Journal of Clinical & Experimental Cardiology

Salem et al., J Clin Exp Cardiolog 2016, 7:11
DOI: 10.4172/2155-9880.1000476

Case Report Open Access

Fatal Myocarditis in a Male with Systemic Sclerosis

Thouraya Ben Salem[1*], Molka Tougorti[2], Imed Ben Ghorbel[2] and Mohamed Habib Houman[2]

[1]*Department of Internal Medicine, La Rabta University Hospital, Tunis, Tunisia*

[2]*Faculty of Medicine Tunis, University Tunis El Manar, Tunisia*

[*]**Corresponding author:** Thouraya Ben Salem, Department of Internal Medicine, La Rabta University Hospital, Tunis, Tunisia, Tel: +216 71 570 851; Fax: +216 71 570 851; E-mail: bensalemthouraya@yahoo.fr

Received date: June 02, 2016; **Accepted date:** October 26, 2016; **Published date:** November 01, 2016

Abstract

Cardiac involvements in systemic sclerosis have a poor outcome. We report here a case of 28 year-old-man with history of systemic sclerosis developing a fatal myocarditis.

Initially patient has disabling joint manifestation. Systemic sclerosis is diagnosed after progressive development of cutaneous, pulmonary, and gastrointestinal manifestations. One year after systemic sclerosis diagnosis, our patient develops heart failure signs when he is already treated with methotrexate (15 mg/week) and coticosteroids (15 mg/day). Echocardiography show global hypokinesia with low left ventricular ejection fraction (32%). Natriuretic peptides and troponin levels are high. Anti-centromere and anti-SRP antibodies are positive. Corticosteroids dose is increased to 1 mg/kg/day, and methotrexate was given 25 mg/week without improvement. Cyclophosphamide was started but patient died within six months. Despite immunosuppressive therapy, myocarditis outcome is poor since patient was in heart failure at presentation, and has anti-SRP antibodies.

Keywords: Systemic sclerosis; Myositis; Myocarditis; Anti-SRP antibody

Introduction

Cardiac manifestations (CM) are common in systemic sclerosis (SS) and cause death in up to 15% of patients. Their prevalence varies widely (15-35%) [1,2] and depends on whether they are screened systematically or only noted when there are clinical symptoms. CM may be under-estimated in SS because cardiac symptoms aren't easily distinguished from pulmonary and esophageal symptoms. Pericarditis and myocardial fibrosis are frequent in SS [3]. Myocardial fibrosis in SS is the consequence of multiple focal ischemic injuries [4] caused by coronary microcirculation disturbance. At the contrary, myocarditis is uncommon in SS and is often associated to muscular involvements. We report herein a case of a young male with SS who developed a rapidly progressive and fatal myocarditis.

Case Report

A 28 year-old-man without medical history was complaining of arthralgia, Raynaud's phenomenon and dysphagia since two years. At presentation, patient had no dyspnea or chest pain. At examination he has a persistent fever and synovitis with joint finger deformities. Sclerotic skin face and sclerodactylia with digital ulcers are apparent. Capillaroscopy show severe organic microangiopathy and foggy aspect without megacapillaries. Thoracic computed tomography confirms interstitial lung disease without forced vital capacity alteration (80%). Gastro-esophageal endoscopy reveals esophagitis. Cardiac echography doesn't show any abnormality. C-reactive protein is high and creatinin phosphokinase is normal. Antinuclear antibodies are positive (1/800) and anti-centromere are negative. Systemic sclerosis with disabling arthritis is diagnosed. Calcium channel blockers and proton pump inhibitors are given. Patient is also treated with corticosteroids (15 mg/day) and methotrexate (15 mg/week) with good improvement. One year later the patient is hospitalized for dyspnea, chest pain, flank dullness with mild abundance ascites, inferior limbs edema and hypotension. There is no myalgia or muscle weakness. Electrocardiogram show a complete left brunch block. Echocardiography reveals global hypokinesia with low left ventricular ejection fraction (32%) and mitral regurgitation. There is no pericarditis. Coronarography is normal. Biological data note high level NT-pro-BNP (10380 ng/L) and increased troponin value (0.24 ng/ml, NV<0.04 ng/ml). Creatinin phosphokinase is two folds normal value. C-reactive protein level is high at 91 mg/l. Anti-centromere, anti-signal recognition particle (anti-SRP) and anti Ro-52 antibodies are positive but anti-polymyositis-scleroderma (anti-PM-Scl) antibodies are negative. Cytomegalovirus serology is negative and there is no evidence of other infection. Angiotensin converting enzyme inhibitor is given. Myocarditis secondary to his SS is retained and patient is treated with high dose corticosteroid (three methylprednisolone pulses than prednisone 1 mg/kg/day) and methotrexate 25 mg/week. His symptoms improve and troponin value decrease to 0.05 ng/ml. But three months later, his condition worsens and her left ventricular ejection fraction decreases to 25%. Cardiac echography shows a severe global hypokinesia and a circumferential pericardial effusion. Methotrexate is stopped and intravenous cyclophosphamide is started without any improvement. Patient died six months after the heart failure diagnosis.

Comments

The first particularity of our case is presence of myocarditis in patient with SS without inflammatory myopathy since our patient doesn't complain of myalgia and there is no muscular weakness.

Myocarditis is a rare clinical condition in patients with SS, only a few cases are reported [5,6]. In a cohort of 181 patients with SS, seven

patients develop acute clinical symptoms of heart disease, among them six have an acute myocarditis (3.3%) [7]. In SS, myocardial involvement is mainly due to myocardial fibrosis. In fact, the micro-circulation alteration, which is an equivalent of Raynaud's phenomenon in the heart, causes micro-ischemic lesions and fibrosis. Myocardial fibrosis can be silent at the beginning of the disease; otherwise it can be responsible of ventricular relaxation abnormalities, conduction or rhythm troubles [3]. These involvements develop progressively, are chronic and appear at a late stage of the disease. Additionally, patients with SS may also develop myocarditis which is an inflammatory phenomenon of the heart muscle. In our patient myocarditis seems obvious because of rapid onset, evident global hypokinesia and elevated muscular enzymes. Myocarditis is more frequent in patient with scleromyositis overlap syndrome than isolated SS. Follansbee et al. select 1095 patients with SS to study relationship between CM and skeletal muscle disease [8]. Authors conclude that however myocardial fibrosis was the predominant histological abnormality at autopsy, patients who died in a context of acute myocarditis, have myocytolisis lesion with contraction band necrosis. They also note that patients with associated myopathy develop more frequently cardiac dysfunction such as rhythm disorder and heart failure.

In scleromyositis overlap syndrome, muscular involvements are rather mild with a modest increase of muscle enzymes. Digital ulcers, joint manifestations, interstitial lung disease and gastrointestinal involvements are frequent manifestations. Cardiac manifestations are also observed [9]. Although considered as a disease serological marker, anti-PM-Scl antibody is not disease specific [9] and isn't positive in all cases. In the study of Ranque et al. concerning patients with myopathies related to systemic sclerosis, only 10% of patients have anti-PM-Scl antibodies [10]. Anti-PM-Scl antibody is absent in our case. Surprisingly, in addition to anti-centromere antidody, our patient has anti-SRP antibody which is a muscle-specific autoantibody. Positive anti-SRP in a patient with SS is another particularity of our case.

Prevalence of anti-SRP antibodies in patients with cardiac manifestation in inflammatory myopthies is evaluated from 6 to 75% and they are considered as a poor prognostic factor. This particular form of myopathy is characterized by necroziting myositis and severe cardiac involvement [11,12]. But anti-SRP antibody is rare in patients with SS and other connective tissue diseases. Hanaoka et al. study anti-SRP positivity in 6180 patients with diverse connective tissue diseases and find that anti-SRP antibody is detected in only 0.5% of these patients. No one of the 440 patients with SS have this antibody [13]. Recent findings show that association between positive anti-SRP antibody and cardiac involvement in inflammatory myopathies is not evident. In a study of patients with polymyositis (n=134), dermatomyositis (n=129) and connective tissue diseases, predominantly with SS (n=790), 19 patients have positive anti-SRP antibody. After a mean follow up of 4.5 years, only two patients develop cardiac involvement [14]. Hengstam et al., when comparing two groups of patients according to the presence or not of anti-SRP antibody, find that there is no association between positive anti-SRP and an increasing risk of cardiac involvement [15].

In our patient, myocarditis is associated to pericarditis which is a frequent manifestation in SS. In addition, pericardial effusion is identified as a useful criterion for noninvasive diagnosis of myocarditis in patients with recent onset of clinical symptoms and normal left ventricular function [16].

CM are difficult to manage in patients with SS. Symptomatic treatment is based on classic medications. Diuretics are considered in cases of heart failure but should be used with caution due to the risk for development of renal failure [3]. Angiotensin converting enzyme inhibitors and calcium channel blockers are given to improve myocardial perfusion [3]. These treatments are also used to improve digital blood flow patterns and reduce symptoms of digital spasm.

Regarding the rarity of myocarditis in SS, there's no standard specific treatment and physician treat according to their own experience. But all authors agree that corticosteroids are mandatory to treat muscular inflammation. High dose steroid (1 mg/kg/day) is often needed in SS like in all inflammatory myopathies [6,17], it may be or not started with intravenous methylprednisolone. In these patients, high risk of scleroderma renal crisis decreases if angiotensin converting enzyme inhibitors are given.

Additional immunosuppressive drugs are used when there is evidence of myocarditis with heart failure [18] but the choice of the drug is controversial.

For our patient, methotrexate was chosen to treat florid arthritis. When patient develops myocarditis, methotrexate dose is increased because we were thinking that methotrexate works in both joint and muscular involvements. As methotrexate is an established therapy for inflammatory arthritis and inflammatory myopathies, it is generally preferred for the management of SS overlap syndrome [18].

Other authors use cyclophosphamide in SS patients with myocarditis [7,17], probably for a more rapid effect than methotrexate. Mycofenolate mofetil and azathioprine may also be used.

Four patients of Pieroni receive cyclophosphamide (2 mg/kg/day up to a cumulative dose of 6 g) followed by Azathioprine, while 3 patients are treated immediately with azathioprine (2 mg/kg/day) for 12 months [7]. After one year follow up, clinical improvement is noted in all patients except one who is in heart failure at the time of diagnosis. The same outcome is seen in our patient, since myocarditis is severe at presentation and doesn't improve after treatment.

Stack et al. report a similar case concerning a 38-year-old man who present with rapidly progressive diffuse cutaneous SS, lung involvement and myocarditis. Patient is given cyclophosphamide pulses (10 mg/kg monthly) and intravenous methylprednisolone with a total of nine doses of cyclophosphamide and three courses of methylprednisolone. Good clinical and biological evolution is noted [6]. Allanore treat the same way, scleromyositis overlap syndrome and polymyositis related myocarditis with intravenous cyclophosphamide with a good outcome [17]. After six month of treatment, patients are asymptomatic and cardiac MRI dramatically improves.

In our patient, heart involvement is rapidly progressive and cardiac dysfunction causes death six months after myocarditis diagnosis and 30 months after SS diagnosis. It is well known that cardiac involvements in SS cause death in the first five years and that mortality rate is 60% in the two first year and rise to 75% after five years. Specific data for myocarditis are not available but it seems that myocarditis with severe heart failure have a poor prognosis [7].

It seems that in SS, myocarditis have a poorer prognosis than myocardial fibrosis since this last take a slow course lead to mild ventricular dysfunction whereas myocarditis may develop rapidly with heart failure.

Myocarditis is a life-threatening manifestation in SS, it must be screened early especially in patients with associated myopathy and who have specific antibodies (anti-PM-Scl or anti-SRP). Despite association of corticosteroids and immunosuppressive drugs, the outcome may be poor.

References

1. Allanore Y, Avouac J, Kahan A (2008) Systemic sclerosis: an update in 2008. Joint Bone Spine 75: 650-655.
2. Steen VD, Medsger TA (2000) Severe organ involvement in systemic sclerosis with diffuse scleroderma. Arthritis Rheum 43: 2437-2444.
3. Lambova S (2014) Cardiac manifestations in systemic sclerosis. World J Cardiol 6: 993-1005.
4. Allanore Y, Meune C, Kahan A (2008) Outcome measures for heart involvement in systemic sclerosis. Rheumatology 47: 51-53.
5. Clemson BS, Miller WR, Luck JC, Feriss JA (1992) Acute myocarditis in fulminant systemic sclerosis. Chest 101: 872-874.
6. Stack J, McLaughlin P, Sinnot C, Henry M, MacEneaney P, et al. (2010) Successful control of scleroderma myocarditis using a combination of cyclophosphamide and methylprednisolone. Scand J Rheumatol 39: 349-350.
7. Pieroni M, De Santis M, Zizzo G, Bosello S, Smaldone C, et al. (2014) Recognizing and treating myocarditis in recent-onset systemic sclerosis heart disease: Potential utility of immunosuppressive therapy in cardiac damage progression. Semin Arthritis Rheum 43: 526-535.
8. Follansbee WP, Zerbe TR, Medsger TA (1993) Cardiac and skeletal muscle disease in systemic sclerosis (scleroderma): a high risk association. Am Heart J 125: 194-203.
9. Iaccarino L, Gatto M, Bettio S, Caso F, Rampudda M, et al. (2013) Overlap connective tissue disease syndromes. Autoimmun Rev 12: 363-373.
10. Ranque B, Bérezné A, Le-Guern V, Pagnoux C, Allanore Y, et al. (2010) Myopathies related to systemic sclerosis: a case-control study of associated clinical and immunological features. Scand J Rheumatol 39: 498-505.
11. Targoff IN, Johnson AE, Miller FW (1990) Antibody to signal recognition particle in polymyositis. Arthritis Rheum 33: 1361-1370.
12. Thiébaut M, Terrier B, Menacer S, Berezne A, Bussone G, et al. (2013) Antisignal recognition particle antibodies-related cardiomyopathy. Circulation 127: e434-436.
13. Hanaoka H, Kaneko Y, Suzuki S, Takada T, Hirakata M, et al. (2016) Anti-signal recognition particle antibody in patients without inflammatory myopathy: a survey of 6180 patients with connective tissue diseases. Scand J Rheumatol 45: 36-40.
14. Kao AH, Lacomis D, Lucas M, Fertig N, Oddis CV (2004) Anti–signal recognition particle autoantibody in patients with and patients without idiopathic inflammatory myopathy. Arthritis Rheum 50: 209-215.
15. Hengstman GJ, ter Laak HJ, Vree Egberts WT, Lundberg IE, Moutsopoulos HM, et al. (2006) Anti-signal recognition particle autoantibodies: marker of a necrotising myopathy. Ann Rheum Dis 65: 1635-1638.
16. Ong P, Athansiadis A, Hill S, Kispert EM, Borgulya G, et al. (2011) Usefulness of pericardial effusion as new diagnostic criterion for noninvasive detection of myocarditis. Am J Cardiol 108: 445-452.
17. Allanore Y, Vignaux O, Arnaud L, Puéchal X, Pavy S, et al. (2006) Effects of corticosteroids and immunosuppressors on idiopathic inflammatory myopathy related myocarditis evaluated by magnetic resonance imaging. Ann Rheum Dis 65: 249-252.
18. Nihtyanova SI, Ong VH, Denton CP (2014) Current management strategies for systemic sclerosis. Clin Exp Rheumatol 32: 156-164.