

Stem-Cell-Derived Exosome Alleviates Hyperlipidemia in a Patient with Pectus Excavatum

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A 46-year-old man received a diagnosis of pectus excavatum (PE), which was then corrected through surgery. After surgery, this patient still had chest pain and high triglyceride (TG), total cholesterol (TC), and low-density lipoprotein (LDL) levels. To solve these problems, eight intravenous infusions of a stem-cell-derived exosome mixture (named TELOXOME) were conducted. In addition to achieving a moderate reduction in chest pain, the treatment significantly reduced the patient's TG, TC, and LDL levels. To our knowledge, this is the first case of a stem-cell-derived exosome reducing the pain of a patient with PE and improving their hyperlipidemia. This result indicates that our exosome mixture (TELOXOME) is a potential regimen for the treatment of hyperlipidemia.

Key words: exosome, hyperlipidemia, hypertriglyceridemia, hyperlipidemia, triglyceride, lipid metabolism, TELOXOME

Introduction

Pectus excavatum (PE), also known as funnel chest, is characterized by a caved-in and funnel-shaped chest and is the most common congenital anterior chest wall deformity. The incidence of PE among newborns is 1 in 400 (1, 2). The most commonly recommended treatment for PE is surgery to reposition the breastbone (2-4). After surgery, the patient's cardiopulmonary function, dyspnea, chest pain, and exercise intolerance should be dramatically improved. For an unknown reason, some patients with PE have severe hyperlipidemia, which results in chest pain and increases the patients' risks of cardiovascular diseases and acute pancreatitis (5-7). Statins are the

conventional treatment for hyperlipidemia, but they only reduce triglyceride (TG) levels by 5% to 15% and may increase the risk of intracranial hemorrhage (5, 8). Therefore, patients who have high TG, total cholesterol (TC), and low-density lipoprotein (LDL) levels typically require a combination treatment (9, 10). Stem-cell-derived exosomes have been proven to affect lipid metabolism by influencing the synthesis, transportation, and degradation of lipids (11-13). In this report, we indicate that our exosome mixture (named TELOXOME) can be used as an alternative treatment for hyperlipidemia.

Materials and Methods

Our patient underwent an intravenous infusion of 5 mL of TELOXOME (a novel stem-cell-derived agent developed by ContiNew Medical, Taipei, Taiwan) diluted in 150 mL of sterile normal saline (14). TELOXOME was administered every 7 days for 8 weeks. Blood samples were collected before and after completion of the TELOXOME infusion, and these samples were analyzed by Le Zen Reference Lab and Central Clinic and Hospital (No. 77, Sec. 4, Zhongxiao E. Rd., Taipei City, Taiwan).

Results

In the Central Clinic and Hospital (CCH), a 46-year-old man received a diagnosis of PE and subsequently underwent the Nuss procedure. After this corrective surgery, his physical condition improved, and no severe clinical symptoms (myocardial infarction or aortic dissection) were observed, as revealed by

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Table 1. Laboratory data

Variable Blood	Reference Range	Before Infusion	After 8 th Infusion
Glucose AC (mg/dL)	74-109	75	92
HbA1c (%)	4.0-6.0	5.3	5.4
Triglyceride, TG (mg/dL)	<150	356	151
Cholesterol, TC (mg/dL)	<200	294	235
HDL-C (mg/dL)	>40	55.3	42.7
LDL-C (mg/dL)	<130	191	155
LDL/HDL Ratio	M: <3.55	3.45	3.63
TC/HDL Ratio	<5.0	5.32	5.05

data from CCH. The only symptom that was not resolved through the surgery was chest pain. After the operation, blood tests revealed high TG (356 mg/dL, normal <150 mg/dL), TC (294 mg/dL, normal <200 mg/dL), and LDL (191 mg/dL, normal <130 mg/dL) levels. After eight intravenous TELOXOME infusions, the patient's chest pain was unexpectedly less severe, and the patient's TG level had significantly decreased from 356 to 151 mg/dL (a 48% reduction). In addition, his TC level had decreased from 294 to 235 mg/dL (20% reduction), and his LDL level had decreased from 191 to 155 mg/dL (19% reduction). The changes in laboratory findings are presented in Table 1. Our proteomic and micro-RNA sequencing of TELOXOME indicated that the factors it contains may reduce TG levels, which has been proved in our speculations.

Discussion

An association between hyperlipidemia and PE has been reported (2, 15). However, the mechanism underlying this association remains unclear. The standard approach to treating hypertriglyceridemia and hyperlipidemia is to combine a statin with omega-3 fatty acids (16, 17). Some patients cannot tolerate statins (18-20); therefore, alternative therapies should be considered. Herein, we report that for a patient who had undergone surgery to correct PE, short-term TELOXOME infusion not only reduced his blood lipid levels to normal ranges but also ameliorated his severe chest pain. Studies conducted using animal models have shown that stem-cell-derived exosomes reduce blood lipid levels through promotion of PPAR α -mediated β -oxidation and through CAMKK1-mediated reduction of fatty acid synthesis (13, 21). This paper is the first report of an exosome mixture used in a human for treating hyperlipidemia. We provide a novel perspective in that we indicate that TELOXOME could be an effective treatment for hyperlipidemia, although the precise

mechanisms or pathways must be investigated further. We did not investigate whether the diameters of our patient's blood vessels were different after exosome treatment. Unexpectedly, our patient reported that his chest pain was dramatically reduced. This is a short communication of a case study. From July 2022 to the time this manuscript was submitted, the patient did not complain about any side effects from the TELOXOME infusion. Long-term tracking will be conducted.

Conflicts of Interest

The authors declare no conflict of interest.

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