Therapy with multipotent allogeneic mesenchymal stromal cells for refractory scleroderma: Case report.

Rossana Mejia7 , Luz M. Avila-Portillo1,2, Ospino Benjamin3 , Luis A. Castro4 , Jenniffer P. Avila1 , Ana M. Santos5 , Jhon Londoño5 , Claudio Villaquirán8 , Gonzalo Gutiérrez-García6 , Edwin Jáuregui7 1. Grupo de Células Stem Adultas, Stem Medicina Regenerativa, Bogotá, Cundinamarca, Colombia. 2. CryoHoldco, LATAM, Guadalajara, Mexico. 3. Blood and Marrow transplantation unit, CIOSAD, Bogotá, Colombia. 4. Dermatology unit, Faculty of Medicine, Universidad Militar Nueva Granada, Bogotá, Colombia. 5. Grupo de Espondiloartropatias, Faculty of Medicine, Universidad de la Sabana, Bogotá, Colombia. 6. Transplantation unit of hematopoietic progenitors, Universidad de Barcelona, Barcelona, Spain. 7. Riesgo de Fractura S.A-CAYRE, Bogotá, Colombia. 8. Pulmonologist, Pontificia Universidad Javeriana, Bogotá, Colombia

Introduction

Systemic sclerosis (ES) is an autoimmune disease that involves vasculopathy and extensive fibrosis. A significant percentage of patients are refractory to treatment with immunosuppressants, autologous hematopoietic stem cell transplantation and this conditions an unfavorable prognosis. Since 2008, the use of multipotent mesenchymal stromal cells (MSCs) that have immune regulatory and repair properties that make them promising for the treatment of autoimmune diseases has been evaluated.

Patients and methods

8 years ago
Raynaud's phenomenon, linear morphea in the abdomen, and gortron papula in the elbow. She received vasodilators, phototherapy and methotrexate with adequate efficacy.

6 year later
She presented rapidly progressive diffuse systemic sclerosis and severe pulmonary hypertension (PH). Treatment with pulses of cyclophosphamide (6), endothelin receptor antagonist, sildenafil and diuretics with favorable evolution.

1 year later
Hospitalized for concomitant adult Still's disease. Present negative: ANAS, Anti Scl-70, Anti Jo-1, anti mitochondrial antibody, anti Miu2, anti-synthetase, anti smooth muscle antibody 1/80, elevated ferritin, increase of 1.5 times the value of transaminases, normal renal function and elevated acute phase reactants. Intravenous methyl-prednisolone, prednisolone 1 mg/Kg/day and CSA.

A 45 years old woman

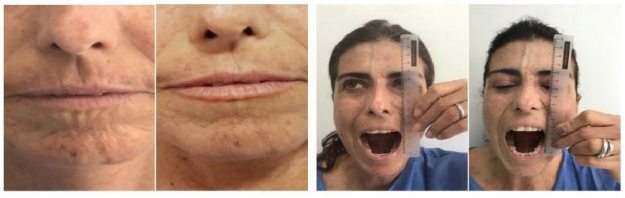
Skin progression of the scleroderma was evidenced.
Infuse MSCs obtained from Wharton's gelatin (GW) from a alogenic donor (HLA 3/6). Compliance with the characteristics of the cells was verified according to the ISCT criteria, the expanded MSCs presented 46XX normal karyotype.Two doses of 1x108 MSC/Kg were produced, which were re-suspended in 100 ml of 5% saline solution with human serum albumin, and were infused via EV added to CYC cycles after signing the informed consent.

Results

The therapy with allogeneic MSCs of GW was well tolerated by the patient, the only adverse event observed was the appearance of fever 2 hours after the first infusion, which resolved without treatment. One month later, we observed a marked decrease in perioral wrinkles, increase in incisor mouth opening -incisive in 3 mm, decrease in trunk telangiectasias, the Rodnan Index modified by 7 points, decrease in atrial natriuretic peptide of 128.8 pg/ml at 74.4 pg/ml. The patient is still under clinical observation, to determine the long-term effects of the therapy.

Table 1. Clinic parameters.
Exist positive changes in the clinic parameters between before to cell therapy and 6 months later.

Parameter	Baseline	6 Months
Brain natriuretic peptide (BNP)	128.80 pg/ml	62.30 pg/ml
Six minutes walk test	572 meters	625 meters
DLCO	76%	94%
PsAP	55 mmHg	52 mmHg
Modified Rodnan skin score (mRSS)	27	17
Inter-incisor distance	3 Cms.	3.5 Cms.



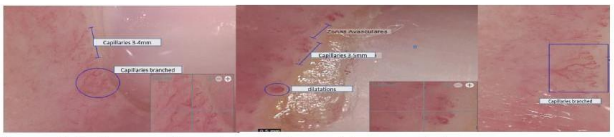


Imagen 2. Capiloscopy. A) Baseline, B) y C) 6 month later of cell therapy.

Table 2. Capiloscopy parameters.
Decrease of capillaries parameters was observed 6 months later Of cell therapy.

CAMPHOR		
	BASELINE	6 MONTHS
Sympthons	3	0
Activities	5	0
Life quality	3	2
	Total 11	Total 2

Decrease in the previous total score Vs post from 11 to 2 points. There was a decrease in each one of the previous sub scales Vs post, in sympthons (3 Vs 0), in activities /5 Vs 2), in quality life (3 Vs 2)

Conclusions

Stem cell therapy is not available as a treatment for patients with refractory scleroderma. However, there are reasons that support its effectiveness and safety in those patients without other available alternatives.