონევროზული შრის ბადებრივი ალოტრანსპლანტატის ელემენტების ირგვლივ ოპერაციისშემდგომი დისტანციური გამა-თერაპიის გამოყენებისას ექსპერიმენტში.

ექსპერიმენტი ჩატარდა 168 ლაბორატორიულ ვირთაგვაზე, რომელთაც მუცლის წინა კედლის კუნთოვან-აპონევროზულ შრეში იმპლანტირებული ჰქონდა პროლენის ბადებრივი ალოტრანსპლანტატი.

ძირითადი ჯგუფის ცხოველები (n=96) ბადებრივი ალოტრანსპლანტატის იმპლანტაციიდან მე-13-19 დღეს იღებდნენ ამ მიდამოს დასხივებას გამა-თერაპიული აპარატით АГАТ Р1-У ("Baltiec", ესტონეთი). ბიოლოგიური მასალის აღება განხორციელდა ოპერაციული ჩარევიდან მე-20,30-ე,მე-40 და 50-ე დღეს. ჰისტოლოგიური სინათლუროპტიკური კვლევისთვის ბიოპტატები ფიქსირდებოდა 10%-იან ნეიტრალურ ფორმალინში. პარაფინული ანათლები შეღებილი იყო ჰემატოქსილინით და ეოზინით. კოლაგენური ბოჭკოების იდენტიფიკაციისათვის გამოყენებული იყო ჰისტოლოგიური ანათლების შეღებვის მეთოდიკა ქრომოტროპ 2В-ით.

მორფომეტრიული კვლევისათვის თავდაპირველად მიიღებოდა ოპტიკური გამოსახულებების ციფრული ასლები (1600x1200) მიკროსკოპის Delta Optical Evolution 100 (პოლონეთი) და ციფრული კამერის Olympus SP-550UZ (იაპონია) გამოყენებით. ოპტიკური გამოსახულებების ციფრულ ასლებზე გარემოში და კომპიუტერული პროგრამის Image J (1.48, W. Rasband, National Institutes of Health, USA) ინსტრუმენტებით განხორციელდა სხვადასხვა ტიპის უჯრედების თვლა, მათი შემდგომი %-ული გამოხატვით, ასევე, კოლაგენური ბოჭკოების და სისხლძარღვების ხვედრითი მოცულობის განსაზღვრა მათი გამოყოფის და მათზე გავლილი პიქსელების რაოდენობის ავტომატური თვლით და შემდგომი გადაყვანით %-ში.

მიღებული შედეგები მიუთითებს, რომ დისტანციური გამა-თერაპიის გამოყენება ბადებრივი ალოტრანსპლანტატის იმპლანტაციის შემდეგ იწვევს გრანულაციური ქსოვილის არათანაბარ მომწიფებას, მის შეშუპებას, ფიბრობლასტების პროცენტის სარწმუნო შემცირებას, ლიმფოიდური უჯრედების მატებას, პლაზმური უჯრედებისა და მაკროფაგების გაჩენას დაკვირვების მე-40 და 50-ე დღეს. ჰისტოლოგიური პრეპარატების შეღებვისას ქრომოტროპ 2В-ით აღინიშნება კოლაგენური ბოჭკოების და სისხლძარღვების სარწმუნო ზრდა დაკვირვების 50-ე დღეს.

ОСОБЕННОСТИ РАЗВИТИЯ РЕПРОДУКТИВНОЙ СИСТЕМЫ ПРИ ИСПОЛЬЗОВАНИИ ГЕНЕТИЧЕСКИ МОДИФИЦИРОВАННЫХ ИСТОЧНИКОВ (ЭКСПЕРИМЕНТАЛЬНОЕ ИССЛЕДОВАНИЕ)

[1]Харисова Н.М., [2]Смирнова Л.М., [3]Кузьмин А.Ф., [1]Рыспаева Г.К., [1]Лепесбаева Г.А.

[1]Карагандинский медицинский университет, кафедра морфологии и физиологии, Караганда, Казахстан; Костромский государственный университет им. Н.А. Некрасова, [2]кафедра физической культуры и спорта; [3]кафедра биологии и экологии, Россия

В наши дни биотехнология стремительно развивается благодаря использованию современных методов для создания новых биопрепаратов, способов их синтеза и распознавания. Одним из методов, применяемых в биотехнологии, является метод генной инженерии, позволяющий создать и модифицировать различные новые продукты, используемые в пищевой промышленности, медицине, сельском хозяйстве, фармацевтической и химической промышленности. С помощью генной инженерии получают микроорганизмы-продуценты антибиотиков, ферментов аминокислот витаминов; рекомбинантные вакцинные штаммы бактерий и вирусов; трансгенные растения, более продуктивные и устойчивые к вредителям, менее требовательные к условиям выращивания; трансгенные животные, вырабатывающие с молоком биологически активные вещества лекарственного назначения. Вместе с тем вмешательство в структуру генома молекулы ДНК и генов вызывает серьезное беспокойство в обществе [6,26].

Прежде чем использовать генно-модифицированные сорта и продукты на их основе для питания человека или в