Clinical Case Reports

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CASE REPORT

Human embryonic stem cells (hESCs) in the treatment of emphysematous COPD: a case report

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Funding Information
No sources of funding were declared for this study.

Received: 26 February 2015; Revised: 4 May 2015; Accepted: 13 May 2015

Clinical Case Reports **2015; 3(7): 632–634**

doi: 10.1002/ccr3.310

Key Clinical Message

Emphysema results in narrowing of the small airways due to inhaling of cigarette smoke and other noxious particles. Oxygen therapy, corticosteroids, and bronchodilators increase the risk of pneumonia, arrhythmia, and fractures in long term. Therapy with human embryonic stem cells resulted in improved symptoms of a patient with emphysema.

Keywords

COPD, emphysema, human embryonic stem cell therapy.

Introduction

Emphysema is a lung disease [1] that results in narrowing of the small airways and breakdown of the lung tissues. It is due to long-term exposure of irritants like inhaling of cigarette smoke, and other toxic particles that cause lung inflammation. Emphysema is a phenotype of COPD [2] and is amongst the leading cause of deaths in most of the countries [3].

Emphysema is categorized as centriacinar emphysema, panacinar emphysema, and distal acinar emphysema. The connection among these subtypes of emphysema's is yet to be clarified [4]. The panacinar emphysema shows higher compliance with lungs then the centriacinar emphysema [5]. It occurs more commonly in people who smoke heavily [6].

There is no effective cure for COPD. Treatments like methylxanthines [7], long-term oxygen therapy, corticosteroids, and bronchodilators are used as a conventional therapy. But long-term usage of these treatments increases the risk of pneumonia, arrhythmia, and fractures [3, 8].

Previous studies have shown that cell-based therapies have a potential for lung repair and rehabilitation of lungs after injury [9]. Cell-based therapies play an important role and reduce both alveolar damage and inflammation of the airways [10].

In our previous studies, we have shown improvement in patients with cerebral palsy [11] patients with cortical visual impairment [12] and patients with other conditions after human embryonic stem cell (hESC) therapy [13]. Here, we present a case of 52-year-old male with emphysema having paraseptal emphysematous changes seen in bilateral upper lobes. The patient had an uneventful recovery.

Methodology

hESCs used in this study were chromosomally stable and free from animal product(s). The cell lines were cultured and maintained as per our in-house patented technology in a GMP, GLP, and GTP certified laboratory (Patent-WO 2007/141657A PCT/1B 2007 Published 13 December 2007). The evidence for the use of hESCs at Nutech Mediworld has been submitted in written and accepted at House of Lords, Regenerative Medicine, Science and Technology Committee [14].

The patient provided with a written consent form before the start of the treatment. A complete examination of the patient was done and video recordings were made before and after the treatment.

The treatment consisted of three phases in which 0.25 mL hESCs were administered through intramuscular route twice daily and 1 mL of hESCs were administered

through intravenous route twice daily for 7 days. He was also nebulized with hESCs suspended in normal saline. The treatment phases were separated by a gap phase of 4–6 months.

Case Presentation

A 52-year-old male was admitted at the Nutech Mediworld on 6 August, 2012 with chief complaints of shortness of breath, pain radiating to the neck, increased cough and wheezing especially at night and after getting up from sleep for the past 9 months. The patient and his wife noticed that he had increased shortness of breath after mild physical exertion (like walking). A visit to a local physician revealed that he had emphysema COPD with not much hope of cure, and only symptomatic treatment was given.

The patient was a heavy smoker since last 30 years and drank alcohol frequently. The family history of patient revealed that the patient's father died of carcinoma of the lungs and his mother died of stomach cancer.

The first contrast-enhanced computed tomography (CEST) performed on 06 August, 12 showed paraseptal and panacinar emphysematous changes in bilateral lung fields with flattening of the diaphragm.

On examination of the central nervous system (CNS) and other parameters, the patient was clinically normal. The patient had no organomegaly and the bowel sample was normal. The patient was conscious, alert, well oriented to time and with fair nutritional status.

The patient was given hESC therapy as a primary treatment at our facility. After 101 days of the hESC therapy, the patient showed an improvement in symptoms like absence of cough and phlegm. His sleeping and overall stamina also improved. A CEST of chest performed after the therapy on 25 September, 2012 showed paraseptal emphysematous changes in bilateral upper lobes and rest of parenchyma appeared normal. He was also able to completely quit smoking during his stay at our facility.

On his last follow-up on (2014, November), he did not report cough, phlegm, or wheezing, was able to work full time and to walk long distances.

Discussion

In the present study, an improvement in cough, phlegm, and overall stamina was observed in a patient with emphysema after hESC therapy. CEST performed after the therapy showed normal parenchyma of the lungs. No adverse events (AEs) were seen in patient following the treatment with hESC.

Previous studies have shown that there is a potential in cell lines to consummate multipotent lung progenitors in association with combined growth factors and novel markers (LIFRα and NRP1) [15]. The mesenchymal stem cells (MSCs) release chemokines, cytokines, and growth factors to the injury site and act as migratory cues. These cues influence selectins and result in activation of integrins on the stem cell surface. This permits the stem cells to interact, adhere, and transmigrate through endothelium [16]. A study by Lee and colleagues stated that MSCs can mitigate the inflammatory and lung injury in isolated perfused human lungs. MSCs released anti-inflammatory mediators to the injury site and repair the damaged cells [17]. The study showed a base for therapeutic use of hESCs in a variety of lung diseases. So, we might possibly explain that hESCs used in our study also rely on the same mechanism of action. We assume that our hESCs also penetrate across the parenchyma and migrate to the affected region. These cells then differentiated into lung epithelial cells and replaced the damaged cells. The use of stem cells is restricted due to the fear of AEs as teratoma formation and immune rejection. In our patient, we have not observed any AE. We have already established the safety of hESC therapy in patients with terminal/incurable conditions [18].

No study till date assessed the therapeutic potential of hESCs in the treatment of patients with emphysema. This is the first study to report the use of hESCs as therapy in lung repair. The patient had an uneventful recovery. Our patient showed remarkable clinical improvement and an improved quality of life. Though he quit smoking, but improvement observed in the patient cannot be justified for his improvement that was observed in a very small span of time. He had been a heavy smoker for last 30 years and his stay at our facility was about 3.5 months only. It has also been reported previously that after smoking cessation, the inflammation, apoptosis, and oxidative stress can remain and sustain to contribute to COPD [19]. There is an ethical concern regarding the use of hESCs like using fertilized embryo, misuse of cells and use in experimental purposes. The fertilized ovum for the present hESCs was donated willingly by a woman undergoing IVF and she was cognizant that it would be used for experimental and research purpose. Moreover, we have used this therapy on patients with incurable conditions and nothing can be more unethical than denying a ray of hope to the patients who have tried all treatments and still shown no improvement. However, we were not able to perform bronchoalveolar lavage sample examination of the patient before and after the treatment. Future well-designed studies can further clarify the role of hESC therapy in patients with emphysematous lung disease.

Conclusion

Therefore, it is summarized that hESCs showed good therapeutic potential in the treatment of patients with

emphysematous COPD. Clinical trials reveal that cell-based therapies have a potential for lung repair and rehabilitation of lungs after injury. However, more clinical trials and follow-up studies are needed to prove the long-term efficacy and safety of hESCs in the treatment of patients with emphysema COPD.

Acknowledgments

The author acknowledges all the doctors, staff, and patients of the Nutech Mediworld. The author also acknowledges Knowledge Isotopes Pvt. Ltd. (www.knowledgeisotopes.com), for the Medical writing assistance.

Conflict of Interest

Authors have no conflict of interest.

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