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Case report of atypical seronegative scleroderma

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Abstract

Introduction: Scleroderma is a rare, systemic, clinically heterogeneous connective tissue disorder. It is accompanied by various degrees of tissue fibrosis and chronic inflammatory infiltration in numerous visceral organs, prominent fibroproliferative vasculopathy and humoral and cellular immune alterations. Virtually all organs can be affected in scleroderma, particularly lungs, heart, kidneys and gastrointestinal tract, which is clearly shown in our patient who had pulmonary fibrosis, liver fibrosis and pericardial effusion, probably due to scleroderma.

Case: A 73 year old woman presented with recurrent presyncope, worsening dysphagia and dyspnea on exertion with general examination highly suggestive of scleroderma in the absence of specific antibodies such as anti-Scl70 antibodies, anti-centromere antibodies and anti RNA polymerase III antibodies. Further investigations with imaging revealed involvement of other organs including heart, lungs and gastrointestinal tract.

Significance: The case highlights the importance to consider seronegative scleroderma when patients present features of scleroderma with multiorgan involvement, even in the absence of specific antibodies to allow early diagnosis and regular follow-up.

Keywords

seronegative scleroderma; tissue disorder

Case Report

A 73 years old Asian woman was admitted to our geriatric department in February 2018 withpresyncope on a background of recent hospital admission for small subdural haematoma from fall a month ago, which was treated conservatively. She had been suffering ongoing lightheadedness and loss of balance since her previous admission. She has a background history of pulmonary fibrosis, liver fibrosis, bronchial asthma and GORD. Her regular medications were terbutaline, budesonide/formoterol inhalerand panto-

prazole. She was previously on prednisone for her pulmonary fibrosis but prednisone was ceased recently. She has never smoked and denies alcohol use.

General examination revealed bilateral pitting oedema of lower limbs, skin thickening and tightening over fingers, chest and mouth with decreased oral aperture as well as facial telangiectasia. Neurological examination was unremarkable. On further exploration of history, she also reported positive Raynaud's phenomenon and worsening of shortness of breath on exertion. Her BSL was found to be 2.7mmol/L on admission. Her hypoglycaemia was treated with IV 50% dextrose solutionin the Emergency Department.

Blood tests revealed hypokalaemia and hyponatraemia. Repeated CT Brain showed the previously documented subdural haematoma had nearly completely resolved and no evidence of new intracranial haemorrhage was found. The patient was admitted for monitoring of BSL, correction of electrolytes imbalance and further investigations for clinical features that were highly suggestive of Scleroderma.

During admission, she had further episodes of hypoglycaemia that were treated with hypokit and IV dextrose solution. Investigations for causes of recurrent hypoglycaemia such as Insulinoma and Adrenal insufficiency were negative, with C-peptide of 0.61nmol/L and morning serum cortisol of 381 nmol/L.

Her hypokalaemia resolved with increased oral intake and regular potassium tablets. Further investigations revealed her hyponatraemia was secondary to SIADH. Her serum osmolality was 274mmol/Kg, urine sodium was 75 mmol, urine osmolality was 361. Her SIADH resolved with fluid restriction of 1.2L daily.

Further investigations to confirm diagnosis of Scleroderma were carried out. Blood tests showed that ANA was positive with titre of >1:2560 and speckled pattern detected, positive anti-Ro60 antibodies, positive anti-Ro52 antibodies, raised ESR and gradually lowering of normocytic anaemia; but anti-Scl70 antibodies, anti-centromere antibodies and anti RNA polymerase III antibodies were negative. Rheumatoid factor, anti-CCP and anti-RNP antibodies were also negative. Vasculitic screen was unremarkable.

Investigations for hepatic fibrosis found a positive AMA suggesting an autoimmune etiology. Hepatitis panel was negative and iron studies were normal.

With respect to her pulmonary fibrosis, a high-resolution computed tomography of her chest found ground glass opacities and traction bronchiectasis in multiple lobes indicative of predominantly interstitial pneumonitis pattern. It also revealed a large pericardial effusion and extensive mediastinal lymphadenopathy were found. Tranthoracic echocardiogram showed fibrinous pericardial effusion with no signs of cardiac tamponade. Pericardiocentensis was not performed as the effusion was not large enough. CT chest abdomen pelvis with contrast was done and confirmed extensive mediastinal lymphadenopathy. However, no solid organ tumor was found.

The patient was started on 500 micrograms of colchicine BD. Repeat transthoracic echocardiogram after a week showed that the effusion size was stable. She was discharged home on colchicine.

Figures

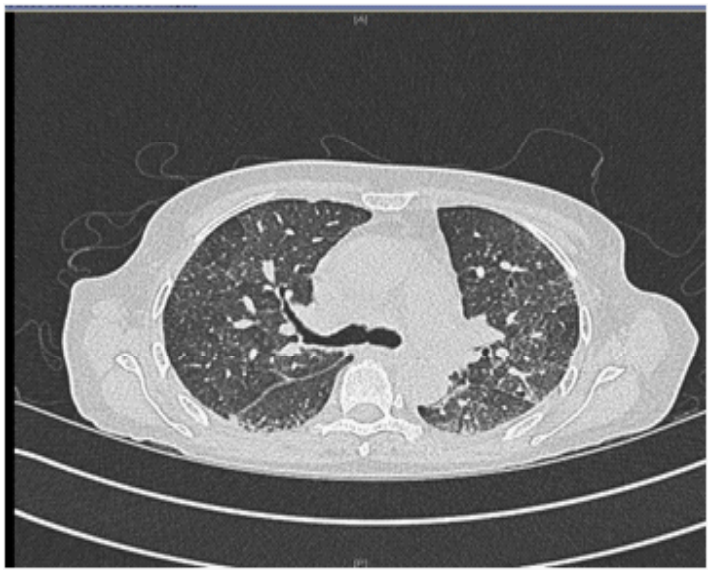

Figure 1

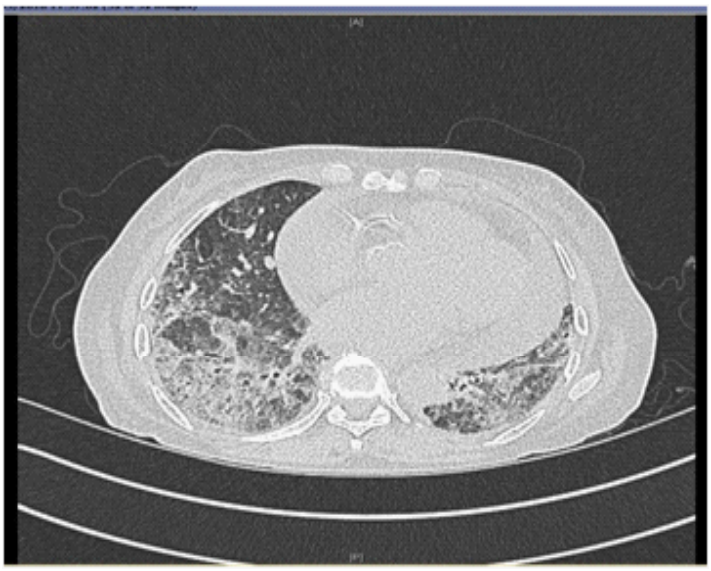

Figure 2

High resolution chest computed tomography, axial slices, showing bilateral lower lobe consolidations (right larger than left) on background of bibasal honeycombing (left more than right) , traction bronchiectasis and ground-glass change in multiple lobes. Figure 2 also show significant large pericardial effusion

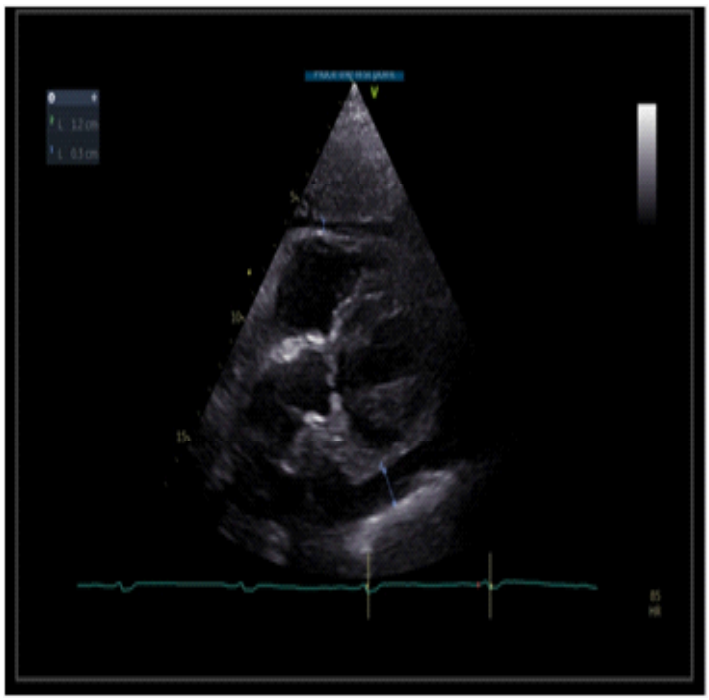

Figure 3

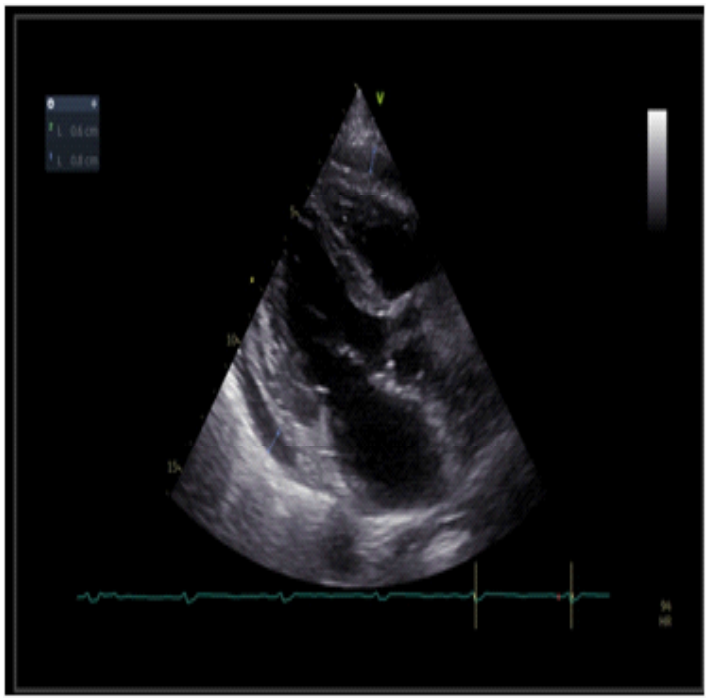

Figure 4

Figure 3 and 4 are Transthoracic Echocardiogram showing small global pericardial effusion without echocardiographic evidence of cardiac tamponade.

Discussion

We report a case with clinical features highly suggestive of scleroderma with multiorgan involvement. Scleroderma is a rare, systemic, clinically heterogeneous connective tissue disorder. It is accompanied by various degrees of tissue fibrosis and chronic inflammatory infiltration in numerous visceral organs, prominent fibroproliferative vasculopathy and humoral and cellular immune alterations [1,2]. Virtually all organs can be affected in scleroderma, particularly lungs, heart, kidneys and gastrointestinal tract, which is clearly shown in our patient who had pulmonary fibrosis, liver fibrosis and pericardial effusion probably due to scleroderma.

Serum autoantibodies are present in >95% of patients and are helpful biomarkers for establishing an early diagnosis [3]. However the highly specific antibodies including anti-topoisomerase I (anti-scl-70), anticentromere antibody and anti-RNA polymerase III antibody are not sensitive as these antibodies are negative in 20-50% of reported scleroderma cases [4,5,6]. Anti-RO antibodies that were positive in our case, on the other hand, can often be found in scleroderma patients with specificity of 50% [7,8].

Studies that look at clinical relevance of anti-RO antibodies in scleroderma also noted an association between anti-RO antibodies and interstitial lung disease. Anti-RO52 antibodies are independently associated with poor survival in patients with scleroderma in the presence of interstitial lung disease [9-12].

Gastrointestinal involvement in particularly abnormal esophageal motility is present in almost all patients with scleroderma. The decreased oral intake and dysphagia described in our case that contributed to recurrent hypoglycemia are secondary from esophageal dysmotility.

Cardiac involvement is one of the most serious visceral organ complications of scleroderma due to its associated high mortality rate [13]. According to the large European League Against Rheumatism (EULAR) Scleroderma Trials and Research (EUSTAR) database, 33(26%) out of 128 scleroderma related deaths were of cardiac origin [13].

Cardiac involvement may be due to either primary sclerosing process of the heart or secondary to involvement from disease of the lungs or kidneys [2]. Manifestation of cardiac complications of scleroderma can involve all structures of the heart and may present in the form of myocardial fibrosis, ischaemia, pericarditis, pericardial effusion/tamponade, arrhythmias, systolic and diastolic dysfunction. Cardiac involvement is reported in at least 15% of scleroderma patients, but up to 70% of patients were found to have myocardial involvement after autopsy [14,15]. Necropsy studies report 33%-72% of patients with scleroderma had pericardial involvement, only 7%-20% of patients reported symptoms of pericarditis or pericardial effusion [16,17]. Pericardial involvement in scleroderma has been described to present with two clinical variants, which are acute pericarditis and chronic pericardial effusion. Presence of pericardial effusion and congestive heart failure has been described to be associated with renal failure in the majority of the patients with scleroderma [18].

Although clinical presentations of pericardial involvement in patients with scleroderma can vary

from asymptomatic to right-sided heart failure and cardiac tamponade, most pericardial involvement in patients with scleroderma is subclinical. Pericardial effusion can only be detected with echocardiogram in 41% of patients [19]. Pericardial effusion in majority of patients with scleroderma is small and often happens after manifestations of the other systemic clinical features of scleroderma. Moderate pericardial effusion is the most commonly detected pericardial manifestations in scleroderma patients, whereas large pericardial effusion that usually led to cardiac tamponade is very rare [20].

Use of glucocorticoid is avoided in our case due to concern of scleroderma renal crisis. A retrospective case-control study of 110 patients with scleroderma renal crisis suggested use of glucocorticoid was associated with markedly increased risk [21]. Multiple studies also suggested that 60% of patients with scleroderma renal crisis have had prior recent exposure to glucocorticoids.

Conclusion

We are describing a case with clinical features that are highly suggestive of scleroderma. Although the initial presenting symptoms are non-specific symptoms with multiorgan involvement, it is important to think of seronegative scleroderma to allow early diagnosis of the disease. Positive ANA and positive anti-RO antibodies are suggestive of scleroderma even though the highly specific antibodies were negative.

References

1. Longo DL, Fauci AS, Kasper DI, et al. Harrison's principles of internal medicine. 19th edn. New York: McGraw-Hill Medical, 2014:chapter 382.

2. Itolikar S, Salagre S, Phatak S, Itolikar M. Recurrent cardiac tamponade in a young woman. Case Reports, 2013(nov29 1), bcr2013201472-bcr2013201472.

3. Kayser C and Fritzler MJ (2015) Autoantibodies in systemic sclerosis: unanswered questions. Front. Immunol.6:167

4. Reveille J, and Solomon D. (2003). Evidence-based guidelines for the use of immunologic tests: Anticentromere, Scl-70, and nucleolar antibodies. Arthritis & Rheumatism, 49(3), pp.399-412.

5. Kuwana, M., Okano, Y., Pandey, J., Silver, R., Fertig, N. and Medsger, T. (2005). Enzyme-linked immunosorbent assay for detection of Anti-RNA polymerase III antibody: Analytical accuracy and clinical associations in systemic sclerosis. Arthritis & Rheumatism, 52(8), pp.2425-2432.

6. Russo K, Hoch S, Dima C, et al. Circulating anticentromere CENP-A and CENP-B antibodies in patients with diffuse and limited systemic sclerosis, systemic lupus erythematosus, and rheumatoid arthritis. J Rheumatol 2000; 27:142.

7. Villalta, D., Imbastaro, T., Di Giovanni, S., Lauriti, C., Gabini, M., Turi, M. and Bizzaro, N. (2012). Diagnostic accuracy and predictive value of extended autoantibody profile in systemic sclerosis. Autoimmunity Reviews, 12(2), pp.114-120.

8. Montalvá, A., &Luque, A. (2014). Anti-SSA/Ro52 autoantibodies in scleroderma: Results of an observational, cross-sectional study. Clinical and Experimental Rheumatology,32. Retrieved from https://www.clinexprheumatol.org/article.asp?a=8265.

9. Gunnarsson, R., El-Hage, F., Aaløkken, T. M., Reiseter, S., Lund, M. B., Garen, T., &Molberg, Ø. (2015). Associations between anti-Ro52 antibodies and lung fibrosis in mixed connective tissue disease. Rheumatology,55(1), 103-108. doi:10.1093/rheumatology/kev300

10. Wodkowski, M., Hudson, M., Proudman, S., Walker, J., & Stevens, W. (2015). Monospecific anti-Ro52/TRIM21 antibodies in a tri-nation cohort of 1574 systemic sclerosis subjects: Evidence of an association with interstitial lung disease and worse survival. Clinical and Experimental Rheumatology,33.

11. Ferreira, J. P., Almeida, I., Marinho, A., Cerveira, C., & Vasconcelos, C. (2012). Anti-Ro52 Antibodies and Interstitial Lung Disease in Connective Tissue Diseases Excluding Scleroderma. ISRN Rheumatology,2012, 1-4.

12. Fischer A, Swigris JJ, Groshong SD, et al. Clinically significant interstitial lung disease in limited scleroderma: histopathology, clinical features, and survival. Chest 2008; 134:601.

13. Tyndall AJ, Bannert B, Vonk M, Airò P, Cozzi F, Carreira PE, et al. Causes and risk factors for death in systemic sclerosis: a study from the EULAR Scleroderma Trials and Research (EUSTAR) database. Ann Rheum Dis. 2010;69:1809 –15.

14. Steen VD, Medsger TA Jr. Severe organ involvement in systemic sclerosis with diffuse scleroderma. Arthritis Rheum. 2000;43:2437–44.

15. Follansbee WP, Miller TR, Curtiss EI, Orie JE, Bernstein RL, Kiernan JM, et al. A controlled clinicopathologic study of myocardial fibrosis in systemic sclerosis (scleroderma). J Rheumatol. 1990;17:656–62.

16. Byers, R., Marshall, D., & Freemont, A. (1997). Pericardial involvement in systemic sclerosis. Annals Of The Rheumatic Diseases, 56(6), 393-394.

17. Deswal A, Follansbee WP. Cardiac involvement in scleroderma. Rheum Dis Clin North Am. 1996;22:841–60.

18. Perez-Bocanegra, C., Fonollosa, V., Simeon, C., Candell, J., Solans, R., Gomez, A., &Vilardell, M. (1995). Pericardial tamponade preceding cutaneous involvement in systemic sclerosis. Annals Of The Rheumatic Diseases, 54(8), 687-688.

19. Gowda RM, Khan IA, Sacchi TJ, et al. Scleroderma pericardial disease presented with a large pericardial effusion—a case report. Angiology 2001;52:59–62.

20. Kitchong charoenying, P. (2013). Pericardial fluid profiles of pericardial effusion in systemic sclerosis patients. Asian Pacific Journal Of Allergy And Immunology, 31(4).

21. Steen VD, Medsger TA Jr. Case-control study of corticosteroids and other drugs that either precipitate or protect from the development of scleroderma renal crisis. Arthritis Rheum 1998; 41:1613.

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