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Low back pain treated with disc decompression and autologous micro-fragmented adipose tissue: a case report

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Abstract

Background: **Pathologies affecting the vertebral disk are extremely common in western industrialized countries. Although the causes can be multiple, it has been demonstrated that this disorder is associated with a degeneration of the intervertebral disk. Current therapies are focused on the relief of the symptoms but cannot repair the damage nor stop the degenerative process. Recently, new strategies for the regeneration of the intervertebral disk, such as the use of mesenchymal stem cells, have been identified.**

Objective: **To evaluate the efficacy and potential benefits of using autologous, micro-fragmented and minimally manipulated adipose tissue graft (Lipogems®) associated with nucleoplasty for the decompression of the disk in a patient suffering for recurrent low back pain.**

Materials and Methods: **Micro-fragmented adipose tissue was obtained using a minimal manipulation technique in a closed system (Lipogems®), without the addition of enzymes or any other additives. Under radioscopic control and with Seldinger technique a minimal part of the nucleus pulposus was emptied to reduce excessive compression level inside the disk, thus creating a virtual cavity. With a specific instrument, manually rotated at 360°, heat ablation of terminal nerve fibers with a radiofrequency probe was performed. At the end, autologous micro-fragmented adipose tissue was injected into the cavity.**

Results: **In the immediate post injection period, the patient reported a significant decrease in pain and the disappearance of the paresthesia at the left lower limb. The ODI score at 6 months revealed a decrease of the disability, switching from 46% at baseline to 24%, i.e. from "severe" to "minimal". The MRI at 6 months revealed a decompression of the treated disk and an increase in the signal intensity of the T2 sequences at the level of the nucleus pulposus.**

Conclusions: **Although this is a single case report, part of a larger study, the results are very encouraging. The decrease of the ODI score and the decompression of the disk shown by the MRI gave evidence of the efficacy and potential benefits of using micro-fragmented, autologous, and minimally manipulated adipose tissue associated with nucleoplasty for the decompression of the disk.**

Introduction

Pathologies affecting the vertebral disk are extremely common in western industrialized countries. Low back pain affects 60 to 80% of the adult population and is the most relevant cause of working infirmity and disability under 45 years of age, with a big economic burden due to prolonged absences from work and costs of the treatments.

Although the causes of low back pain can be multiple, it is clear that this disorder is associated with a degeneration of the intervertebral disk (IVD), which, in turns, can contribute to facet joint disorder, radiculopathy and, eventually, can induce myelopathies. In a healthy disk, there is an equilibrium between anabolic and catabolic processes regulated by enzymes, cytokines, and endogenous cells. The degeneration of the disk is triggered by a decrease of nucleus pulposus (NP) cell number. Current therapies, both surgical (excision of the disc and arthrodesis) and not surgical (physical therapy, nerve root blocks), are focused on the relief of the symptoms but cannot repair the damage nor stop the degenerative process at the adjacent levels. Recently, new strategies for the regeneration of the intervertebral disk have been identified[1-3], mainly because of the new advances in the understanding of the molecular mechanisms responsible for tissue regeneration. It seems that the replacement of autologous NP cells can be a possible solution to slow down the degeneration process. In analogy with the ACI (autologous chondrocytes implant) technique, procedures for harvesting and expanding cells from NP of healthy disks have been tested. These techniques are invasive and only a low number of cells with low proliferative potential can be harvested. Because of these limitations, the use of accessible and abundant sources of cells with high regenerative potential is preferable, and mesenchymal stem cells (MSCs) are good candidates because of their high self-renewal capacity and multilineage differentiation potential[4]. Because of their abundance, the easy access, and the simple isolation procedures[5,6], adipose tissue-derived MSCs (ADMSCs) have been considered as good candidates for tissue regeneration[7]. ADMSCs are routinely obtained enzymatically from fat lipoaspirates as SVF[8], and/or may undergo prolonged *ex vivo* expansion, with significant senescence and decline in multipotency. Besides, these techniques have complex regulatory issues[9,10], and often lead to clinical results below expectations[11]. Hence, availability of a minimally manipulated, autologous adipose tissue would have remarkable biomedical and clinical relevance. For this reason, a new device, named Lipogems®, has been developed[12-14]. The technique is non-traumatic and intra-operatively provides micro-fragmented adipose tissue in a short time (15-20 minutes), without expansion and/or enzymatic treatment.

The purpose of this case report is to demonstrate the efficacy and potential benefits of using autologous, micro-fragmented, and minimally manipulated adipose tissue graft, associated with the minimally invasive procedure of nucleoplasty, for the decompression of the disk in a patient suffering for recurrent low back pain and with little or no benefits from conservative medical treatments. This minimally invasive procedure, associated with the radiofrequency ablation of the "annulus", allows the mechanical removal of a small part of nucleus pulposus at the central part of the disk. The entire procedure is performed under local anesthesia and fluoroscopic control and is indicated for disk bulging and contained disk herniation that, on MRI, appears as black disc. The aim of the procedure is to decompress the disk, create a retraction of the "annulus" by decreasing the compression of the nerve root, and desensitize the terminal nociceptors, thereby reducing the sensation of pain.

Case presentation

T.E., a 43-year-old male, 85 kg x 177 cm with a prior history of total hip arthroplasty 3 years before due to a car accident. The patient suffered for a recurrent serious chronic low back pain due to an L3-L4 intervertebral disk degeneration. The MRI revealed a dehydrated disk, reduced in volume and height. The patient suffered pain while walking, during and after work and was very poorly responsive to the pharmacological treatment (diclofenac+tiocolchicoside daily). Patient quality of life was consistently decreased and the working capacity and effective performance of duties seriously compromised. In addition, the common and very easy daily living activities were functionally impaired, preventing even the most basic actions such as tying the shoes.

Materials and methods

Harvesting and processing of the adipose tissue

The procedure was performed under local anesthesia. Before harvesting the fat tissue, the selected site is injected with local anesthesia and adrenaline at high dilution. Two small incisions were performed with an 18G needle, and the fluid was injected using a 17G blunt cannula. The fat (40 cc) was then harvested using a 13G blunt cannula attached to a Vaclock 20 ml syringe and introduced into the Lipogems® processing kit. Lipogems® has been developed to improve the classical fat graft lipofilling technique[15] with the aim of providing transplantable clusters of lipoaspirate with reduced size for the improvement of their post-transplant engraftment[16,17]. The system con-

sists of a disposable kit for the aspiration, processing and reinjection of autologous adipose tissue in both human and veterinary medicine[18-23]. Its core is a disposable and closed device filled with saline solution that progressively reduces the size of the clusters of adipose tissue by means of mild mechanical forces and eliminates oil and blood residues responsible for the inflammation processes. The technique is non-traumatic and intra-operatively provides micro-fragmented fat in a short time (15-20 minutes), without expansion and/or enzymatic treatment. The vasculo-stromal niches of Lipogems® survive in the site of the injection and improve tissue health[24-28].

Surgical procedure

The awake, slightly sedated patient (midazolam i.v. 3 mg) is placed prone on the surgical bed and injected topically with 6 cc of Mepivacaine 2% and adrenaline (1:200.000) at the L3-L4 level, about 8 cm sideways the interspinous line. The intervertebral disk is localized with an 18G spinal needle under radioscopic control. With Seldinger technique, the needle is replaced with an operative cannula and a grasper is inserted to remove a minimal part of the NP, in order to obtain a retraction in the external size of the "annulus" fibrosus, thus creating a virtual cavity where the autologous micro-fragmented adipose tissue will be placed. Then, a radiofrequency probe is introduced to perform a 360° ablation. At the end, 2 ml of autologous micro-fragmented adipose tissue is injected. Total surgical time was 45 minutes.

Outcome measures

Clinical outcomes were determined using Oswestry Disability Index and MRI imaging. The Oswestry Disability Index (ODI) by Fairbank has become one of the principal condition-specific outcome measures used in the management of spinal disorders. It is a self-rating condition-specific outcome measure for the evaluation of low back pain disability. It consists of ten sections with six alternative responses describing functional impairment in a series of daily activities. Clinical outcomes were taken as following: ODI immediately before surgery (baseline), after the treatment, 1 week, 1, 3 and 6-months' follow-up; the MRI immediately before surgery (baseline) and at 6-months' follow-up.

Ethics

The procedure mentioned in this case report is in accordance with the ethical standards and with the Helsinki Declaration of 1975, as revised in 2000. The patient has been informed about risks, benefits and alternative options to the proposed treatment, and expressed and signed the informed consent form.

Results

In the immediate post injection period, the patient reported a significant decrease in pain and the disappearance of the paresthesia at the left lower limb. At the same time, the measurement of the treated disk, compared with pre-operative imaging, showed an increase of 1.3 mm at the same level. This evidence might be interpreted as a precocious sign of a lively metabolic response of the transplanted tissue, viable and proliferating in the new target site.

The ODI score at 6 months indicated a decrease of the disability, switching from 46% at baseline to 24%, i.e. from "severe" to "minimal" following Fairbank scores. The MRI at 6 months revealed an increase in the signal intensity in the T2 sequences at the level of the NP of the treated disk.

Measurements of the disk height at the same level, compared between pre- and post-op showed a significant augmentation (Figure 1).

From a subjective point of view, the patient referred a significant improvement in the quality of life and mood, and a disappearance of pain. The patient started to carry out normal daily activities and duties, stopped any pharmacological treatment and increased his work capability, i.e. carrying out of heavy manual tasks. At 6-months' follow-up, the clinical condition was stable and unchanged.

Discussion

The clinical results obtained for the single patient, together with the strong rationale that underlies the entire procedure, may represent a further step in regenerative medicine. The conventional treatment for a bulging and dehydrated disk (black disk) consists in the removal of the inactivated tissues in order to decrease the internal pressure and disk protrusion.

Nucleoplasty is a mini-invasive procedure that has been demonstrated to be effective in this kind of diseases, with good outcomes for the patient, and very low incidence of collateral effects[29]. At the end of the procedure, autologous micro-fragmented adipose tissue graft appears to be a strong base to create an optimal environment[30] where local tissues may augment their hydration, as seen at time distance of 6 months with MR imaging. The expected outcome found its basis on the mechanical decompression of the bulging disk, obtained by a partial subtraction of the nucleous polposus tissue, fol-

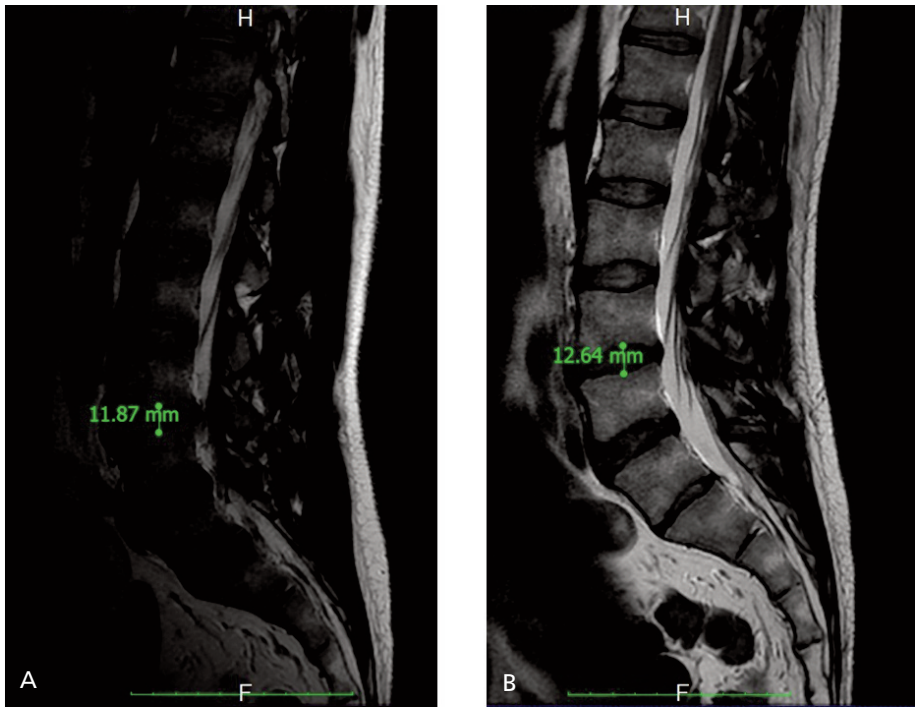

Figure 1. *A*, Pre-surgical sagittal T2-weighted MRI showing disc protrusion at L3-L4. *B*, Post-operative sagittal T2-weighted MRI. Note the consistent improvement of protrusion and the residual discal bulging, with increased intervertebral disc height, compared to preoperative images.

lowed by radiofrequency ablation of nerve fibers around the area submitted to decompression. These two actions are followed by the injection at the same site of a prepared solution of adipose tissue, rich with mesenchymal cells and other precursor cells.

This procedure represents a three-step treatment of the disk, providing decompression and revitalizing the inner part of the disk with a new population of cells.

No collateral effects have been reported, and this can be justified by the fact that this technique utilizes an autologous and not enzymatically or chemically treated tissue.

Conclusions

Tissue regeneration and, in this context, disk regeneration, represents the new challenge of modern medicine. An effective, efficient, and minimally invasive treatment, such as the nucleoplasty associated with radiofrequency – applied for years with very good success – find its completion within the autologous adipose tissue graft. Although this is a single case report, part of a larger study, the results are very encouraging. The decrease of the ODI score and the MRI gave evidence of the efficacy and potential benefits of using autologous, micro-fragmented and minimally manipulated adipose tissue graft associated with nucleoplasty for the treatment of the "black disk".

Conflict of Interest Statement

All authors declare that there are no conflicts of interest regarding the publication of this paper.

Ethical Approval

The study has been approved by the Ethical Commettee.

References

1. Liang C, Li H, Tao Y, Zhou X, Li F, Chen G, Chen Q. Responses of human adipose-derived mesenchymal stem cells to chemical microenvironment of the intervertebral disc. J Transl Med 2012; 10: 49.
2. Marfia G, Campanella R, Navone SE, Zucca I, Scotti A, Figini M, Di Vito C, Alessandri G, Riboni L, Parati E. Potential use of human adipose mesenchymal stromal cells for intervertebral disc regeneration: a preliminary study on biglycan-deficient murine model of chronic disc degeneration. Arthritis Res Ther 2014; 16: 457.
3. Wei A, Shen B, Williams L, Diwan A. Mesenchymal stem cells: potential application in intervertebral disc regeneration. Transl Pediatrics 2014; 3: 71-90.
4. Caplan AI. Adult mesenchymal stem cells for tissue engineering versus regenerative medicine. J Cell Physiol 2007; 213: 341-347.
5. Casteilla L, Planat-Bénard V, Cousin B, Silvestre JS, Laharrague P, Charrière G, Carrière A, Pénicaud L. Plasticity of adipose tissue: a promising therapeutic avenue in the treatment of cardiovascular and blood diseases? Arch Mal Coeur Vaiss 2005; 98: 922-926.
6. Oedayrajsingh-Varma MJ, van Ham SM, Knippenberg M, Helder MN, Klein-Nulend J, Schouten TE, Ritt MJ, van Milligen FJ.Adipose tissue-derived mesenchymal stem cell yield and growth characteristics are affected by the tissue-harvesting procedure. Cytotherapy 2006; 8: 166-177.

7. Zuk PA, Zhu M, Ashjian P, De Ugarte DA, Huang JI, Mizuno H, Alfonso ZC, Fraser JK, Benhaim P, Hedrick MH. Human adipose tissue is a source of multipotent stem cells. Mol Biol Cell 2002; 13: 4279-4295.
8. Gimble JM, Bunnell BA, Chiu ES, Guilak F. Concise review: adipose derived stromal vascular fraction cells and stem cells: let's not get lost in translation. Stem Cells 201; 29: 749-754.
9. Components P. Understanding adipose-derived stromal vascular fraction (AD-SVF) cell biology and use on the basis of cellular, chemical, structural and paracrine components: a concise review. J Prolother 2012; 4: e855-e869.
10. Centeno CJ, Bashir J. Safety and regulatory issues regarding stem cell therapies: one clinic's perspective. PM R 2015; 7: S4-S7.
11. Strem BM, Hicok KC, Zhu M, Wulur I, Alfonso Z, Schreiber RE, Fraser JK, Hedrick MH. Multipotential differentiation of adipose tissue-derived stem cells. Keio J Med 2005; 54: 132-141.
12. Garcìa-Contreras M, Messaggio F, Jimenez O, Mendez A. Differences in exosome content of human adipose tissue processed by non-enzymatic and enzymatic methods. CellR4 2014; 3: e1423.
13. Carelli S, Messaggio F, Canazza A, Hebda DM, Caremoli F, Latorre E, Grimoldi MG, Colli M, Bulfamante G, Tremolada C, Di Giulio AM, Gorio A. Characteristics and properties of mesenchymal stem cells derived from micro-fragmented adipose tissue. Cell Transpl 2015; 24: 1233-1252.
14. Bianchi F, Maioli M, Leonardi E, Olivi E, Pasquinelli G, Valente S, Mendez AJ, Ricordi C, Raffaini M, Tremolada C, Ventura C. A new nonenzymatic method and device to obtain a fat tissue derivative highly enriched in pericyte-like elements by mild mechanical forces from human lipoaspirates. Cell Transpl 2013; 22: 2063-2077.
15. Sultan SM, Stern CS, Allen RJ Jr, Thanik VD, Chang CC, Nguyen PD, Canizares O, Szpalski C, Saadeh PB, Warren SM, Coleman SR, Hazen A. Human fat grafting alleviates radiation skin damage in a murine model. Plast Reconstr Surg 2011; 128: 363-372.
16. Coleman SR. Structural fat grafts: the ideal filler? Clin Plastic Surg 2001; 28: 111-119.
17. Coleman SR. Structural fat grafting: more than a permanent filler. Plast Reconstr Surg 2006; 118: 108S-120S.
18. Bianchi F, Maioli M, Leonardi E, Olivi E, Pasquinelli G, Valente S, Mendez AJ, Ricordi C, Raffaini M, Tremolada C, Ventura C. A new nonenzymatic method and device to obtain a fat tissue derivative highly enriched in pericyte-like elements by mild mechanical forces from human lipoaspirates. Cell Transpl 2013; 22: 2063-2077.
19. Canaider S, Maioli M, Facchin F, Bianconi E, Santaniello S, Pigliaru G, Ljungberg L, Burigana F, Bianchi F, Olivi E, Tremolada C, Biava PM, Ventura C. Human stem cell exposure to developmental stage zebrafish extracts: a novel strategy for tuning stemness and senescence patterning. Cell 2014; 2: e1226.
20. Maioli M, Rinaldi S, Santaniello S, Castagna A, Pigliaru G, Delitala A, Bianchi F, Tremolada C, Fontani V, Ventura C. Radioelectric asymmetric conveyed fields and human adipose-derived stem cells obtained with a nonenzymatic method and device: a novel approach to multipotency. Cell Transpl 2014; 23: 1489-1500.
21. Raffaini M, Tremolada C. Micro fractured and purified adipose tissue graft (Lipogems®) can improve the orthognathic surgery outcomes both aesthetically and in postoperative healing. CellR4 2014; 2: e1118.
22. Tremolada C, Palmieri G, Ricordi C. Adipocyte transplantation and stem cells: plastic surgery meets regenerative medicine. Cell Transpl 2010;19: 1217-1223.
23. Tassinari R, Canaider S, Pasquinelli G, Tremolada C, Ventura C. Lipogems, a new modality of fat tissue handling to enhance tissue repair in chronic hind limb ischemia. CellR4 2014; 2: e1289.
24. Benzi R, Marfia G, Bosetti M, Beltrami G, Magri AS, Versari S, Tremolada C. Microfractured lipoaspirate may help oral bone and soft tissue regeneration: a case report. CellR4; 3: e1583.
25. Bosetti M, Borrone A, Follenzi A, Messaggio F, Tremolada C, Cannas M. Human lipoaspirate as autologous injectable active scaffold for one-step repair of cartilage defects. Cell Transpl 2015 Sep 21. [Epub ahead of print].
26. Cestaro G, De Rosa M, Massa S, Amato B, Gentile M. Case report Intersphincteric anal lipofilling with microfragmented fat tissue for the treatment of faecal incontinence: preliminary results of three patients. Videosurgery Miniinv 2015; 10: 337-341.
27. Striano RD, Chen H, Bilbool N, Azatullah K, Hilado J, Horan K. Non-responsive knee pain with osteoarthritis and concurrent meniscal disease treated with autologous microfragmented adipose tissue under continuous ultrasound guidance. CellR4 2015; 3: e1690.
28. Giori A, Tremolada C, Vailati R, Navone SE, Marfia G, Caplan AI. Recovery of function in anal incontinence after micro-fragmented fat graft (Lipogems®) injection: two years follow up of the first 5 cases. CellR4 2015; 3: e1544.
29. Gerges FJ, Lipsitz SR, Nedeljkovic SS. A systematic review on the effectiveness of the nucleoplastytm procedure for discogenic pain. Pain Physician 2010; 13: 117-132.
30. Marfia G, Navone SE, Di Vito C, Tabano S, Giammattei L, Di Cristofori A, Gualtierotti R, Tremolada C, Zavanone M, Caroli M, Torchia F, Miozzo M, Rampini P, Riboni L, Campanella R. Gene expression profile analysis of human mesenchymal stem cells from herniated and degenerated intervertebral discs reveals different expression of osteopontin. Stem Cells and Development 2015; 24: 320-328.