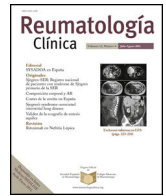




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## Case report

### Heart Transplantation in Systemic Sclerosis: A Therapeutic Option. Presentation of a Case and Literature Review



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#### ABSTRACT

Cardiac involvement in systemic sclerosis (SSc) is rare but leads to poor short-term prognosis. Evidence regarding heart transplantation (HT) is scarce and is based on experience with isolated cases. We present this case with the aim of analysing the characteristics of a patient with SS who has undergone a successful transplant.

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### Trasplante cardíaco en esclerosis sistémica: una opción terapéutica. Presentación de un caso y revisión de la bibliografía

#### RESUMEN

El compromiso cardíaco en la esclerosis sistémica (ES) es raro, pero conlleva un mal pronóstico a corto plazo. La evidencia relativa al trasplante cardíaco (TC) es escasa y se basa en la experiencia con los casos aislados. Presentamos este caso con el objetivo de analizar las características de un paciente con esclerosis sistémica sometido a un trasplante exitoso.

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#### Introduction

SSc is a systemic autoimmune disease of heterogeneous pathogenesis in which vascular, cutaneous and internal organ fibrosis are prominent.<sup>1</sup> Primary symptomatic cardiac involvement occurs in 15–35% of patients and is estimated to cause up to 30% of deaths.<sup>1,2</sup>

#### Case

We present the case of a 58 year-old male diagnosed with anti-SCL70 positive diffuse cutaneous SSc (dcSSc). At diagnosis he presented with myositis, arthralgias and scleroderma (Rodman index 23/51), as well as interstitial disease of subpleural predominance in both lung bases. No oesophageal or renal involvement was observed. After 11 months of evolution it presented elevation of myocardial damage markers (CK, CK-Mb, Troponin and NT-proBNP). Echocardiogram and cardiac resonance showed pericardial effusion, dilation and biventricular systolic dysfunction. The initial affectation was mild (LVEF 51% and RVEF 40% without pathological gadolinium enhancement or myocardial

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**Table 1**

Published cases of heart transplantation in patients with Systemic Sclerosis: demographic, laboratory and clinical characteristics, used immunosuppressive therapies and progression.

Author	Sex	Age at Dx	Sub-type	ANA	ILD	Other organs involved	Enhancement on IRM	FEVI pre-HT	Interval Dx-HT	ISx. pre-HT	Follow-up	Dead
Turcotte (2020) <sup>a</sup>	W	42	dcSSc	NS	No	uDT; RP	Yes	25%	6 y and 6 mo	NR	4 y	No
Faust (2019) <sup>6</sup>	W	32	dcSSc	NI	No	FR, uDT	NI	40%	12 y	MMF	2 wk	No
Faust (2019) <sup>6</sup>	W	30	dcSSc	NI	Yes	FR, uDT	NI	53%	14 y and 2 mo	GC, CFM, CSA	6 semanas	Yes
Martens (2012) <sup>7</sup>	M	31	NI	NI	No	No	Yes	42%	3 y	MTX, MMF	1 y	No
Bennasar (2015) <sup>8</sup>	W	16	dcSSc	NS	No	RP; myositis; xerophthalmia; xerostomía	Yes	25%	3 y	AZA, GC	15 d	Yes
Johnson (2013) <sup>9</sup>	W	14	dcSSc	NS	No	Arthritis	NI	42%	4 y and 7 mo	MTX; CFM	22 mo	Yes
Ikic (2014)	W	15	dcSSc	Scl-70	No	uDT; arthritis; miositis	Yes	35%	NI	MMF, GC	0.5 y	No
Ikic (2014) <sup>10</sup>	W	12	dcSSc	NS	No	uDT; iDT; arthritis; myositis	NI	25%	NI	D-PEN	3 y	No
Ikic (2014) <sup>10</sup>	W	35	lcSSc	NS	No	TDs; arthritis; myositis	No	17%	NI	GC	0.1 y	Yes
Ikic (2014) <sup>10</sup>	M	46	lcSSc	Neg	No	uDT	NI	27%	NI	No	10 y	No
Ikic (2014) <sup>10</sup>	M	32	lcSSc	Neg	No	uDT	No	15%	NI	No	12 y	No
Ikic (2014) <sup>10</sup>	W	24	Overlap – RA	NS	No	Arthritis	No	15%	NI	TCZ, MTX, GC	2.5 y	No
Lenaerts (2018) <sup>11</sup>	M	50	dcSSc	Neg	No	No	Yes	20%	5 mo	NR	109 mo	No
Lenaerts (2018) <sup>11</sup>	M	49	lcSSc	RNA – polimerasa III	No	Myositis	Yes	40%	5 y	GC, MTX	23 mo	No
Lenaerts (2018) <sup>11</sup>	M	47	dcSSc	PM – Scl – 100	No	NI	Yes	40%	27 mo	NR	23 mo	No
De Diego (2020) <sup>a</sup>	M	58	dcSSc	Scl-70	Yes	Myositis, arthralgias	Yes	26%	14 mo	MTX, CFM, RTX	36 mo	No

Dx: diagnosis; ANA: anti-nuclear antibody; ILD: interstitial lung disease; Interval Dx-TC: interval between Dx and HT; ISx: immunosuppressant; y: years; mo: months; wk: week; M: man; W: woman; NI: not included; NS: no specificity; uDT: upper digestive tract; iDT: inferior digestive tract; RP: Raynaud’s phenomenon; lcSSc: limited cutaneous SSc; cdSSc: cutaneous diffuse SSc; Neg: negative; RA: rheumatoid arthritis; MTX: methotrexate; MMF: mycophenolate mofetil; D-PEN: D-penicillamine; AZA: azathioprine; GC: glucocorticoids; CFM: cyclophosphamide; CSA: cyclosporine A; TCZ: tocilizumab; RTX: rituximab.

<sup>a</sup> Case reported in this article.

oedema) but despite the support treatment with neurohumoral inhibitors (ACEI, beta-blockers and aldosterone antagonists) and immunosuppressive treatment (corticosteroids, mycophenolate mofetil, cyclophosphamide pulses and Rituximab) it progressed unfavourably to severe affectation (LVEF 26% and RVEF 24% with patchy subendocardial gadolinium enhancement). Interstitial lung involvement was controlled with immunosuppressors, whereas residual myocardial involvement triggered episodes of cardiogenic shock and malignant ventricular arrhythmias. Five months after the diagnosis of cardiomyopathy, HT was chosen as the therapeutic option. Thirty-six months after HT the patient is in stage I of the NYHA, with good biventricular function of the graft, respiratory stable and has presented regression of the skin affectation (Rodman’s index of 17/51 at 16 months post-transplant) with the usual immunosuppressive treatment.

**Discussion**

Myocardial involvement is associated with ventricular systolic dysfunction in 10% of patients<sup>3</sup> with a two-year mortality

of 60%.<sup>4</sup> Although it can occur in both subtypes it is more severe in patients with cdSSc, often evolving in parallel with skin progression.<sup>5</sup> It is also more frequently associated with certain antibodies: anti-SCL70, anti-U3 RNP, anti-Ku and anti-Th/To. Due to the importance in terms of mortality of pulmonary involvement, pulmonary and cardio-pulmonary transplantation are accepted options in the face of therapeutic failure. In the case of cardiac affectation there are fewer reported cases of CT, being an option frequently limited by the concomitant affectation of other organs. After a systematic search, another 15 cases of CT were identified in patients with cardiac involvement by ES (Table 1). Eight presented a diagnosis of EScd (53.3%), 5 EScl (33.3%), 1 (6.6%) overlap syndrome with rheumatoid arthritis and in another case the ES subtype was not included. No cardiac recurrence of ES was reported in any case. Only one other published case presented associated pulmonary involvement,<sup>6</sup> although its evolution is not assessed since it died 6 weeks after the CT scan due to infectious complications. It is worth noting the skin improvement after immunosuppression for CT, also observed in other published cases.

## Conclusions

Although the literature is limited, the case presented, along with those previously published, demonstrates that HT is a valid therapeutic option in SSc with severe cardiac involvement especially if non-cardiac systemic involvement is ruled out and/or controlled.

## Consents and approval of the ethics committee

The publication of the case was approved by the ethics committee of the Donostia University Hospital. Informed consent was obtained from the patient for the publication of his case.

## Conflict of interest

The authors declare that they have no conflicts of interest. Also, all authors read and approved the final manuscript.

## References

- Carreira Delgado P.E. Diagnóstico, diagnóstico diferencial y clasificación de la esclerosis sistémica. En: Rúa-Figueroa I, González-Gay MA, directores. Tratado SER de diagnóstico y tratamiento de enfermedades sistémicas autoinmunes. Panamericana; 2018, p. 201-207.
- Hung G, Mercurio V, Hsu S, Mathai SC, Shah AA, Mukherjee M. Progress in understanding diagnosing, and managing cardiac complications of systemic sclerosis. *Curr Rheumatol Rep*. 2019;21:68, <http://dx.doi.org/10.1007/s11926-019-0867-0>. Published 2019 Dec 7.
- Allanore Y, Meune C, Vonk MC, Airo P, Hachulla E, Caramaschi P, et al. Prevalence and factors associated with left ventricular dysfunction in the EULAR Scleroderma Trial and Research group (EUSTAR) database of patients with systemic sclerosis. *Ann Rheum Dis*. 2010;69:218–21.
- Turcotte-Gosselin F, Turgeon PY, Ilic A, Beaudoin J, Joubert P, Dubois M, et al. Is heart transplantation a valuable option in patients with diffuse systemic sclerosis and primary cardiac involvement? *Clin Case Rep*. 2020;8:137–41, <http://dx.doi.org/10.1002/ccr3.2600>.
- Domsic RT, Rodríguez-Reyna T, aLucas M, Fertig N, Medsger TA Jr. Skin thickness progression rate: a predictor of mortality and early internal organ involvement in diffuse scleroderma. *Ann Rheum Dis*. 2011;70:1.
- Faust I, Weile J, Fujita B, Kandolf R, Hendig D, Vollmer T, et al. Heart transplantation in systemic sclerosis: new impulses for conventional scleroderma transplantation regimen and scleroderma diagnostic monitoring: 2 case reports. *Transplant Proc*. 2019;51:865–70, <http://dx.doi.org/10.1016/j.transproceed.2019.01.025>.
- Martens E, Lange P, Pohl T, Nickel T, Juchem G, Kaczmarek I, et al. Heart transplantation in a 36-year-old experiencing terminal heart failure caused by systemic sclerosis. *Transplantation*. 2012;94:13–5, <http://dx.doi.org/10.1097/TP.0b013e3182575df>.
- Bennasar G, Carlevaris L, Secco A, Romanini F, Mamani M. Trasplante cardíaco en una paciente joven con diagnóstico de esclerosis sistémica difusa. *Reumatol Clin*. 2016;12:285–7, <http://dx.doi.org/10.1016/j.reuma.2015.10.001>.
- Johnson JN, Kvistad BS, Reed AM, Porter J, O'Learly PW, Driscoll DJ. Cardiac transplantation in a pediatric patient with systemic sclerosis. *Congenit Heart Dis*. 2013;8:1–4, <http://dx.doi.org/10.1111/j.1747-0803.2011.00554.x>.
- Ilic A, Chatelus E, Epailly E, Kremer H, Sibilia J, Gottenberg J, et al. Heart transplantation in 6 patients with systemic sclerosis and a primary cardiac involvement. In: *ACR/ARHP annual meeting*. 2014.
- Lenaerts JC, Lenaerts JL, Westhovens R, Droogne W, Ciarka A, Van Cleemput J, et al. Cardiac transplantation in systemic sclerosis: single-centre experience of three cases. *Rheumatology*. 2018;57:1122–4, <http://dx.doi.org/10.1093/rheumatology/key055>.