Case report

Stiff skin syndrome and myeloma successfully treated with autologous haematopoietic stem cell transplantation (HSCT)

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ABSTRACT

Stiff skin syndrome (SSS) is a rare scleroderma-like syndrome characterised by stone hard skin, joint limitation and progressive restriction of chest that may lead to death. We describe the efficacy of haematopoietic autologous stem cell transplantation (HSCT) in a case of SSS secondary to a smouldering myeloma (SM), with severe joint disability, lung interstitial disease and oesophageal dysfunction. The patient was evaluated at 1, 12 and 18 months after HSCT, clinically (joint motility, HAQ and NYHA for dyspnoea) and instrumentally (DLCO, chest HRCT, oesophagus x-ray). After 18 months since HSCT, we observed a high improvement, contemporaneously to SM remission, of HAQ, joint motility, lung (at DLCO and HRCT) and oesophageal abnormalities.

Introduction

Stiff skin syndrome (SSS) is a scleroderma-like (SSc) rare disease of unknown aetiology, characterised by progressive motility limitation of areas with abundant fascia – proximal limbs, shoulders and thorax – often culminating in a severe chest restriction that may lead to death (1).

Highly variable features are reported in literature (1), with sporadic familiar aggregation (2), visceral involvement (1) and absence of inflammatory infiltrate in skin, fascia and muscle (3).

Haematogical disorders are rarely associated to SSc-like syndromes (4) but, until now, never to a SSS-like disorder.

Report

We describe a case of successful treatment of a SSS associated to smouldering myeloma (SM) with haemopoietic autologous stem cell transplantation (HSCT).

A 56-year-old man, had a five-year history of progressive and symmetric limitation of shoulders, hips, knees and trunk, exiting in severe disability (difficulty in standing up and sitting down) (Fig. 1A), with a similar familiar case (father's sister, deceased), and complained of joint and muscle pain, severe thigh and buttock skin indurations, dyspnoea and dysphagia.

Two previous biopsies (deltoid and quadriceps) revealed thickness of skin and fascia, without inflammatory or amyloid infiltrate. Antinuclear autoantibodies and muscle enzymes were normal. At capillaroscopy, capillaries were tortuous but without a scleroderma pattern. Ultrasound of the skin of hand and arms revealed dermal thickness (5).

Chest high resolution computerised tomography (HRCT) showed a diffuse bilateral interstitial lung involvement (severe at superior and mild at inferior lobe) (Fig. 2A) and DLCO, at functional respiratory tests, was low (67%). Dynamic x-ray demonstrated a distal oesophageal peristalsis reduction.

All previous treatments (methotrexate, hydrossiclorochine, azathioprine, cyclophosphamide, immunoglobulin and plasmapheresis) were unsuccessful.

Elevated kappa chains IgG (2345 mg/dl) were detected and bone marrow biopsy showed a CD138+ kappa plasma-cellular multiple myeloma (MM) with 30% of plasma cells and a low mitotic index.

Despite high dosage steroids treatment, symptoms worsened rapidly and HSCT was prescribed, with approval of the ethics committee of Florence and patient's written consent, according to the Helsinki declaration.

The patient received 50 mg/kg cyclophosphamide, since day -5 to day -2, 2.5 mg/kg thymoglobulin at day -3, mesna 120% since day -5 to -2 and 30 mg/mq melphalan at day -1, followed by the in-

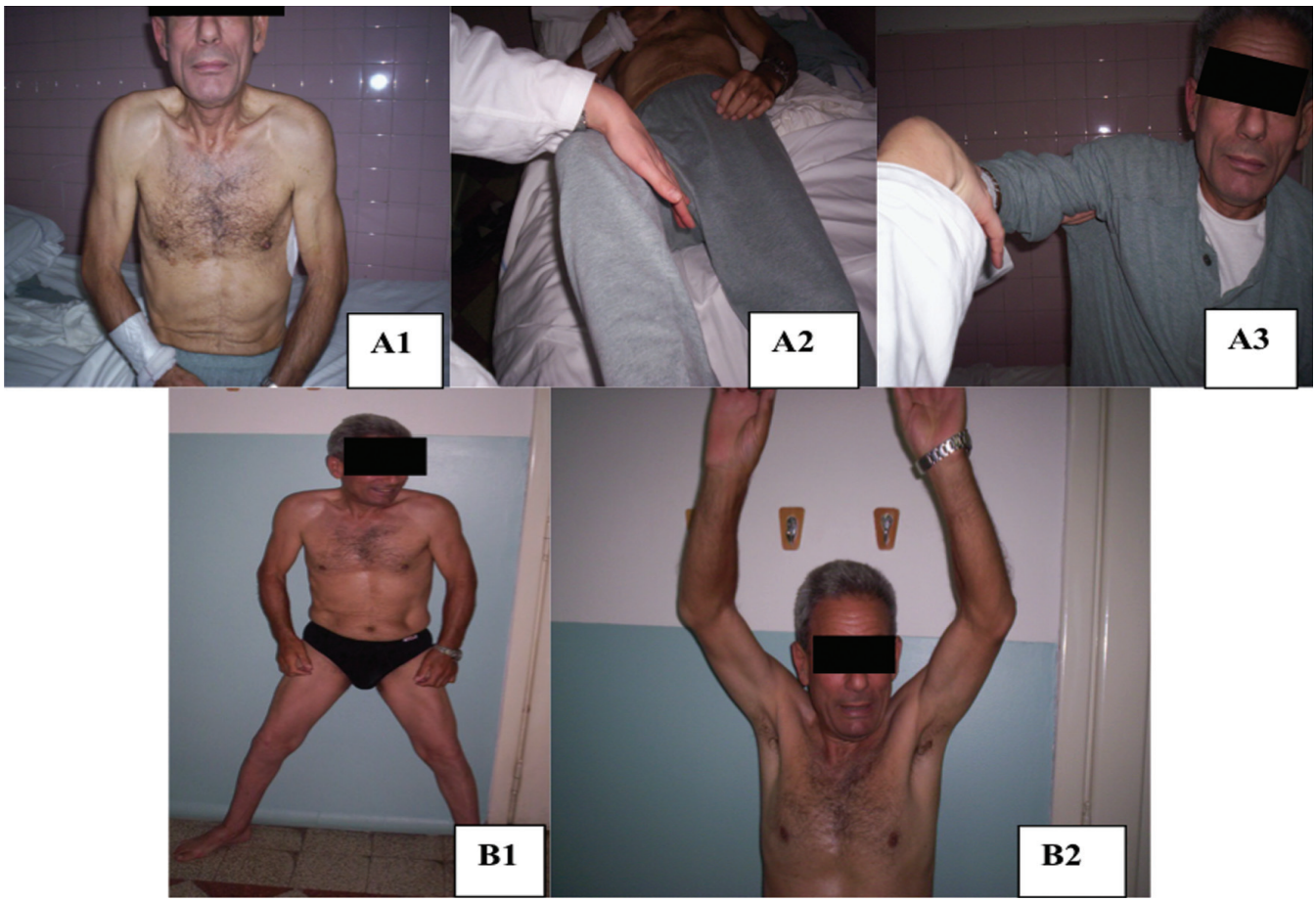

Fig. 1. Clinical improvement of SSS-like patient after HSCT. Joint limitation of SSS-like patient before (**A1**: impossibility to stand up and difficulty to sit down, **A2**, **A3**: limitation of hips and shoulders extra-rotation, respectively) and after 18 months (**B1**: ability to stand up and ameliorated extrarotation of hips; **B2**: increase extra-rotation of shoulders) since HSCT.

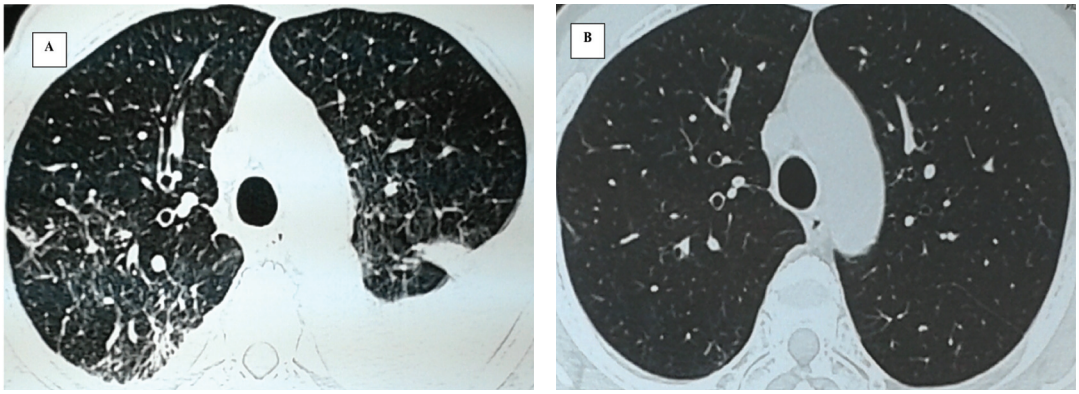

Fig. 2. Interstitial fibrosis at HRCT of lung before (**A**) and after (**B**) 18 months since treatment with HSCT.

fusion of 4.29x10E6/kg purified CD34+ cells (6).

Before HSCT and successively – at 1, 12 and 18 months – the patient was evaluated for joint motility (Fig. 1A-B) and filled the Health Assessment Questionnaire (HAQ).

Chest HRCT, pulmonary functional tests (PFR) and dynamic oesophageal x-ray, were performed at baseline and 18 months.

At 18 months, a complete haematological remission (absence of k and lambda chains in blood and urine), contemporaneously to the maximal clinical (Fig. 1B) and instrumental improvement (Table I), was achieved.

After one month and progressively over time, motility ameliorated (Fig. 1B and Table I). Dyspnoea gradually decreased (NYHA 4, before HSCT decreased progressively to 1, at 18 months), associated to the enhancement of DLCO/FVC and interstitial involvement regression at HRCT (Fig. 2B), at 18 months. Also dysphagia disappeared, with normal oesophageal x-ray at 18 months.

Discussion

HSCT demonstrated to be an effective treatment in our case, according to previous evidences (6-7), even if the basic mechanisms are poorly understood.

Table I. Clinical and instrumental improvement of SSS-like patient before and after HSCT.

	Before	One month later	12 months later	18 months later
HAQ	3	3	2.4	1.2
SHOULDER				
Intrarotation (C7-index)	Left : 47 cm Right: unable	Bilateral: 52 cm	Right 39 cm Left 46 cm	Bilateral 35 cm
Extrarotation	Right: 80° Left: 100°	Right: 90° Left: 70°	Right: 140° Left: 140°	Bilateral 180°
HIP				
Intrarotation	Left : 10° Right: unable	invaried	Left : 10° Right: 10°	invaried
Extrarotation	Left : 0° Right: 10°	invaried	Left : 30° Right: 10°	Left : 30° Right: 30°
KNEE				
Flexion	Left : 120° Right: 130°	Bilateral 60°	Bilateral 90°	Bilateral 90°
NYHA	4	3	2	1
PFR	DLCO 67% FVC 60%	–	–	DLCO 80% FVC 90%
Chest HRCT	Severe fibrosis of superior lobe and mild fibrosis of inferior lobe	–	–	Regression of fibrosis of superior and inferior lobe
Oesophagus x-ray	reduction of peristalsis in particular in distal tract	–	–	Normal

It was hypothesised that immunosuppression plus HSCT might substantially decrease or even eliminate the illness effectors cells, leaving a "minimal residue" (8).

HSCT has not been used previously in SSS but only in severe SSc. According to the first register, HSCT results were controversial in SSc (9): more than 50% ameliorated, 15% relapsed and 5% worsened.

Later, other reports (10-11), showed a DLCO enhancement, in agreement with our case.

Otherwise, while in SSc the DLCO improvement was not supported by a significant change in HRCT (10), our patient presented a regression of lung interstitio-pathy. Furthermore, in our case, HSCT determined a significant progressive resolution of joint and oesophageal abnormalities that was never demonstrated in SSc.

The reason of this full recovery in our patient is probably linked to the reconstitution of bone marrow abnormalities secondary to SM. Even if previous treatment with cyclophosphamide had no given significant results in this case, the higher dose-intensity of the chemotherapy administered within the conditioning regimen might also account for the positive clinical impact.

Up to now, SSS has been described in childhood and usually, is a diagnosis of exclusion (1-3). We firstly reported a SSS in the adulthood, suggesting that it might be associated to MM. Even if there was a similar familiar case, the relationship with MM, might be also supported by the contemporaneous improvement of MM and SSS at 18 months since HSCT. Probably, other future cases might be lead to a better knowledge of this rare manifestation.

Key message

- Our case showed a significant improvement after HSCT of joint, lung and oesophageal disease in SSS associated to SM.

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