Case Report

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A Case Study depicting Management of Diabetes Mellitus with Autologous Stem Cells

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Abstract

Diabetes mellitus type 2 is a long-term disorder of the metabolism characterized by elevated levels of sugar in blood, insulin resistance, and relative lack of insulin. Insulin is the main culprit for diabetes mellitus. Beta cells of the pancreatic islets are the producers of this peptide hormone which is considered to be the main anabolic hormone of the body regulating the carbohydrates, fats and protein metabolism by promoting the absorption of, especially, glucose from the blood into fat, liver and skeletal muscle cells. From this study, it seems that stem cell therapy can be a promising approach to manage the long term condition diabetes mellitus. The patients were administered stem cells derived from their bone marrows during the procedure. The levels of blood glucose and glycated hemoglobin (HbA1c) were decreased significantly post procedure in both the patients.

Keywords: Diabetes mellitus, Autologous, Stem Cells, HbA1c.

Abbreviations

HbA1c: Glycated hemoglobin
β-islet: Beta-islet
TSCs: Tissue stem cells
ESCs: Embryonic stem cells
iPSCs: Induced pluripotent stem cells
MSCs: Mesenchymal stem cells
ADSCs: Adipose-derived stem cells
VSC: Vascular stem cells
SVF: Stromal vascular fraction

Introduction

Diabetes Mellitus or diabetes is a long term condition that belongs to a group of metabolic disorders characterized by an increase in blood glucose levels (blood sugar), either due to insufficient insulin production in the body, or improper response of ones body's cells to insulin, or both [1]. Patients with high blood sugar levels typically experience an urge to urinate frequently (polyuria), increased thirst (polydipsia) and hunger (polyphagia), unusual weight gain or weight loss, fatigue, non-healing cuts and bruises, male-infertility, numbness and tingling in hands and feet and blurred vision [2]. There are three types of diabetes, namely, type-1, type-2 and gestational diabetes. From the total diabetes cases reported around the globe, 10% are the cases of type-1 diabetes, during which the patient's body stops producing insulin [3]. Type-1 diabetes is also termed as insulin-dependent, or juvenile diabetes as it develops mainly in children and teenagers, though it can develop at any age. The patients suffering from type-1 diabetes are required to follow a healthy diet plan, indulge in a regular exercise regime and take insulin shots in order to lead a normal healthy [4]. Type-2 diabetes is the most common form of diabetes across the world ranging to approximately 90% of the diabetes cases reported worldwide. In this condition the body is unable to produce enough amount of insulin required for the normal functioning of the body or the body is unable to use the insulin properly. This condition is also termed as insulin resistance [5]. At first, one's pancreas makes extra insulin to make up for it. But, over time it isn't able to keep up and can't make enough insulin to keep body's blood glucose at normal levels. To lead a healthy life, patients suffering from type-2 diabetes need to eat healthy, be physically active and may be required to take oral medication, and/or insulin shots in order to control their blood glucose levels. The third type of diabetes is gestational diabetes that affects females during pregnancy [6]. Such women have comparatively very high levels of glucose in their blood, and their bodies are unable to produce enough insulin to make up for it. The majority of gestational diabetes patients can control their diabetes with a proper exercise and diet regime. Around 10-20% of them will need to take some kind of blood-glucose-controlling medications. Undiagnosed or uncontrolled gestational diabetes can raise the risk of complications during childbirth. The baby may be bigger than he/she should be. Poor management of diabetes may have adverse effects on other parts of our body; it might lead to eye disorders like glaucoma, diabetic retinopathy, cataracts to name some; foot complications like ulcers, neuropathy, and sometimes gangrene sometimes leading to foot amputation; skin problems; heart diseases like ischemic heart disease, during which the blood supply to the heart muscle is diminished; peripheral arterial disease that includes tingling, pain in the leg, and sometimes problems walking properly; stroke; and ketoacidosis, a combination of acidosis and ketosis during which the ketone bodies and acid accumulation takes place in the blood [5].

For the better management of diabetes of both types, stem cell therapy is proving out to be a potential option available these days. Stem

cells are the foundation for every organ and tissue in our body and are found in multicellular organisms. These cells are unspecialized cells which are capable of renewing themselves through cell division without limit as long as the person is alive. Each new cell has the potential either to remain a stem cell or become another type of cell [7]. There are three commonly accessible sources of autologous adult stem cells in humans; bone marrow, which requires extraction by harvesting, that is, drilling into bone (typically the femur or iliac crest); adipose tissue (lipid cells), which requires extraction by liposuction and peripheral blood, which requires extraction through apheresis, wherein blood is drawn from the donor (similar to a blood donation), and passed through a machine that extracts the stem cells and returns other portions of the blood to the donor. Stem cells can also be taken from umbilical cord blood just after birth and skin and dental pulp of the patient. There are three different types of stem cells, namely, embryonic stem cells (ESCs), adult tissue stem cells (TSCs) and induced pluripotent stem cells (iPSCs).

Embryonic stem cells are isolated from the inner cell mass of blastocysts of preimplantation-stage embryos. These cells require specific signals to differentiate to the desired cell type; if simply injected directly, they will differentiate into many different types of cells, resulting in a tumor derived from this abnormal pluripotent cell development (a teratoma). A tissue derived stem cell is an undifferentiated cell, capable of proliferation, self-renewal, production of a large number of differentiated functional progeny, regenerating tissue after injury. Adult stem cells have been identified in many organs and tissues, including brain, bone marrow, peripheral blood, blood vessels, skeletal muscle, skin, teeth, heart, gut, liver, ovarian epithelium, and testis. They are thought to reside in a specific area of each tissue (called a "stem cell niche"). The adult stem cells occur in many tissues and enter normal differentiation pathways to form the specialized cell types of the tissue in which they reside. Induced pluripotent stem cells are somatic cells that have been genetically reprogrammed to an embryonic stem cell-like state by being forced to express genes important for maintaining the defining properties of embryonic stem cells. Although additional research is needed, iPSCs are already useful tools for drug development and modeling of diseases, and scientists hope to use them in transplantation medicine. In addition, tissues derived from iPSCs will be a nearly identical match to the cell donor and thus probably avoid rejection by the immune system. Adipose-derived stem cells (ASCs) are mesenchymal stem cells (MSCs) that are obtained from abundant adipose tissue, adherent on plastic culture flasks, can be expanded *in vitro*, and have the capacity to differentiate into multiple cell lineages [8]. These cells are routinely isolated from the stromal vascular fraction (SVF) of homogenized adipose tissue. Similar to other types of mesenchymal stem cells (MSC), ADSC remain difficult to define due to the lack of definitive cellular markers. Still, many types of MSC, including ADSC, have been shown to reside in a perivascular location, and increasing evidence shows that both MSC and ADSC may in fact be vascular stem cells (VSC) (9). Locally, these cells differentiate into smooth muscle and endothelial cells that are assembled into newly formed blood vessels during angiogenesis and neovasculogenesis. Additionally, MSC or ADSC can also differentiate into tissue cells such as adipocytes in the adipose tissue. Systematically, MSC or ADSC are recruited to injury sites where they participate in the repair/regeneration of the injured tissue [9].

Of all stem cell types, autologous harvesting involves the least risk. By definition, autologous cells are obtained from one's own body, just as one may bank his or her own blood for elective surgical procedures. Adult stem cells are frequently used in various medical therapies (e.g., bone marrow transplantation). Stem cells can now be artificially grown and transformed (differentiated) into specialized cell types with characteristics consistent with cells of various tissues such as muscles or nerves [10].

Case Description

Two patients, who had a history of type-2 diabetes mellitus, got in touch with GM Nursing Home, Chandigarh, India in May 2017 to undergo the cell therapy procedure for the better management of their disease. Both the patients signed an informed written consent before the procedure. Patient details and outcome data has been summarized in **(Table 1)**.

Biochemical examination was performed before the procedure in which three different parameters were checked, namely, blood sugar fasting, blood sugar (PP) and glycated hemoglobin (HbA1c) (H.P.L.C). The procedure was done using bone marrow derived mononuclear cells for which about harvesting of 60 mL of bone marrow aspirate was done from each patient from the posterior iliac crest, making the patient lay down in prone position under general anesthesia. The bone-marrow was harvested using a marrow needle (size 11 G • 100 mm) inserted 3 cm deep pointing anterolateral into the marrow in the direction of the iliac crest. 5mL of bone marrow was aspirated into a 20mL heparinized plastic syringe and the procedure was repeated, through the same skin opening with several perforations made into different points in the iliac crest, 60 mL of bone marrow aspirate was received. The marrow was aspirated in small fractions from different points to maximize the harvesting of the marrow stromal cells and to reduce dilution by peripheral blood. Further this bone marrow aspirate was processed using an advanced and fully automated bone marrow processing system, namely, The Arthrex Angel System™ to harvest the bone marrow concentrate. In the end, the bone marrow concentrate was administered intravenous to both the patients. The patients were kept under observation for 4-5 hours post procedure and discharged after that.

Results

Both the patients were advised to maintain their regular routine involving exercise, medication course, and diet immediately before and for 90 days after the treatment. The subjects received the treatment once and their glucose levels were monitored daily at home and once a month NABL accredited laboratory. The table below summarizes the results of this study **(Table)**.

Table 1: Patient Details and outcome data.

Patient	Age	Gender	Parameter	Results			
				Pre Procedure	1 month after treatment	2 months after treatment	3 months after treatment
1.	83 yrs	Male	HbA1c (in %)	6.6	-	-	5.9
			Glucose Fasting (in mg/dl)	104	140	95	100
			Glucose PP (in mg/dl)	205	174	170	140
2.	74 yrs	Female	HbA1c (in %)	6.9	-	-	6.0
			Glucose Fasting (in mg/dl)	114	110	115	125
			Glucose PP (in mg/dl)	205	159	174	140

Patient 1 is an 83 years old male with type-2 diabetes. He's is currently taking Gluconorm G4 Forte to manage his blood sugar levels. Patient 2 is a 74 years old female with type-2 diabetes. She's is currently taking Glyzid M Forte to manage her blood sugar levels. Both of them do not take additional vitamins or supplements, and maintain an active lifestyle by light exercise 2-3 times per week. HbA1c levels for patient 1 and patient 2 were alleviated from 6.6% and 6.9% before the procedure to 5.8% and 6.0% respectively after the cell therapy procedure.

Conclusion

The results of these case studies revealed the efficacy of bone marrow derived stem cells in diabetes patients. In both the patients, the blood glucose and HbA1c levels were decreased significantly after cell therapy treatment.

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