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INDIVIDUALIZATION OF ART PROTOCOLS IN PATIENTS WITH DIFFERENT OVARIAN RESERVE

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ABSTRACT

Infertility remains one of the most important challenges in modern reproductive medicine and requires an individualized approach to improve the effectiveness of assisted reproductive technologies (ART). The aim of this study was to evaluate ART outcomes in patients with different ovarian reserve levels and to determine the role of personalized treatment protocols. This prospective study included 60 infertile women treated at the “Beshik” Reproductive Medicine Clinic (Samarkand, Uzbekistan) during 2025–2026. The participants were divided into two groups according to ovarian reserve: normal ovarian reserve (n=30) and diminished ovarian reserve (n=30). Ovarian reserve was assessed using anti-Müllerian hormone levels and antral follicle count, and all patients were additionally stratified according to the POSEIDON concept. Although patients with diminished ovarian reserve demonstrated lower numbers of retrieved oocytes and less favorable embryological outcomes, individualized ovarian stimulation protocols allowed satisfactory rates of oocyte maturation, fertilization, and blastocyst formation to be achieved. The findings indicate that personalization of ART protocols based on ovarian reserve assessment and POSEIDON stratification contributes to improved reproductive outcomes.

Keywords: infertility, assisted reproductive technologies, IVF, ICSI, ovarian reserve, AMH, POSEIDON, personalization

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ИНДИВИДУАЛИЗАЦИЯ ПРОТОКОЛОВ ВРТ У ПАЦИЕНТОК С РАЗЛИЧНЫМ ОВАРИАЛЬНЫМ РЕЗЕРВОМ

АННОТАЦИЯ

Бесплодие является одной из наиболее актуальных проблем современной репродуктивной медицины и требует индивидуализированного подхода для повышения эффективности вспомогательных репродуктивных технологий (ВРТ). Целью исследования явилась оценка результатов ВРТ у пациенток с различным овариальным резервом и определение значения

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HISTOCHEMICAL FEATURES OF CONNECTIVE TISSUE FORMATION IN FACIAL SOFT TISSUES FOLLOWING XENOGRAFT IMPLANTATION

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ABSTRACT

Objective: To comparatively evaluate the dynamics of connective tissue formation and remodeling in the surrounding soft tissues following subcutaneous implantation of xenografts derived from different biological sources-porcine, bovine, and ovine pericardium-in rabbits using Van Gieson histochemical staining. **Materials and Methods:** The experimental study included 20 rabbits. Incisions were made in the frontal region of the rabbits, and xenograft materials derived from porcine, bovine, and ovine pericardium were implanted. Tissues from the implantation sites were examined morphologically and histochemically on days 3, 7, 14, 21, and 35 after implantation. To identify connective tissue components, particularly the formation and distribution of collagen fibers, histological sections were stained using the Van Gieson method. At different observation periods, the appearance of collagen fibers around the implants, their density and orientation, as well as the maturation characteristics of the connective tissue framework, were comparatively evaluated. **Results:** The tissue response following xenograft implantation was characterized by a gradual, stage-dependent progression. During the early post-implantation period, inflammatory and cellular reactions predominated around the implant, whereas at later stages, increased fibroblastic activity and enhanced collagen fiber formation were observed. By day 21, connective tissue matrix formation had entered an active phase, while by day 30, organization of collagen fibers and formation of a mature connective tissue framework were observed. The characteristics and dynamics of these processes were comparatively assessed among xenografts of different biological origins. **Conclusion:** Van Gieson staining enables the identification and assessment of the sequential stages of collagenogenesis and connective tissue remodeling in the tissues surrounding xenografts following implantation. The obtained findings are of considerable importance for the morphological evaluation of the integration characteristics of xenografts derived from different biological sources with surrounding soft tissues.

Keywords: xenograft, soft tissue, Van Gieson staining, histochemistry, collagen, collagenogenesis, fibroblast, connective tissue, regeneration, remodeling, implantation.

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ГИСТОХИМИЧЕСКИЕ ОСОБЕННОСТИ ФОРМИРОВАНИЯ СОЕДИНИТЕЛЬНОЙ ТКАНИ В МЯГКИХ ТКАНЯХ ЛИЦА ПОСЛЕ ИМПЛАНТАЦИИ КСЕНОТРАНСПЛАНТАТОВ

АННОТАЦИЯ

Цель. Провести сравнительную оценку динамики формирования и ремоделирования соединительной ткани в окружающих мягких тканях после подкожной имплантации кроликам ксенотрансплантатов, полученных из перикарда сердца различных биологических видов свиньи, крупного рогатого скота и овцы, с использованием гистохимического метода окраски по Ван Гизону. **Материал и методы**. Экспериментальное исследование проведено на 20 кроликах. В лобной области кроликов выполняли разрезы с последующей имплантацией ксенотрансплантационных материалов, полученных из перикарда свиньи, крупного рогатого скота и овцы. Ткани в области имплантации исследовали морфологическими и гистохимическими методами на 3-и, 7-е, 14-е, 21-е и 35-е сутки после имплантации. Для выявления компонентов соединительной ткани, в частности оценки формирования и распределения коллагеновых волокон, гистологические срезы окрашивали по методу Ван Гизона. В различные сроки наблюдения проводили сравнительную оценку появления коллагеновых волокон вокруг имплантата, их плотности и ориентации, а также особенностей созревания соединительнотканного каркаса.

Результаты. Установлено, что тканевая реакция после имплантации ксенотрансплантатов характеризовалась стадийным течением. В ранние сроки вокруг имплантата преобладали воспалительная и клеточная реакции, тогда как в последующие сроки отмечалось усиление фибробластической активности и образования коллагеновых волокон. На 21-е сутки формирование соединительнотканного матрикса переходило в активную фазу, а к 30-м суткам наблюдались упорядочивание коллагеновых волокон и формирование зрелого соединительнотканного каркаса. Проведена сравнительная оценка особенностей течения данных процессов при использовании ксенотрансплантатов различного биологического происхождения. **Заключение.** Метод окраски по Ван Гизону позволяет выявлять этапы коллагеногенеза и ремоделирования соединительной ткани в окружающих тканях после имплантации ксенотрансплантатов. Полученные результаты имеют важное значение для морфологической оценки особенностей интеграции ксенотрансплантатов, изготовленных из различных биологических материалов, с окружающими мягкими тканями.

Ключевые слова: ксенотрансплантат, мягкие ткани, окраска по Ван Гизону, гистохимия, коллаген, коллагеногенез, фибробласт, соединительная ткань, регенерация, ремоделирование, имплантация.

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KSENOTRANSPLANTATLAR IMPLANTATSIYASIDAN SO‘NG YUZ YUMSHOQ TO‘QIMALARDA BIRIKTIRUVCHI TO‘QIMA SHAKLLANISHINING GISTOKIMYOVIY XUSUSIYATLARI

ANNOTATSIYA

Maqsad. Turli biologik manbalardan-cho‘chqa, qoramol va qo‘y yurak perikardidan olingan ksenotransplantatlar quyonlarning teri ostiga implantatsiyasidan keyin atrof yumshoq to‘qimalarda

biriktiruvchi to‘qima shakllanishi va remodellanishining dinamikasini Van Gieson gistokimyoviy usuli yordamida qiyosiy baholash. **Material va usullar.** Eksperimental tadqiqotda 20 dona quyonlar olindi. Quyonlarning peshona sohasidan kesmalar tayyorlanib, cho‘chqa, qoramol va qo‘ydan olingan perikard ksenotransplantant materiallar implantatsiya qilindi. Implantatsiya sohasidagi to‘qimalar 3, 7, 14, 21, va 35-sutkalarda morfologik va gistokimyoviy jihatdan o‘rganildi. Biriktiruvchi to‘qima komponentlarini, xususan kollagen tolalarining shakllanishi va taqsimlanishini aniqlash maqsadida gistologik kesmalar Van Gieson usulida bo‘yaldi. Turli kuzatuv muddatlarida implantat atrofida kollagen tolalarining paydo bo‘lishi, ularning zichligi, yo‘nalishi va biriktiruvchi to‘qima karkasining yetilish xususiyatlari qiyosiy baholandi. **Natijalar.** Ksenotransplantat implantatsiyasidan keyingi to‘qima reaksiyasi bosqichma-bosqich kechishi kuzatildi. Erta muddatlarda implantat atrofida yallig‘lanish va hujayraviy reaksiyalar ustunlik qilgan bo‘lsa, keyingi muddatlarda fibroblastik faollik va kollagen tolalarining shakllanishi kuchayishi qayd etildi. 21-sutkalarda biriktiruvchi to‘qima matriksining shakllanishi faol bosqichga o‘tib, 30-sutkada kollagen tolalarining tartiblanishi va yetuk biriktiruvchi to‘qima karkasining shakllanishi kuzatildi. Turli kelib chiqishga ega ksenotransplantatlar o‘rtasida mazkur jarayonlarning kechish xususiyatlari qiyosiy baholandi. **Xulosa.** Van Gieson usuli ksenotransplantat implantatsiyasidan keyin atrof to‘qimalarda kollagenogenez va biriktiruvchi to‘qima remodellanishining bosqichlarini aniqlash imkonini beradi. Olingan natijalar turli biologik manbalardan tayyorlangan ksenotransplantatlarning yumshoq to‘qimalar bilan integratsiyalanish xususiyatlarini morfologik jihatdan baholashda muhim ahamiyatga ega.

Kalit so‘zlar: ksenotransplantat, yumshoq to‘qima, Van Gieson, gistokimyo, kollagen, kollagenogenez, fibroblast, biriktiruvchi to‘qima, regeneratsiya, remodellanish, implantatsiya.

KIRISH

Yuz sohasidagi yumshoq to‘qimalar deformatsiyalarini rekonstruktiv tiklash zamonaviy plastik va rekonstruktiv xirurgiyaning dolzarb muammolaridan biri hisoblanadi. To‘qima nuqsonlarini bartaraf etishda biologik materiallardan foydalanish nafaqat yetishmayotgan to‘qima hajmini to‘ldirish, balki implantatsiya sohasida yangi biriktiruvchi to‘qima karkasining shakllanishi uchun biologik matritsa yaratish imkonini ham beradi [3, 8, 9, 13]. Shu sababli hayvon to‘qimalaridan olinadigan ksenotransplantatsion materiallarning regenerativ imkoniyatlari alohida ahamiyat kasb etadi. Ksenotransplantatning samaradorligi uning implantatsiya sohasidagi to‘qimalar bilan o‘zaro ta’siri, yallig‘lanish reaksiyasining darajasi, fibroblastlar faolligi, angiogenez, hujayradan tashqari matriks komponentlarining sintezi hamda kollagen tolalarining shakllanish va remodellanish xususiyatlariga bog‘liq [7, 10, 12, 14]. Ksenotransplantatning to‘qimaga integratsiyalanishini baholashda kollagen tolalarining shakllanish dinamikasi muhim morfologik mezonlardan biri hisoblanadi. Kollagen hujayradan tashqari matriksning asosiy tarkibiy komponenti bo‘lib, regeneratsiya jarayonida to‘qimaning mexanik mustahkamligi va struktur barqarorligini ta’minlaydi [1, 5]. Biriktiruvchi to‘qimaning shakllanishi dastlab fibroblastlarning proliferatsiyasi va migratsiyasi, keyinchalik hujayradan tashqari matriks komponentlarining sintezi va kollagen tolalarining hosil bo‘lishi bilan kechadi. Regeneratsiyaning keyingi bosqichlarida kollagen tolalari qayta tashkillanib, ularning yo‘nalishi va zichligi o‘zgaradi hamda yetuk biriktiruvchi to‘qima karkasi shakllanadi [2, 4, 6].

Bunda, morfologik baholashda Van Gieson bo‘yash usuli muhim gistokimyoviy usullardan biri bo‘lib, u biriktiruvchi to‘qimaning kollagen komponentlarini boshqa to‘qima tuzilmalaridan differensial ajratib ko‘rsatish imkonini beradi.

Tadqiqot maqsadi, cho‘chqa, qoramol va qo‘ydan olingan ksenotransplantatlar implantatsiyasidan keyin atrof yumshoq to‘qimalarda kollagen tolalari va biriktiruvchi to‘qima karkasi shakllanishining dinamikasini Van Gieson gistokimyoviy usuli yordamida qiyosiy baholash.

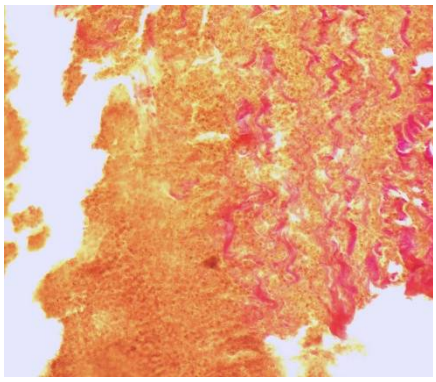
Material va usullar

Eksperimental tadqiqotda biologik kelib chiqishiga ko‘ra uch xil yani cho‘chqa, qoramol va qo‘y perikardidan tayyorlangan ksenotransplantatsion materiallardan foydalanildi. Ksenotransplantatlar eksperimental quyonlarlarning (20 dona) peshona teri osti yumshoq

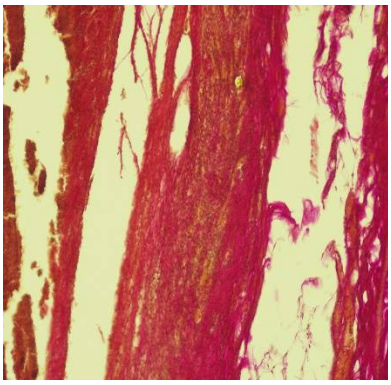
to‘qimalariga implantatsiya qilindi. Implantatsiyadan keyingi morfologik o‘zgarishlarni dinamik baholash maqsadida material 3, 7, 14, 21, 28 va 35-sutkalarda olindi.

Olingan to‘qima namunalari belgilangan gistologik protokol asosida fiksatsiya qilinib, parafin bloklarga joylashtirildi va tegishli qalinlikda gistologik kesmalar tayyorlandi. Biriktiruvchi to‘qima komponentlarini aniqlash maqsadida kesmalar Van Gieson usulida bo‘yaldi. Ushbu usul kollagen tolalarini atrofdagi boshqa to‘qima elementlaridan differensial ajratish va implantatsiya sohasida fibroz to‘qimaning shakllanishini baholash imkonini berdi. Mikroskopik tahlil jarayonida quyidagi mezonlarga e’tibor qaratildi: implantat atrofida kollagen tolalarining paydo bo‘lishi; ularning tarqalish darajasi va zichligi; tolalarning yo‘nalishi va tartiblanishi; implantat atrofida biriktiruvchi to‘qima kapsulasining shakllanishi; implantat va resipient to‘qima chegarasidagi struktur qayta qurilish; kuzatuv muddati ortishi bilan biriktiruvchi to‘qimaning yetilish belgilari.

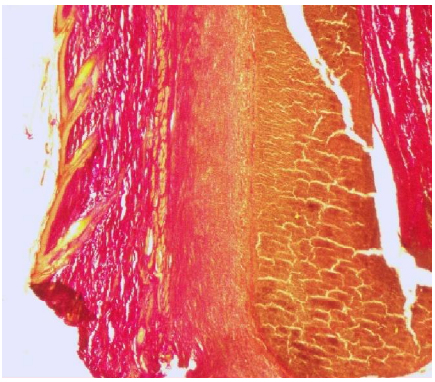
Natijalar 3-sutka. Ksenotransplantat implantatsiyasidan keyingi 3-sutkada uchala eksperimental guruhda ham implantatsiya sohasida biriktiruvchi to‘qima komponentlarining notekis taqsimlanishi kuzatiladi. Van Gieson usulida kollagen saqlovchi tuzilmalar qizil-pushti rangda namoyon bo‘lib, ularning arxitekturasi hali yetuk biriktiruvchi to‘qimaga xos tartibli tuzilishga ega emas. Implantat va resipient to‘qima chegarasida struktur geterogenlik, to‘qima elementlarining ajralishi hamda bo‘sh sohalar aniqlandi. Bu morfologik manzara implantatsiyadan keyingi erta reaktiv bosqichga mos keladi. Qoramol ksenotransplantati qo‘llanilgan 3-sutkalik preparatda (1-rasm) implantatga tutash sohada intensiv qizil-pushti bo‘yalgan yirik tolali tuzilmalar ko‘rinadi.



1-rasm. Qoramol ksenotransplantati implantatsiyasidan keyingi 3-sutka. Implantat-resipient to‘qima chegarasida notekis joylashgan kollagenli tuzilmalar. Van Gieson usulida bo‘yash. Kattalashtirish: 10x40.



2-rasm. Cho‘chqa ksenotransplantati implantatsiyasidan keyingi 3-sutka. Implantat-resipient to‘qima chegarasida notekis joylashgan kollagenli tuzilmalar. Van Gieson usulida bo‘yash. Kattalashtirish: 10x40.



3-rasm. Qo‘y ksenotransplantati implantatsiyasidan keyingi 3-sutka. Implantat-resipient to‘qima chegarasida notekis joylashgan kollagenli tuzilmalar. Van Gieson usulida bo‘yash. Kattalashtirish: 10x40.

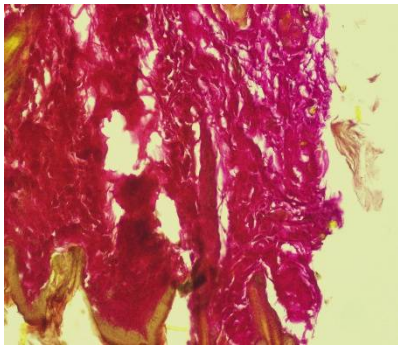
Kollagenli strukturalar notekis joylashgan, ayrim qismlarda uzunasiga yo‘nalgan tutamlar ko‘rinishida namoyon bo‘ladi. Implantat-to‘qima chegarasida struktur ajralishlar saqlanib qolgan. Cho‘chqa ksenotransplantati qo‘llanilgan guruhda (2-rasm) qizil-pushti bo‘yalgan biriktiruvchi to‘qima komponentlari nisbatan kam maydonni egallaydi. Ayrim sohalarda umumiy arxitektonika hali notekis. Implantat bilan atrof to‘qima orasida keng ajralish sohasi ko‘rinadi.

Qo‘y ksenotransplantatida (3-rasm) implantatsiya sohasidagi to‘qima tuzilishi geterogen bo‘lib, Van Gieson-pozitiv tolali komponentlar ayrim sohalarda zich to‘plangan. Tolali strukturalar orasida bo‘shliqlar mavjud va ularning yo‘nalishi notekis. Demak, 3-sutkada uchala guruhda ham yetuk biriktiruvchi to‘qima karkasi hali shakllanmagan, asosiy morfologik belgi esa implantat-resipient to‘qima interfeysining qayta tashkillana boshlaganligidir. 14-sutkaga kelib Van Gieson reaksiyasida kollagen saqlovchi tuzilmalarning maydoni va struktur shakllanganligi 3-sutkaga nisbatan yaqqolroq namoyon bo‘ldi. Tolalarning yirikroq tutamlarga birlashishi, ayrim sohalarda

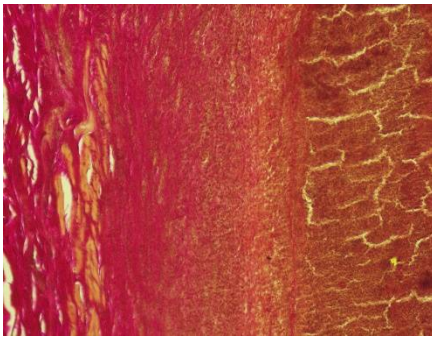
parallel yo‘nalishi va implantatsiya zonasi bo‘ylab biriktiruvchi to‘qima qatlamining shakllanishi kuzatildi. Bu davrni ksenotransplantat atrofida faol fibroplastik qayta qurilish va biriktiruvchi to‘qima matriksining shakllanish bosqichi sifatida baholash mumkin.

Qo‘y ksenotransplantatida implantat bilan chegaradosh sohada Van Gieson-pozitiv tolali komponentlar keng qatlam hosil qildi. Kollagenli strukturalarning zichligi oshgan va ayrim qismlarda tolalarning implantat yuzasi bo‘ylab yo‘nalishi ko‘rinadi. Qoramol ksenotransplantatida implantat atrofida qizil-pushti bo‘yalgan to‘lqinsimon tolali tuzilmalar aniqlanadi. Ular ayrim sohalarda bir-biriga nisbatan parallel joylashib, implantat bilan atrof to‘qima o‘rtasida struktur bog‘lanish shakllanayotganini ko‘rsatadi. Biroq to‘qimaning ayrim qismlarida geterogenlik saqlanadi.

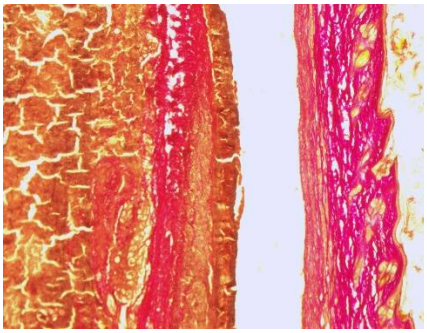
Cho‘chqa ksenotransplantatida Van Gieson-pozitiv tolalar nisbatan uzun va yo‘naltirilgan tutamlar shaklida kam sonli ko‘rinadi. Implantatga yaqin sohalarda tolali biriktiruvchi to‘qima komponentlarining tartiblanishi nisbatan sust. Kuzatuvning 35-sutkasida 3 va 14-sutkalarga nisbatan tolali biriktiruvchi to‘qimaning arxitektonikasi ancha shakllangan. Van Gieson bo‘yicha intensiv bo‘yalgan kollagenli tuzilmalar yirik va nisbatan tartibli tutamlar hosil qilgan. Ayrim maydonlarda tolalarning parallel yo‘nalishi va zichlashishi kuzatilishi biriktiruvchi to‘qima matriksining remodellanishi va yetilishi bilan mos keladi. Cho‘chqa ksenotransplantati qo‘llanilgan guruhda (6-rasm) implantatsiya sohasi bo‘ylab shakllangan biriktiruvchi to‘qima qatlamida kollagen komponentlarining siyrak joylashishi kuzatiladi.



4-rasm. Qo‘y ksenotransplantati implantatsiyasidan keyingi 35-sutka. Implantat-resipient to‘qima chegarasida notekis joylashgan kollagenli tuzilmalar. Van Gieson usulida bo‘yash. Kattalashtirish: 10x40.



5-rasm. Qoramol ksenotransplantati implantatsiyasidan keyingi 35-sutka. Implantat-resipient to‘qima chegarasida notekis joylashgan kollagenli tuzilmalar. Van Gieson usulida bo‘yash. Kattalashtirish: 10x40.



6-rasm. Cho‘chqa ksenotransplantati implantatsiyasidan keyingi 35-sutka. Implantat-resipient to‘qima chegarasida notekis joylashgan kollagenli tuzilmalar. Van Gieson usulida bo‘yash. Kattalashtirish: 10x40.

Tolali tuzilmalarning nisbatan tartiblangan arxitektonikasi erta muddatlardagi geterogen manzaradan farq qiladi. Qoramol ksenotransplantatida (5-rasm) implantat bilan tutash sohada biroz zichlashgan tolali biriktiruvchi to‘qima qatlami yaqqol namoyon bo‘ladi. Van Gieson-pozitiv strukturalarning zichligi o‘rtacha bo‘lib, implantat chegarasi bo‘ylab uzluksizroq to‘qima zonasi kuchsiz shakllangan. Qo‘y ksenotransplantatida (4-rasm) qizil-pushti rangda intensiv bo‘yalgan yirik kollagen tutamlari kuzatiladi. Ular turli yo‘nalishda joylashgan bo‘lsada, ayrim sohalarda zich va yirik tolali tuzilmalarni hosil qiladi. Bu ko‘rinish biriktiruvchi to‘qima matriksining kechki bosqichda qayta qurilishi bilan mos keladi.

Implantatsiyadan keyingi 3-sutkada olinganda, ya’ni kuzatuvning erta bosqichida implantatsiya sohasidagi morfologik manzara asosan to‘qimalarning shikastlanishga nisbatan dastlabki reaksiyasi bilan tavsiflandi. Implantat atrofida yallig‘lanish hujayralari va interstitsial o‘zgarishlar kuzatildi. Van Gieson usulida bo‘yalganda implantat atrofida yangi shakllanayotgan kollagen komponentlarining miqdori nisbatan kam bo‘lib, biriktiruvchi to‘qima karkasi hali to‘liq shakllanmagan holatda bo‘ladi.

Muhokama. Olingan gistokimyoviy ma’lumotlar ksenotransplantat implantatsiyasidan keyin atrof to‘qimadagi regenerativ jarayonlar vaqtga bog‘liq ravishda bosqichma-bosqich kechishini ko‘rsatadi. Erta muddatlarda to‘qimaning implantatsiyaga dastlabki reaksiyasi ustunlik qilsa, keyingi bosqichlarda fibroblastik faollik, hujayradan tashqari matriks sintezi va kollagen tolalarining shakllanishi yetakchi ahamiyat kasb etadi.

Ayniqsa, 14-21-sutkalar biriktiruvchi to‘qima matriksining faol shakllanish bosqichi sifatida, 28-35-sutkalar esa kollagen tolalarining tartiblanishi va to‘qima remodellanishi bosqichi sifatida baholanishi mumkin. Bunda faqat kollagen miqdorining ko‘payishini ijobiy natija sifatida baholash yetarli emas. Implantat atrofida haddan tashqari zich va chegaralangan fibroz kapsulaning shakllanishi bilan implantat strukturasiga yo‘nalgan tartibli biriktiruvchi to‘qima integratsiyasini morfologik jihatdan farqlash muhim. Shu sababli Van Gieson bo‘yicha kollagenning bo‘yalish darajasi bilan birga tolalarning arxitektonikasi, yo‘nalishi, zichligi va implantat-to‘qimada joylashishi kompleks baholanishi lozim.

Cho‘chqa, qoramol va qo‘ydan olingan ksenotransplantatlarda mazkur ko‘rsatkichlarning farq qilishi materiallarning to‘qima bilan biologik integratsiyalanish xususiyatlaridagi tafovutlarni aks ettirishi mumkin.

Xulosa

Ksenotransplantat implantatsiyasidan keyin atrof yumshoq to‘qimalarda biriktiruvchi to‘qima shakllanishi bosqichma-bosqich kechadi va uning dinamikasini Van Gieson gistokimyoviy usuli yordamida baholash mumkin. Erta kuzatuv muddatlarida (3-7 sutka) biriktiruvchi to‘qima karkasining dastlabki shakllanish belgilari kuzatilsa, 14-21-sutkalarda kollagenogenez va hujayradan tashqari matriks shakllanishi faollashadi. 28-35-sutkalarda kollagen tolalarining zichlashishi, tartiblanishi va biriktiruvchi to‘qima strukturasining yetilishi remodellanish jarayonini aks ettiradi. Cho‘chqa, qoramol va qo‘ydan olingan ksenotransplantatlarni Van Gieson usulida qiyosiy o‘rganish ularning to‘qima integratsiyasi va biriktiruvchi to‘qima hosil bo‘lishiga ta’sirini morfologik jihatdan farqlash imkonini beradi. Ksenotransplantat samaradorligini baholashda kollagen miqdori bilan bir qatorda uning arxitekturasi, tolalarning tartiblanishi va implantat-to‘qima interfeysidagi struktur tashkillanishi ham hisobga olinishi maqsadga muvofiq.

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