Gynecologic Oncology Reports 18 (2016) 36–39

Contents lists available at ScienceDirect

Gynecologic Oncology Reports

journal homepage: www.elsevier.com/locate/gynor

Case report

A surgical multi-layer technique for pelvic reconstruction after total exenteration using a combination of pedicled omental flap, human acellular dermal matrix and autologous adipose derived cells

Anna Myriam Perrone [a,*], Alessandra Livi [a], Milena Fini [b], Elena Bondioli [c], Sergio Concetti [d], Alessio Giuseppe Morganti [e], Federico Contedini [f], Pierandrea De Iaco [a]

[a] Oncologic Gynecology Unit, Sant'Orsola-Malpighi Hospital, via Massarenti 13, 40138 Bologna, Italy
[b] Laboratory of Preclinical and Surgical Studies, Rizzoli Orthopaedic Institute, via di Barbiano 1/10, 40136 Bologna, Italy
[c] Burns Intensive Care Unit and 'Regione Emilia Romagna' Skin Bank, Bufalini Hospital, viale Ghirotti 286, 47023 Cesena, Italy
[d] Complex Pelvic Surgery Unit, Sant'Orsola-Malpighi Hospital, via Palagi 9, 40138 Bologna, Italy
[e] Radiotherapy Unit, Sant'Orsola-Malpighi Hospital, via Massarenti 13, 40138 Bologna, Italy
[f] Department of Plastic and Reconstructive Surgery, S. Orsola-Malpighi Hospital, via Massarenti 13, 40138 Bologna, Italy

ARTICLE INFO

Article history:
Received 25 September 2016
Received in revised form 23 October 2016
Accepted 25 October 2016
Available online 27 October 2016

Keywords:
Cervical cancer
Pelvic exenteration
Human acellular dermal matrix
Omental flap
Pelvic reconstruction
Lipofilling

1. Introduction

Women affected by relapsed gynecological cancer are often treated with pelvic exenteration (PE); this aggressive surgical procedure implies a large hard-to-fill pelvic defect. Moreover patients submitted to PE for gynecologic malignancies present severe postoperative local complications (including abdominal infections, intestinal fistulas, small bowel perforation, terminal colostomy complications, vaginal stump dehiscence, pelvic organ prolapse and even perineal evisceration) in about 21% of cases and a 3% mortality within 30 days (Chiantera et al., 2014).

Because of young age and survival greater than 50% at 5-year in patients with no residual tumor after surgery, a new approach with better clinical results to pelvic reconstruction is needed.

Different reconstruction techniques were proposed to improve abdominal organ support and reduce complications, with conflicting results (Kolehmainen et al., 2013). Synthetic mesh used for pelvic reconstruction, despite increased mechanical support, attempts to adhesions and other relevant complications (Dinsmore et al., 2000). Primary reconstructive myocutaneous flap (MF) from abdomen or thigh is invasive and sometimes it cannot be performed because of previous incisions, hernia or insufficient flap tissue volume that compromise the donor site. Pedicled greater omental flap (PGOF) represents the standard procedure used for pelvic dead space filling, but it cannot provide the required support alone.

As a result of the disadvantages of these techniques, the use of bioprosthetic materials, such as human acellular dermal matrix (HADM) has been explored (Bondioli et al., 2014). Post-operative abdominal adhesion reduction and well tolerability in compromised tissues are its major advantages (Silverman, 2011).

The association of a thigh-based MF with HADM has been proposed by Said H.K. et al. for the pelvic floor reconstruction in recurrent vulvar cancer (Said et al., 2007). More recently, a two-layer reconstruction with a combination of HADM and PGOF has been performed by Momoh A.O. et al. after an anterior PE for bladder cancer (Momoh et al., 2010).

Moreover, some reports have suggested that the mechanical performance of HADM could be enhanced by cell seeding and some Authors have already created matrix seeded with adipose-derived stem cells (ASCs). The structural framework of the HADM is favourable for cell incorporation and this procedure improves the mechanical support of the matrix (Altman et al., 2008). Moreover ASCs combined with HADM were also successfully used to accelerate wound healing because of induced angiogenesis. To obtain these multipotent stem cells and progenitor cells, autologous adipose tissue is harvested from the patient (Komatsu et al., 2013).

We report a surgical multi-layer technique of pelvic reconstruction using a combination of pedicled omental flap and HADM filled with

* Corresponding author at: Unit of Oncologic Gynecology, S. Orsola-Malpighi Hospital, via Massarenti 13, 40138 Bologna, Italy.
E-mail address: myriam.perrone@aosp.bo.it (A.M. Perrone).

http://dx.doi.org/10.1016/j.gore.2016.10.006

microinjection of adipose-derived Stromal Vascular Fraction (SVF) following total pelvic exenteration (TPE) for the treatment of recurrent cervical cancer.

2. Case presentation

A 41-years-old Caucasian woman from Eastern Europe presented to Gynaecologic Unit in January 2014 for a high-grade squamous cell cervical carcinoma (FIGO stage IIIB) and enlarged bilateral common iliac lymph nodes (maximum diameter of 17 mm) suspected for metastasis. The patient underwent right nephrostomy before treatment for right hydronephrosis.

One month later the patient started a combined external beam radiotherapy (46 Gy) on tumor and pelvic lymph nodes and Cisplatin based systemic chemotherapy. The curative treatment was completed by 28 Gy high dose-rate brachytherapy boost.

In order to explore the response to treatment, the patient was submitted to pelvic MRI (4 months after therapy) and 18F FDG-PET/CT (6 months after therapy). MRI showed a complete radiologic response with fibrotic tissue but the 18F FDG-PET/CT showed a focal metabolic uptake ($SUV_{max} = 13.4$) located in the cervical region suspicious for cancer persistence, without nodal uptake. A cold biopsy of the cervix confirmed the persistence of disease.

Therefore, we proposed surgical intervention modulated on the results of intraoperative frozen sections with the possibility of TPE if bowel and bladder were involved. In case of PE, plastic reconstruction with PGOF and HADM filled with adipose tissue would be performed.

After a longitudinal laparotomy we performed peritoneal washing for cytology and a complete exploration of abdominal cavity that showed a local involvement of uterus, bladder and rectum without lymph nodes involvement confirmed by the frozen section biopsies. Indeed the patient underwent to supraelevatoric TPE (type I) according to the classification by Magrina et al. (1997), with lymph nodes dissection extended to common iliac vessels and para-aortic and para-caval lymph nodes. Pelvic peritoneum, fatty tissue among vessels and part of the right levator ani muscle were removed without residual disease based on frozen section results (Fig. 1A). Fecal divertion was obtained with a terminal para-rectal sigmoidostomy on the left side and urinary divertion with an ileo-colonic heterotopic urinary continent pouch (Indiana technique) (Rowland et al., 1987).

Immediate reconstruction of the pelvic floor was achieved using a multi-layer technique. Firstly, the pelvic dead space was partially filled with PGOF on the left gastro-epiploic artery (Fig. 1B). Then, the omentum was covered by a 20×20×2 mm inlay of HADM inserted circumferentially into the pelvic defect with interrupted monofilament resorbable sutures onto the residual pelvic muscle and fascia and their insertions onto the pelvic bone and periosteum (Fig. 1C). Finally, PGOF was filled with adipose tissue to increase its thickness and to create a sort of natural hammock for supporting the intestinal loops and avoiding inter-organs adhesions and pelvic prolapse. Adipose tissue was obtained with the lipoaspiration in abdominal subcutaneous fat tissue (Fig. 2A); the low pressure of aspiration was preferred to minimize damage to the graft. At the end of the procedure, 200–300 cm^3 of adipose tissue was aspirated and centrifugated (by Coleman Technique) to obtain 100–150 cm^3 of processed fat (Coleman, 1995). Finally microinjections of processed fat in the PGOF were performed (Fig. 2B) to increase volume. At the end of the procedure three abdominal tubular drains were inserted.

The final pathology confirmed the persistence of a high grade cervical squamous cell carcinoma with infiltration of uterus, right ovary, right ureter and bilateral proximal parametrium with negative surgical margins and positive peritoneal washing; none of nineteen lymph nodes removed revealed cancer metastasis.

The patient's post-operative course was uneventful and uncomplicated according to Clavien-Dindo classification of surgical complications (Dindo et al., 2004).

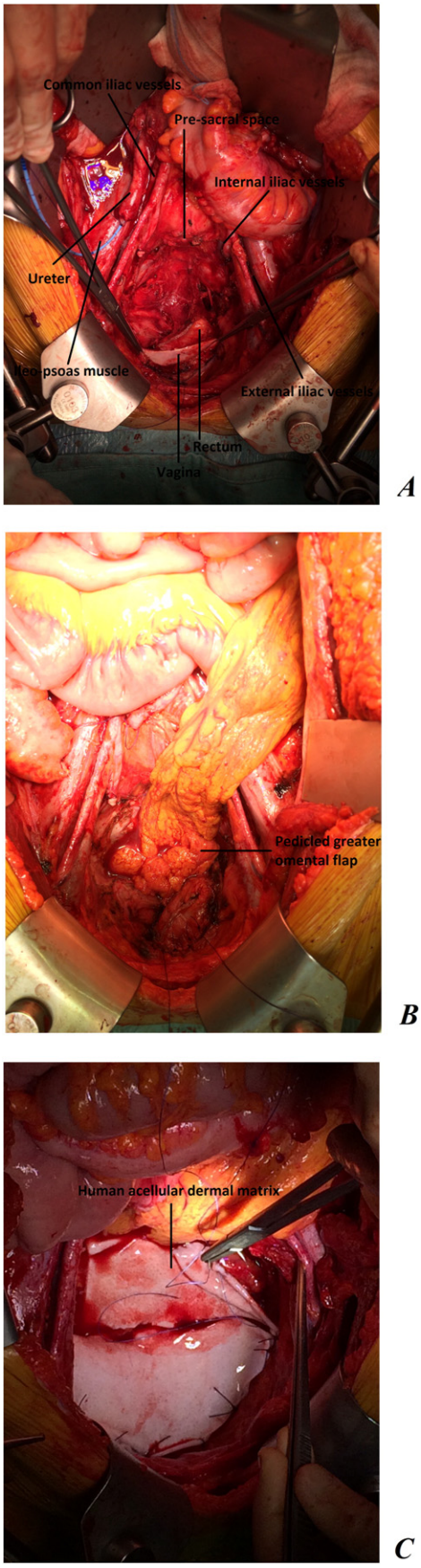
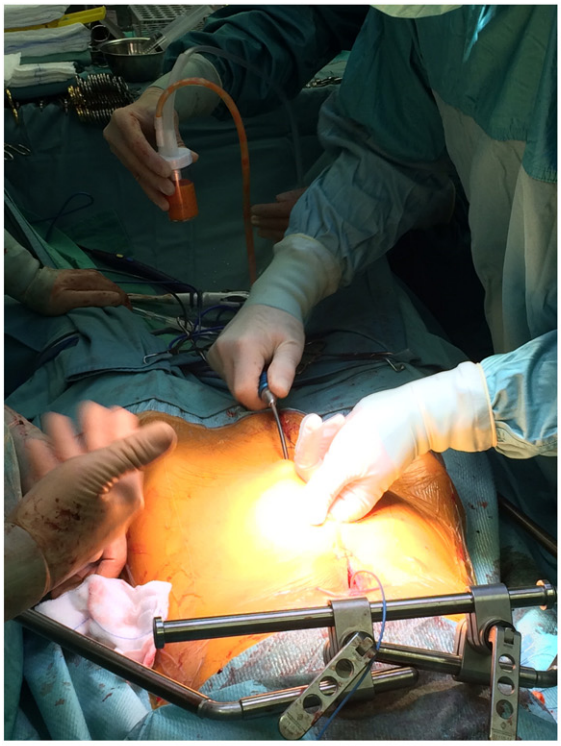
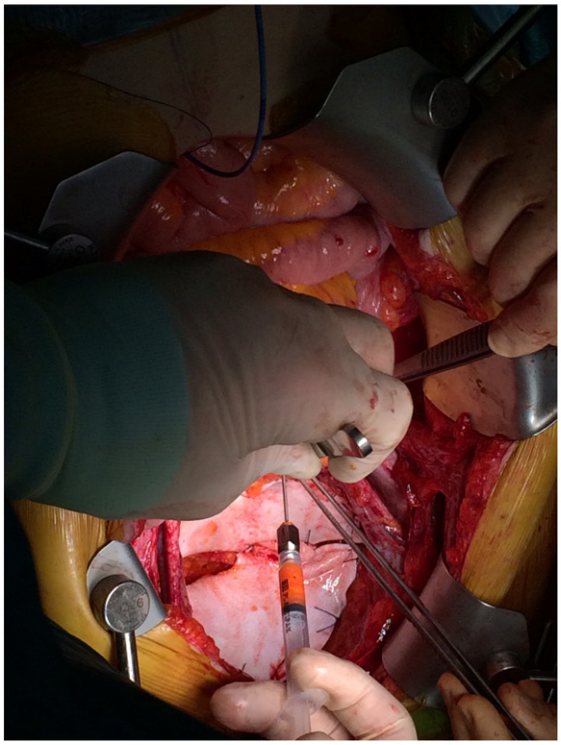


Fig. 1. Demolitive surgery and first step of reconstructive surgery **1A** Pelvic defect after TPE. **1B** Pelvic defect filled with PGOF. **1C** HADM positioned at the pelvic brim and fixed to pelvic fascia.



A



B

Fig. 2. Second step of reconstructive surgery, **2A** Adipose tissue obtained with the lipoaspiration in abdominal subcutaneous fat tissue. **2B** PGOF filled with microinjection of adipose tissue to increase its thickness and create a sort of natural hammock.

Thirty days after surgery patient was submitted to pelvic MRI that showed neither surgical complication nor cancer relapse. Three months later four cycles of adjuvant chemotherapy with Paclitaxel and Cisplatin were completed without significant systemic side effects. Six months after surgery because of the presence of two focal radiotracer's uptakes on the left pelvis (SUV max = 10.7) and in the pre-sacral area (SUVmax = 12.2) at restaging 18F FDG-PET/CT the patient started a second line chemotherapy with Bevacizumab and Topotecan and she was still alive at the last follow-up after 13 months from surgery.

3. Conclusions

A major purpose of pelvic reconstructive surgery is to fill tissue defect and improve structural organs support. Indeed, pelvic dead space is related to a high rate of local complications, especially local infections, pelvic organs herniation, bowel loops prolapse and obstruction (Chiantera et al., 2014; Kolehmainen et al., 2013; Dinsmore et al., 2000; Bondioli et al., 2014; Silverman, 2011; Said et al., 2007; Momoh et al., 2010; Altman et al., 2008; Komatsu et al., 2013; Magrina et al., 1997; Rowland et al., 1987; Coleman, 1995; Dindo et al., 2004; Croak et al., 2004). These adverse events significantly compromise patient's quality of life and sometimes require a second aggressive surgical intervention. Moreover patients submitted to PE for gynecological malignancies frequently have previously received radiotherapy, which might even double the frequency of local complications (Kolehmainen et al., 2013).

In some cases, synthetic mesh is used to provide long-lasting pelvic reconstruction. However, if placed directly over visceral organs, it induces intense host response, dense adhesions and other relevant complications, as bowel obstruction, perforation and fistulas. Moreover it often becomes infected and requires removal, especially if used in contaminated or previously irradiated fields (Albo et al., 2006).

Despite PGOF could sometimes provide soft well-vascularised tissue adequately obliterating pelvic defect, its mechanical support is negligible. Moreover in considerable proportion of patients it is not available because of previous surgeries or its volume is not sufficient (Butler & Rodriguez-Bigas, 2005). Therefore, when additional support or volume is required, the use of bioprosthetic material, such as HADM, seems to be promising. It can provide relevant advantages including excellent structural support and resistance to bacterial infection, even in presence of challenging conditions including bacterial contamination or prior irradiation (Butler et al., 2005).

In our case, the massive pelvic floor defect resulted after TPE and the inadequate volume of omentum, related to the thinness of the patient (BMI: 22), required to use HADM combined with the omental flap and microinject of fat to obliterate pelvic dead space, as previously planned. This technique permitted to completely obliterate the pelvic dead space in a thin patient with small omental flap.

In order to increase the thickness of the omental flap and improve its remodelling capabilities, we performed microinjection of fat and to the best our knowledge, this technique has not been previously reported in literature.

The pelvic MRI performed 30 days after surgery showed the complete obliteration of pelvic defect both by omentum and HADM, without any sign of prolapse or pelvic fluid (Fig. 3A). Moreover, the abdominal CT-scan performed 6 months later confirmed the persistence of omentum and adipose tissue volume (Fig. 3B).

In conclusion, the use of PGOF and HADM with microinjection of adipose cells could represent an efficient combination to provide structural support and volume in the reconstruction of the pelvic floor, with special regards of patients at higher risk of complications because of compromised tissues or with limited flap donor site.

Further comparative studies should evaluate the long-term outcomes of this technique in larger cohort of patients and elucidate indications and contraindications for its use.

Conflict of interest statement

The Authors BE and MF patented the decellularization method.

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

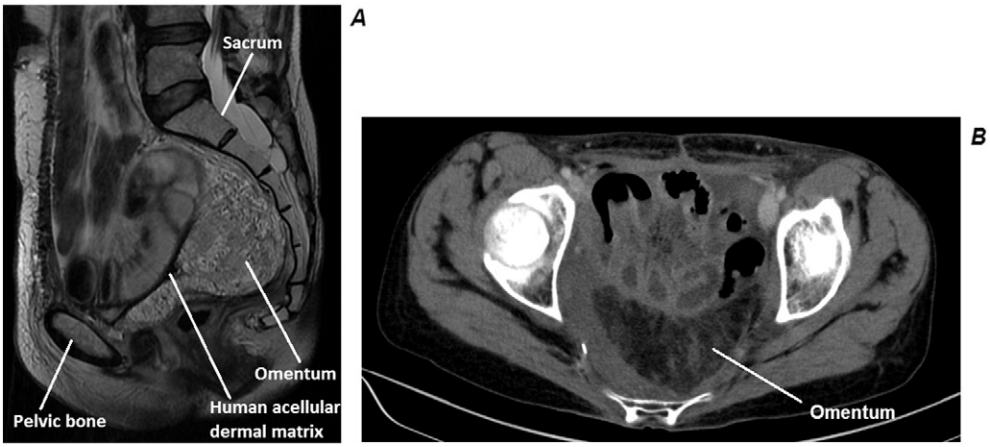


Fig. 3. Final imaging result, **2A** Final result at MRI performed 30 days after surgery. **3B** Final result at CT-scan performed 6 months after surgery.

Transparency document

The Transparency document associated with this article can be found, in the online version.

References

Albo, D., S.S., A., Berger, D.H., et al., 2006. Decellularized human cadaveric dermis provides a safe alternative for primary inguinal hernia repair in contaminated surgical fields. Am. J. Surg. 192 (5), e12–e17 (Nov).

Altman, A.M., Matthias, N., Yan, Y., et al., 2008. Dermal matrix as a carrier for in vivo delivery of human adipose-derived stem cells. Biomaterials 29 (10), 1431–1442 (Apr).

Bondioli, E., Fini, M., Veronesi, F., et al., 2014. Development and evaluation of a decellularized membrane from human dermis. J. Tissue Eng. Regen. Med. 8 (4), 325–336 (Apr).

Butler, C.E., Rodriguez-Bigas, M.A., 2005. Pelvic reconstruction after abdominoperineal resection: is it worthwhile? Ann. Surg. Oncol. 12 (2), 91–94 (Feb).

Butler, C.E., Langstein, H.N., Kronowitz, S.J., 2005. Pelvic, abdominal, and chest wall reconstruction with AlloDerm in patients at increased risk for mesh-related complications. Plast. Reconstr. Surg. 116, 1263–1275.

Chiantera, V., Rossi, M., De Iaco, P., et al., 2014. Morbidity after pelvic exenteration for gynecological malignancies: a retrospective multicentric study of 230 patients. Int. J. Gynecol. Cancer 24 (1), 156–164 (Jan).

Coleman, S.R., 1995. Long-term survival of fat transplants: controlled demonstrations. Aesthet. Plast. Surg. 19, 421–425 (Sept-Oct).

Croak, A.J., et al., 2004. Patients with vaginal rupture and evisceration. Obstet. Gynecol. 103, 572–576.

Dindo, D., Demartines, N., Clavien, P.A., 2004. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann. Surg. 240 (2), 205–213 (Aug).

Dinsmore, R.C., Calton, W.C., Harvey, S.B., Blaney, M.W., 2000. Prevention of adhesions to polypropylene mesh in a traumatized bowel model. J. Am. Coll. Surg. 191, 131.

Kolehmainen, M., Suominen, S., Tukiainen, E., 2013. Pelvic, perineal and genital reconstructions. Scand. J. Surg. 102, 25–31.

Komatsu, I., Yang, J., Zhang, Y., et al., 2013. Interstitial engraftment of adipose-derived stem cells into an acellular dermal matrix results in improved inward angiogenesis and tissue incorporation. J. Biomed. Mater. Res. A 101 (10), 2939–2947 (Oct).

Magrina, J.F., Stanhope, C.R., Weaver, A.L., 1997. Pelvic exenterations: supralevator, infralevator, and with vulvectomy. Gynecol. Oncol. 64, 130Y135.

Momoh, A.O., Kamat, A.M., Butler, C.E., 2010. Reconstruction of the pelvic floor with human acellular dermal matrix and omental flap following anterior pelvic exenteration. J. Plast. Reconstr. Aesthet. Surg. 63 (12), 2185–2187 (Dec).

Rowland, R.G., Mitchell, M.E., Bihrle, R., et al., 1987. Indiana continent urinary reservoir. J. Urol. 137 (6), 1136–1139 (Jun).

Said, H.K., Bevers, M., Butler, C.E., 2007. Reconstruction of the pelvic floor and perineum with human acellular dermal maytrix and thigh flaps following pelvic exenteration. Gynecol. Oncol. 107 (3), 578–582 (Dec).

Silverman, R.P., 2011. Acellular dermal matrix in abdominal wall reconstruction. Aesthet. Surg. J. 31 (7 Suppl), 24S–29S (Sep).