Annals of Clinical Case Reports

Case Report
Published: 01 Aug, 2019

Stromal Vascular Fraction Cell Therapy for Idiopathic Pulmonary Fibrosis - Cure without Side Effects

Jaroslav Michalek[1,2], Zuzana Dudasova[1,2] and Conville Brown[1,3]*

[1]International Consortium for Cell Therapy and Immunotherapy, Czech Republic

[2]Cellthera Clinic, Czech Republic

[3]The Partners Stem Cell Centre, The Bahamas

Abstract

Idiopathic Pulmonary Fibrosis is a progressive lung disease with unknown origin, poor prognosis and limited treatment options. A strategy implementing autologous Stromal Vascular Fraction (SVF) cells from adipose tissue represents a novel approach in this chronic and devastating disease. Here we present a case study of a 71 year old woman who underwent SVF cell therapy during one surgical procedure. Clinical status of the patient was closely monitored with regular spirometry before and up to 14 months after SVF cell therapy. Nine months after SVF therapy patient did not require anti-fibrotic drugs and spirometry showed improvements that continued further at 14 months. SVF therapy is a rapid, safe, and cost-effective method which can be easily applied in patients with pulmonary fibrosis and other chronic lung diseases.

Keywords: Idiopathic pulmonary fibrosis; Chronic lung disease; Chronic asthma; Stromal vascular fraction; Stem cells

Introduction

Idiopathic Pulmonary Fibrosis (IPF) is a chronic and disabling lung disease characterized by irreversible loss of lung function due to scarring of the lung tissue ultimately resulting in death [1]. The median of survival is 3-5 years after diagnosis [2]. Typical pathological features of IPF are scarring and fibrosis of the interstitial lung tissue due to activation of fibroblasts and accumulation of myofibroblasts into the alveolar space, leading to dysfunction and failure of the lung. Clinical manifestations include respiratory deterioration, dyspnea on exertion and heart failure eventually leading to death. Aging, smoking, bacterial or viral infection, industrially processed food and air pollution are the most critical risk factors of IPF. Physical, environmental and genetic factors may also contribute to the pathogenesis and development of the disease [3]. Current conventional therapy relies mainly on the reduction of symptoms or slowing the progression of the disease, including corticosteroids and beta-mimetics, unfortunately is frequently associated with various side effects. Oxygen supplementation is needed for patients with advanced IPF. Typically, conventional medicine cannot cure IPF. A promising novel strategy implements regenerative medicine based on Mesenchymal Stem/stromal Cells (MSCs) which can be easily obtained from adipose tissue together with other regenerative cells as Stromal Vascular Fraction (SVF) cells. MSCs have strong homing effect to the sites of injury and ischemia, inhibit chronic inflammation, and contribute to tissue restoration [4] and so have potential to be used for the treatment of IPF. SVF cells can be readily isolated from adipose tissue obtained by a standard liposuction, and administered during one surgical procedure [5]. Previously, we described that SVF cells containing MSCs have a great regenerative potential in a large cohort of 1128 patients with osteoarthritis [6] including elderly [7]. Here we demonstrate how autologous SVF cell therapy can contribute to lung regeneration and cure of a patient with IPF without any serious side effects.

Case Presentation

Seventy one years old female ex-smoker suffering from IPF for 2 years underwent autologous SVF cell therapy after signing the informed consent. Adipose tissue was obtained by tumescent liposuction under local anesthesia. SVF cells were isolated from adipose tissue and treated as previously described [6,7]. Briefly, 150 ml of adipose tissue was obtained, SVF cells isolated and resuspended in normal saline and administered intravenously during one surgical procedure. Clinical status of the patient was closely monitored during said procedure. For the long-term

OPEN ACCESS

Correspondence:
Zuzana Dudasova, International Consortium for Cell Therapy and Immunotherapy, Videnska 119, 619 00 Brno, Czech Republic, Tel: +420-511-181-444;
E-mail: dudasova@cellthera.org

Received Date: *18 Jun 2019*
Accepted Date: *30 Jul 2019*
Published Date: *01 Aug 2019*

Citation:
Michalek J, Dudasova Z, Brown C. Stromal Vascular Fraction Cell Therapy for Idiopathic Pulmonary Fibrosis - Cure without Side Effects. Ann Clin Case Rep. 2019; 4: 1698.

ISSN: 2474-1655

follow-up, data including spirometry with objective measurements of the Functional Vital Capacity (FVC) of the lungs as well as Forced Expiratory Volume in one second (FEV1) were monitored closely. These data were measured starting 2 months before through 14 months after SVF cell therapy.

Results

Seventy one years old female, ex-smoker with IPF for 2 years preceded by 4 years of chronic asthma, had been suffering from a chronic dry and stifling cough, tiredness, shortness of breath and significant decrease in her quality of life. Her lung functions were also objectively monitored by spirometry on a regular basis. During last 2 years, she was on continuous oxygen therapy *via* nostrils, and underwent pulmonary rehabilitation. She received standard medications including inhaled corticosteroids and beta-mimetics, oral prednisolone 10 mg to 80 mg per day, and omeprazole 20 mg/day. She was also taking supplements with calcium 2 mg × 500 mg daily and Vitamin D3 800 IU daily. Her situation was complicated with pneumonia 5 months before SVF cell therapy. Pneumonia required hospitalization and intensified medical care including oxygen, antibiotic and other supportive therapy. After that acute pneumonia resolved, she remained quite weak, in a wheelchair and unable to walk more than about 10 meters due to severe dyspnea. She remained on her medications above and on continuous oxygen delivery at 6 l/min. *via* nostrils. Chest X-ray demonstrated progression of the lung fibrosis with diffuse alveolar changes. Due to constant deterioration of health, the patient decided to undergo autologous SVF cell therapy during one surgical procedure. She underwent autologous intravenous SVF cell therapy using 2.38×10^6/kg of her body weight of nucleated SVF cells with viability 99% isolated from 150 ml of adipose tissue. No serious side effects were documented in association with the cell therapy procedure. Besides SVF cell therapy, she received recommendations to avoid calcium supplementation and initiate magnesium supplementation together with trace minerals containing zinc, selenium and manganese (Anti-Aging Minerals®) and vitamin supplementation containing vitamins B1, B2, B3, B6, B12, folic acid, pantothenic acid, vitamin C, D3, and K2 (Anti-Aging Vitamins®) for 12 months. One month after the SVF therapy, she was able to reduce her standard prednisolone and beta-mimetic medication, and her spirometry showed mild improvement (Figure 1). She was constantly improving further. She was able to stop inhaled beta-mimetics and corticosteroids 5 months after SVF cell therapy, and was able to wean herself off oral prednisolone by 9 months after SVF cell therapy. Nasal oxygen was reduced to 3-4 l/min. At 12 months after SVF cell therapy, she became independent of oxygen only when inside her house, may be psychologically dependent, as she tended to use it when walking outside the house. Spirometric examination 9 months after SVF cell therapy revealed dramatic improvements in lung functions (FVC 104%, FEV1 92%) and similar and stable results were documented at 14 months after SVF cell therapy (FVC 102%, FEV1 97%) (Figure 1). Clinically, the patient felt very good, was able to walk without oxygen, and without a need for anti-fibrotic or anti-asthmatic medications. Her quality of life had improved dramatically. No respiratory tract infection was documented during the 14 months period since SVF cell therapy.

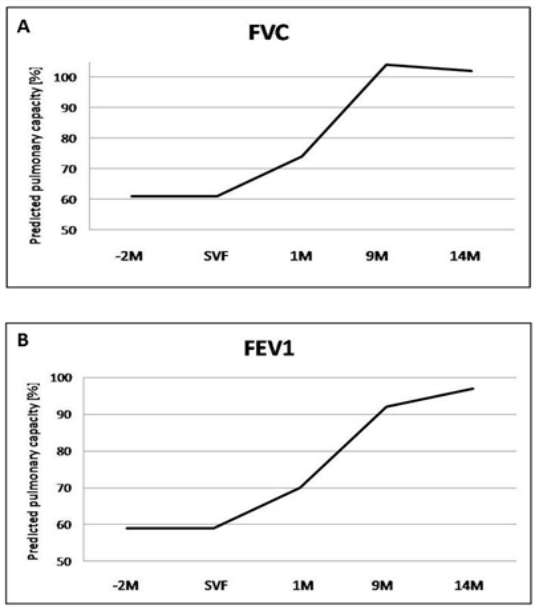

Figure 1: Analysis of the pulmonary vital capacity by (A) Forced Vital Capacity (FVC) and (B) Forced Expiratory Volume-One Second (FEV1) tests.

Discussion

Because current conventional treatment of IPF is limited and ineffective, including serious side effects and the disease progressively deteriorates and often ends with lung transplantation or death, novel therapeutic approaches, including regenerative medicine, are needed. Various stem cells therapies have been used for IPF treatment in clinical studies, for example bone marrow isolated MSCs [8], Adipose Tissue-Derived Stem Cells (ADSCs) [4], placenta-derived MSCs [9] or alveolar type II progenitor cells [10]. As was described previously, adipose tissue-derived MSCs are more genetically stable and can be safely and easily isolated in much higher quantities from adipose tissue by a standard liposuction as a part of SVF [5]. SVF therapy was successfully clinically used in treatment of many disorders including pulmonary diseases such as Chronic Obstructive Pulmonary Disease (COPD) [11], IPF [4] and pulmonary emphysema [12]. As we described previously, SVF cells have a distinctive tissue regeneration potential in patients with osteoarthritis [6,7]. Moreover, International Consortium for Cell Therapy and Immunotherapy has experience with neurodegenerative diseases [13], and pulmonary diseases including COPD.

Stem cells have pleiotropic effects in the place of lung injury that include anti-inflammatory, immunomodulatory, anti-fibrotic and paracrine effects [2]. They are able to differentiate into various local cell types, including cells in bronchioles, alveoli, and pulmonary vasculature and also contribute in activation of the resident stem cells. Typically, large amounts of SVF may be obtained from 200 ml of adipose tissue (10^6 nucleated SVF cells per each ml of the adipose tissue) when CT-SVF-03 Kit is used [6,7] leading to clinical application of more than 2×10^6/kg of body weight nucleated freshly isolated SVF cells. Based on our clinical experience, this amount leads to optimal clinical result, i.e. complete cure of chronic and debilitating disease such as IPF. These non-manipulated autologous SVF cells may be directly administered intravenously to the patient with no serious side effects. Another route, i.e. endotracheal application of SVF cells in IPF patients has also been described [4]. Here we were able to demonstrate that only one application of SVF cells is sufficient to initiate the immunomodulatory and regenerative processes in the lung. Obviously, other parameters may affect the clinical results of the cell therapy, including age, disease stage, extent of tissue damage, and

other diseases of the patient.

Here we document for the first time to our knowledge, the IPF cure using autologous SVF cells isolated and administered during one surgical procedure. This treatment is safe with no serious side effects. It may represent a promising new therapeutic approach for the treatment of IPF. Definitely, this method is still at an experimental stage and large multicenter randomized trials should be performed to further evaluate the efficacy of SVF cells as a treatment for this devastating chronic lung disease.

References

1. Cárdenes N, Álvarez D, Sellarés J, Peng Y, Corey C, Wecht S, et al. Senescence of bone marrow-derived mesenchymal stem cells from patients with idiopathic pulmonary fibrosis. Stem Cell Res Ther. 2018;9(1):257.
2. Tzouvelekis A, Toonkel R, Karampitsakos T, Medapalli K, Ninou I, Aidinis V et al. Mesenchymal stem cells for the treatment of idiopathic pulmonary fibrosis. Front Med (Lausanne). 2018;5:142.
3. Wolters PJ, Collard HR, Jones KD. Pathogenesis of idiopathic pulmonary fibrosis. Annu Rev Pathol. 2014;9:157-79.
4. Tzouvelekis A, Paspaliaris V, Koliakos G, Ntolios P, Bouros E, Oikonomou A, et al. A prospective, non-randomized, no placebo-controlled, phase Ib clinical trial to study the safety of the adipose derived stromal cells-stromal vascular fraction in idiopathic pulmonary fibrosis. J Transl Med. 2013;11:171.
5. Strioga M, Viswanathan S, Darinskas A, Slaby O, Michalek J. Same or not the same? Comparison of adipose tissue-derived versus bone marrow-derived mesenchymal stem and stromal cells. Stem Cells Dev. 2012;21(14):2724-52.
6. Michalek J, Moster R, Lukac L, Proefrock K, Petrasovic M, Rybar J, et al. Stromal vascular fraction cells of adipose and connective tissue in patients with osteoarthritis: a case control prospective multi-centric non-randomized study. Global Surgery. 2017;3(3):1-9.
7. Michalek J, Vrablikova A, Darinskas A, Lukac L, Prucha J, Skopalik J, et al. Stromal vascular fraction cell therapy for osteoarthritis in elderly: Multicenter case-control study. J Clin Orthrop Trauma. 2019;10(1):76-80.
8. Glassberg MK, Minkiewicz J, Toonkel RL, Simonet ES, Rubio GA, DiFede D, et al. Allogeneic human mesenchymal stem cells in patients with idiopathic pulmonary fibrosis via intravenous delivery (AETHER) a phase I safety clinical trial. Chest. 2017;151(5):971-81.
9. Chambers DC, Enever D, Ilic N, Sparks L, Whitelaw K, Ayres J, et al. A phase 1b study of placenta-derived mesenchymal stromal cells in patients with idiopathic pulmonary fibrosis. Respirology. 2014;19(7):1013-8.
10. Serrano-Mollar A, Gay-Jordi G, Guillamat-Prats R, Closa D, Hernandez-Gonzalez F, Marin P, et al. Safety and tolerability of alveolar type II cell transplantation in idiopathic pulmonary fibrosis. Chest. 2016;150(3):533-43.
11. Comella K, Blas JAP, Ichim T, Lopez J, Limon J, Moreno RC. Autologous stromal vascular fraction in the intravenous treatment of end-stage chronic obstructive pulmonary disease: a phase I trial of safety and tolerability. J Clin Med Res. 2017;9(8):701-8.
12. Shigemura N, Okumura M, Mizuno S, Imanishi Y, Nakamura T, Sawa Y. Autologous transplantation of adipose tissue-derived stromal cells ameliorates pulmonary emphysema. Am J Transplant. 2006;6(11):2592-600.
13. Michalek J, Vrablikova A, Heinrich KG, Dudasova Z. Stromal vascular fraction cell therapy for a stroke patient - cure without side effects. Brain Sci. 2019;9(3):55.