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The impact of biomaterials in the reconstructive gynecologic surgery

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Abstract

Pelvic floor disorders comprise a series of pathologies that the urogynecologist surgeon must correct using the latest materials and techniques developed. Stress urinary incontinece and pelvic organ prolapse are major health issues that affect the quality of life of women, all over the world. In the past years there has been a tendency to adopt synthetic and biological materials to enforce the repairs during the surgical interventions. The outcome of the surgical procedure is dictated by the properties of the material used, individual immune response and organic factors. Surgisis pelvic floor grafts are absorbable, non-crosslinked, multi-layered sheets of extracellular matrix collagen derived from porcine small intestinal subcumosa. The biomaterials used should induce a limited inflammatory response in order to achieve optimal reconstructive remodelling. The aim of this paper is to present a case report in which biological tissue grafts were used in the course of the surgical interventions in order to correct structural defects.
Keywords: *reconstructive surgery, surgisis, polypropylene mesh, vaginoplasty*

Introduction

In the view of the occurence of local complications attributed to the use of synthetic materials, such as erosion and pain, the search for alternative materials in the use of reconstructive surgery is in full action[1,2,3].

Biological tissue grafts derived from dermis, pericardium and small intestine submucosa of bovine and porcine origin have been used in the past years for the surgical correction of soft tissue defects such as breast reconstruction[4], hernia repair[5] and orthopedic interventions[6].

The main advantage of biological materials is that they can be used on contaminated granulation tissue as well as normal tissue. This can be explained by the rapid revascularization and clearance of bacteria[7,8]. In contrast, synthetic polymer mesh materials have a greater risk of infection[9].

Biological grafts represent an alternative to synthetic mesh. The use of synthetic mesh has been reported to expose the patient to complications such as vaginal wall erosion, chronic pain and dyspareunia[10]. Acellular animal collagen matrices derived from the porcine small intestine can be used to correct tissue defects. This biological material requires extensive processing in order to eliminate the risk of tissue rejection and avoid complications.

In order to resist degradation after the implantation the biological material need to be decellularized, sterilized and cross-linked[10]. This process is vital step in the preparation of the material in order to render it nonimmunogenic and reduce the risk of viral or prionic transmission[11]. However, due to extensive processing the the biomechanical properties can be affected[12].

The outcome of the surgical intrvention using biological material depends on several factors including: the materials physical properties (porosity and degradability), the mechanical properties (stiffness and strength), the patient's immune response to the implanted material and the individual anatomy and comorbidities[13].

Biomechanical properties and host response of Xenografts

In a study developed in 2010, Rice et al. demonstrated that the tensile strenghts of biomaterials developed from the small inestinal submucosa increases after 60 days of implantation in a rat abdominal wall defect[14]. Similar results were observed by Zhang et al and Badylak et al.[15,16]. Authors concluded that biomaterials derived from small intestinal porcine submucosa appears to increase in strength for as long as 2 years after the surgical intervention. In contrast, porcine dermal collagen matrices appear to be degraded quiclky (about three months).

The available data suggests that the cross-linkage negativelly affects the rate of degradation and the degree of the inflamatory response induced by the host. Due to the fact that cross-linked biological materials induce little cell infiltration the body reacts with a limited response in collagen remodelling and graft degradation[17,18]. In contrast, in non-cross-linked xenografts, cell infiltration was greater thus the collagen production and degradation rates were higher[14,19,20]. Two studies conducted in 2004 and 2010 by Wiedemann et al. and Deprest et al. demonstrated that the biological materials (porcine small intestinal submucosa) used in their study was replaced by native tissue in humans[21,22].

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The key factor for ensuring a desirable outcome during reconstructive surgery using biomaterials is represented by the „biodegradability" and this will assure an active remodelling response rather than a scar. In 2006 Baessler et al. conducted a study using small intestinal porcine submucosa. The authors observed that 60% of the implant was resorbed in 30 days and the collagen scaffold had been completely replaced within 3 months[23,24]. As we mentioned before, the absence of inflammatory response allows macrophage to create a neomatrix that is stronger than the preexisting native tissue[24,25].

First and second-generation organic polymers

First generation organic polymers

The first generation of organic polymers allowed persistence of denatured animal collagen during implantation. This process was due to the fact that scientists cross-linked the component collagen fibers by metallic salt precipitation. The inflammatory macrophage response developed a chronic foreign-body giant-cell reaction. This was the first step precludes the chance of constructive remodeling due to an intense cicatrisation process[26,27]. Healing is characterized by dense but poorly organized fibrous tissue that forms a weak connection to the wall[28].

Second generation organic polymers

The second generation polymers allowed the preservation of a normal collagen structure and viable matrix that created a biodegradable scaffold for the host tissue to colonize. Scientists prepared a collagen scaffold in their natural state. The residual fibroblasts and endothelial animal deoxyribonucleic acid were extracted by gentle osmotic or enzymatic leaching. This allows the implant to be resorbed in 30 days and the matrix to be completely replaced in 3 months. This allows the macrophage to create a new matrix that is stronger than the preexisting tissue.

Mast cells are activated in order to release granules that have a high content of histamine, heaprin and cytokines. This helps create edema, regulate vascular proliferation and and trigger a chemotactic response that is needed in the early stages of wound healing.

Macrophages are white blood cells produced by the division of invading monocytes. Macrophages contribute to the innate immunity through nonspecific phagocytes and by stimualting pathogen-specific cell-mediated response. They play an important role in the regulation of injury response and wound healing. Proinflammatory and cytotoxic macrophages (marked as M1) promote pathogen killing and phagocytosis of foreign materials. The second phenotype of macrophages (marked as M2) encourages an immuno-regulatory response which leads to constructive tissue remodelling[26].

Fibroblasts represent the main component of healing due to the secretion of fibrous and adhesive proteins.

Cse Report

Case Series

Surgisis (by Cook Biodesign) is an absorbable biomaterial, non-crosslinked, multi-layered sheets of extracellular matrix collagen derived from porcine small intestinal submucosa.

In this article we present 4 case reports, one with recurrent obstetric rectovaginal fistula, a patient with mesh extrusion, one with operated carcinoma and another one diagnosed with squamos cell carcinoma stage II A.

During follow-up of the oncological cases we observed good results using Surgisis grafts. It is known that radiation therapy causes numerous epithelial and stromal changes, prominent among which is fibrosis with its early and late consequences. We were pleased to observe, at three month follow-up visit, the local exam of the oncological cases revealed normal epithelium and restored vascularization.

The treatment of post-obstetrical rectovaginal fistulas represent a challenge in gynecologic surgery because the success rate for the traditional techniques is reduced. The patient underwent several surgical attempts to correct the rectovaginal fistula before being hospitalized in our clinic. In the case of mesh extrusion the biomaterial was heplful in correcting and reinforcing the anterior vaginal wall after the excision.

Case 1: Recurrent obstetric rectovaginal fistula treated by surgisis graft

The surgical intervention started out by identifying the fistula. The cranial vaginal extremity of the fistula was revealed through the rectal instillation of 50 ml methylene blue solution and 50 ml of air. The fistula was identified in the vaginal mucous folds at approximately 2 cm from the hymeneal ring. With the aid of a metal grooved probe we identified the rectal extremity of the fistula at 4 cm from the anus. The technique of episyoproctotomy was performed. After excision of the fistulous tract, we dissected and and mobilized 2 cm lateral the vaginal and rectal walls on the entire length of the initial incision. The external anal sphincter muscles delimitation was performed by annular dissection of the tissue planes laterally on each side. Electric stimulation to the visible muscular structures was performed in order to identify

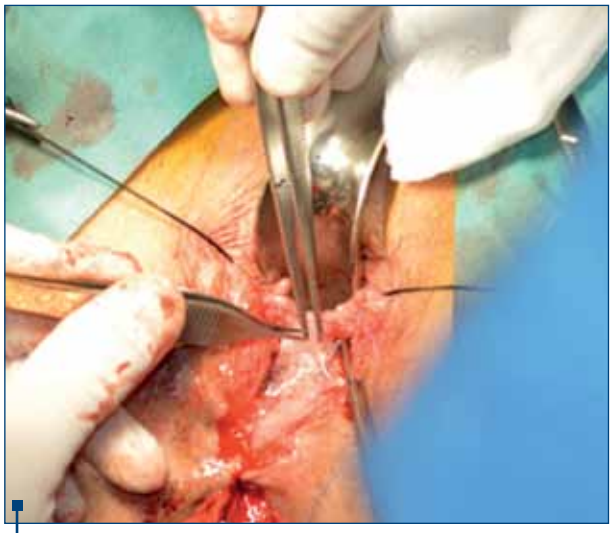

Figure 1. Intraoperative aspect

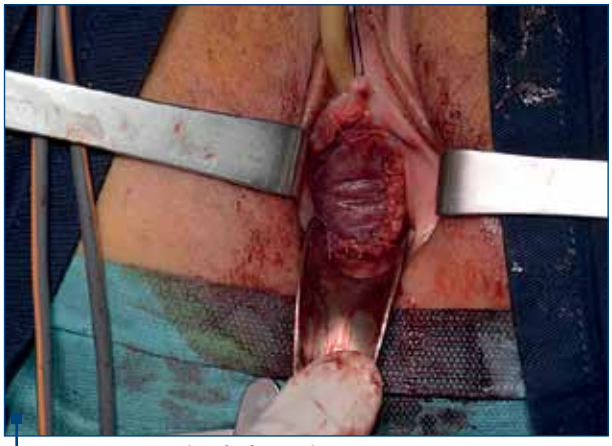

Figure 2. Biomaterial graft after mesh extrusion

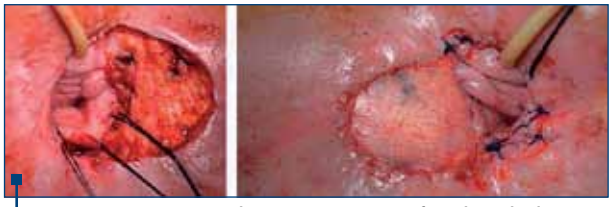

Figure 3. Intraoperative and postoperative aspect after relapsed vulvar carcinoma

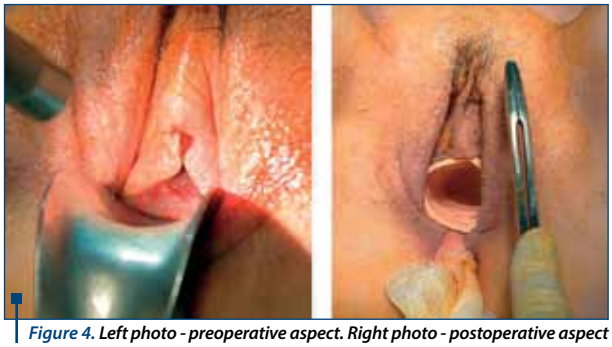

Figure 4. Left photo - preoperative aspect. Right photo - postoperative aspect

the sphincter muscle's contraction. Surgical sutures were used to close the rectal surgical incision in two plans with resorbable monofilament (PDS 3/0) to the level of mucocutaneous junction. At this stage we interposed a fragment measuring 4/3 cm of Surgisis graft which was fixed with resorbable 3/0 sutures at the corners. The external anal sphincter was rebuilt using two "Ü" shaped sutures of PDS 3/0 and Vicryl no.1. The vaginal incision was sutured with interrupted continuous Vicryl 2/0. The scarred perineal skin was excised and the superficial incision was closed using separate sutures (Figure 1).

Case 2: Mesh extrusion

A 45 year old presented with bloody vaginal discharge and dyspareunia. The patient underwent a transobturator sling procedure 1 year before. Clinical examination revealed a short anterior vaginal wall - approximately 2 cm between the urethral meatus and the cervix, as well as mesh extrusion for 3/2cm at this level.

We performed a 4 cm longitudinal incision at the level of the anterior vaginal wall. Sharp and blunt dissection was performed in order to remove the extruded mesh toghether with vaginal wall. We attempted to corect the tissue defect and the distance between the urethral meatus and the cervix by interposing a 4/2 cm Surgisis fragment which was fixed with separate 3/0 Vicryl sutures. The patient was discharged from the hospital and monitored by clinical examination at 2,4, 8 and 12 weeks. After three months the clinical exam revealed the xenogenic scaffold completely replaced with the host's epithelium (Figure 2).

Case 3: Relapsed vulvar carcinoma

This case relates about a 76 year-old patient with an operated vulvar carcinoma. After radiation therapy was performed the patient underwent 6 interventions for local relapse in a 12 year period. The clinical examination revealed a local tumor recurrence for which the patient received radiation therapy. The local anatomy and the margins after excision revealed a large skin defect that proved difficult with conventional means. In this case, Surgisis was an excellent alternative to correct the tissue defect. The local exam at three months postoperative revealed epithelium undergoing restoration (Figure 3).

Case 4: Neovagin reconstruction

A case of 36 year old patient who was diagnosed with squamos cell carcinoma stage II A. The patient underwent radical hysterectomy and pelvic lymphadenectomy followed by radiotherapy. The clinical examination revealed no signs of local relapse after three years from the radical intervention and vaginal length of 2 cm. The surgery repair methods included sharp and blunt dissection with the aim to rebuild a normal anatomy by making a neovagina using surgisis biomaterial mounted on a soft vaginal mould with band separation of the rectum from the urethrovesical space (Figure 4).

Discussion

Choosing the material

It is safe to say that any material that is introduced in the human body will cause complications in some cases due to the fact that the immune response is variable from one individual to another. The principle of biodegradability must be understood by the surgeon in order to achieve the best results.

The biomaterials used must be adjusted so that the degradability overcomes an important aspect. The material used needs to allow enough time for the development of new tissue in on order to provide adequate mechanical support to the pelvic structures. An initial inflammmatory response is required to develop angiogenesis and collagen ingrowth. This correlates with an M1 macrophage response. The biomaterial used in the pelvic reconstructive surgical procedures must be: degradable, provoke an acute inflammatory response, undergo tissue remodeling, permeable to cells and be mechanically robust at the point of implantation.

Synthetic meshes may be a permanent solution but the drawback is represented by a strong and persistent

inflammmatory reaction. This explains the durability of the repair but may also cause long-term complications.

Surgisis is a second generation biomaterial due to extensive acellular processing in order to render the graft non-immunogenic. This process allows to keep the matrix's characteristics that include collagen, glycosaminoglycans and glycoproteins in order for the host cells to repopulate the tissue.

Conclusions

Biological grafts represent a viable alternative in the surgical treatment of pelvic floor disorders. The data derived from the clinical trials shows that both synthethic and biological materials can be used in the treatment of pelvic floor disorders. Polypropylene meshes are associated with a high incidence of complications due to an exacerbated host response.

Biomaterials allow the integration of the graft on to healthy tissue and even contaminated granuation tissue without leaving foreign material in place. Gradually, the scaffold is replace by host cells which remodel the tissue.

The favorable outcome of the surgical intrvention using biological material can be predicted with the following: the material's physical and mechanical properties, the patient's immune response to the implanted material and the individual anatomy and comorbidities. ■

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