

Case Report

Mixed connective tissue disease presenting with isolated pulmonary hypertension, and limited cutaneous sclerosis

Vaishal Kamlesh Shah*, Dhaval Dave, Rushabh Parikh, Divya Lala,
S.T. Nabar, Archana Bhate

Dr. D.Y Patil Medical College, Nerul, Navi Mumbai, India

Received: 20 July 2016

Accepted: 13 August 2016

*Correspondence:

Dr. Vaishal Kamlesh Shah,

E-mail: leo.spacewalker@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Mixed connective tissue disease (MCTD) was first recognized by Sharp and Colleagues in 1972 among a group of patients with overlapping clinical features of systemic lupus erythematosus (SLE), scleroderma and myositis, with the presence of distinctive antibodies against, what now is known to be U1ribonucleoprotein (RNP). We report an unusual case of a 29-year old female with MCTD characterized by the coexistence of signs, symptoms and immunological features of 3 defined autoimmune diseases isolated PHT, cutaneous sclerosis (SSc), hypothyroidism

Keywords: Mixed connective tissue disease, Hypothyroidism, Pulmonary hypertension, Limited cutaneous sclerosis

INTRODUCTION

The term limited cutaneous sclerosis refers to group of patients with demonstrable evidence of muscle necrosis with perivascular cell infiltration, following symptoms of muscle pain and severe tenderness. The presence of erythematous skin rash in few such cases makes the term dermatomyositis more appropriate. This constellation of symptoms is more often referred to polymyositis-dermatomyositis complex (PM-DM Complex).^{1,2} All such conditions presenting together with SLE and SSc is a rarepresentation of MCTD which is reported in the following case.

CASE REPORT

A 29 year old unmarried female, right handed person, student by profession, hailing from Navi Mumbai (India) was brought to the OPD with low grade fever since 8 days not associated with chills and high TLC count of 17,500. There was no history of cough, breathlessness, chest pain, loose stools, pain in abdomen, vomiting,

oliguria, burning micturition, vomiting as well as no history of DM/HTN/BA/IHD/CVA or Koch's /Koch's contact. And there was a history of hypothyroidism since 3 months, on T. Thyronorm (25ug) OD.

Clinically, she was febrile (99°F). The blood pressure was 130/80 mm Hg, the pulse 84 beats per minute, oxygen saturation 98% while she was breathing ambient air. On general examination she had fragile and rough skin, epidermal atrophy, and Sclerodactyl was present. Erythematous patches were seen over the fingers and palms. Other findings included reduced muscle mass and strength, symmetrical pain, stiffness and swelling of the metacarpophalangeal and proximal interphalangeal joints.

Dispersed raised red scaling plaques with central atrophy on the extremities, some of them having resolved causing hyper-pigmentation, atrophy and scarring, friable nails, brittle hair and clubbing was seen. Patches with excessive hair on the forearms and face. Intraoral findings include; fibrosis of the the tongue with reduced mobility, loss of papillae, generalized pallor and blanching of the mucous

membrane, and diffuse fibrosis of the buccal mucosa with loss of normal elasticity. Also, a diminished oral aperture with the interincisal distance of 2.3 cm was noted.



Figure 1: Sclerodactyly and swelling of metacarpophalangeal joints.



Figure 2: Cushingoid face with sparse madarosis and hyperpigmented patches.



Figure 3: Reduced oral aperture.

History of photosensitivity and bluish discoloration of the fingers on exposure to cold was present. RS – Air entry bilaterally equal; CVS- S1, S2 heard, S2 loud; P/A – Soft, Non tender; CNS – Power 5/5 in all limbs; DTR and superficial reflexes present B/L and No sensory peripheral neuropathy.

Her basic investigations were sent and the blood reports showed Hb-13.8g/dl; TLC-14,200; Plt -100000; MCV-96.0 fL; MCHC 31.9 pg. Electrolytes, RFT and urine routine report was normal. LFT showed mildly raised enzymes and hyperbilirubinemia (1.3); Calcium-8.3 mg/dl; ESR – 18 mm/hr; CRP raised-7.3 {Normal 0-6}; HHH – Negative. In view of persistent high TLC Counts, following investigations were sent: Bactec Blood Culture

was found to be normal and urine culture and sensitivity was *enterococcus spp.* ECG showed normal sinus rhythm with peak pulmonale p waves and T wave inversion in v1 to v6.

2 Decho was suggestive of: LVEF-55%; dilated right atrium and right ventricle, severe tricuspid regurgitation; PASP – 120 mm of hg, severe pulmonary hypertension; minimal pericardial effusion. Thyroid profile was WNL; abdominal sonography was within normal limits and in Chest X ray no abnormality was detected. Certain special investigations were sent which were found to be in the abnormal range and are as follows:

The immunological profile revealed a high ANA titer of 56.74 {Normal <20}, ANA Blot was sent. nRNP/Sm positive –

- Systemic lupus erythematosus
- MCTD (Sharp Syndrome)
- Systemic sclerosis
- Polydermatomyositis

Nucleosomes positive - Systemic lupus erythematosus. Cardio reference was taken in view of 2D echo findings and HRCT with Ct pulmonary Angio and LL AV doppler were advised. HRCT with CT Pulmonary Angio – Mild right and minimal left plural effusion; Mild cardiomegaly with dilatation of the right ventricle and right atrium and pericardial effusion. Mediastinal lymphadenopathy; B/L LL AV Doppler - Slow flow in bilateral posterior tibial artery; No evidence of DVT. PFT was advised with showed reduced DLCO and mild restrictive airway disease.

Skin biopsy was not advised as it would lead to non-healing ulcers. As per urine culture sensitivity reports, patient was started on T. Nitrofurantoin. Patient was treated with corticosteroids along with immunosuppressant. The patient was given antibiotics and started on T. Sildenafil. After about 1 month of intensive treatment, the evolution was excellent with significance remission of subjective clinical complaints and an improved general status. An improvement of laboratory parameters was also seen.

The long term prognosis is uncertain due to involvement of multi organic dysfunction. A close follows up of the patients' clinical condition, evolution and therapeutic adjustments are necessary.

DISCUSSION

The prevalence for MCTD it is probably around 10/100000. The female: male ratio is about 9:1. The term “connective tissue disease” (CTD) includes a large group of conditions characterized by considerable clinical diversity, heterogeneity and complexity. Although MCTDs can generally be clinically and serologically defined as distinct and separate entities, many patients

diagnosed with autoimmune rheumatic disease cannot be categorized easily into one of the established conditions.³ The existence of patients with signs, symptoms and certain laboratory test results suggestive of a systemic autoimmune disease but fulfilling more than one classification criteria for well-defined CTDs is a more and more common experience in clinical practice.

As opposed to some early stages of CTDs that might be undefined, unclassifiable or perhaps incomplete, with clinical elements and laboratory results suggestive of a systemic disease but not fulfilling criteria for well-defined CTDs, overlap syndromes define patients exhibiting enough features to meet the diagnosis of several CTDs at the same time. Thus, they “overlap” two or more diseases. Any CTD can be a partner in an overlap disorder.⁴

Mixed connective tissue disease (MCTD) is the prototype of an overlap syndrome. Since its original description by Sharp and collaborators in 1972, as an apparently unique syndrome combining clinical elements of SSc, SLE and PM, associated with antibodies to RNase sensitive extractable nuclear antigen, many clinical, serologic, and genetic studies have analysed the different aspects of this entity.⁵

The relevance of defining MCTD as a separate disease entity has been challenged, some authors considering it just a subset of SLE.⁶ Over the past 30 years there has been a continuing debate as to whether MCTD constitutes a “distinct clinical entity” and it still remains a controversial diagnosis.⁷

Most authors agree that MCTD is a distinctive entity rather than a haphazard association of clinical and serological features and that the presence of high titres of autoantibodies to U1RNP influences the expression of connective tissue disease in ways that are relevant to prognosis and treatment.⁸ In present patient, the clinical examination and the data obtained by investigations did not permit us to include this case in one of the typical, well established CTDs.

Autoimmune condition was then suspected on the basis of detailed clinical examination and the basic laboratory investigations which were done. A high level of suspicion in such cases can usually lead to prompt diagnosis of any CTD. Therefore after reviewing our case we found that our patient is suffering from a MCTD which presented with isolated pulmonary hypertension, and limited cutaneous sclerosis.

In a study on 118 patients, Caramaschi and collaborators evaluated the coexistence of additional autoimmune disease in a population of patients suffering from SSc. Their findings showed that approximately one third of patients affected by SSc developed one or more additional autoimmune diseases. Hence such patients must be carefully evaluated, both at the onset as well as

during follow up for the possible co- existence of multiple autoimmune disorders. We intend to undergo a close follow-up of the patient’s clinical status and to monitor repeatedly, the titers of the autoantibodies in order to obtain an overview of their dynamics.

In practice, the exact immunologic diagnosis makes a big difference because the detection of an autoantibody may help the clinician to anticipate particular complications and to evaluate the outcome of the patient. The identification of overlapping features in a given patient is also important because treatment needs to be directed specifically at some of these features.

Overall, the picture of overlap syndromes with respect to CTDs is complex and heterogeneous. Observer bias might play a role in disease classification, so the presence of specific autoantibody profiles is certainly a useful tool in the diagnosis evaluation of such patients.

CONCLUSION

Present patient presented with isolated pulmonary hypertension with Hypothyroidism with limited cutaneous sclerosis and was furthermore diagnosed to have MCTD which is a very rare incidence in itself. Early diagnosis and appropriate treatment forms the key for the management of this rare disabling condition.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

REFERENCES

1. Bennett RM, O'Connell DJ. Mixed connective tissue disease: a clinicopathologic study of 20 cases. *Semin Arthritis Rheum.* 1980;10:25.
2. Dubowitz V. Inflammatory myopathies. In: *Muscle disorders in childhood.* In the series of Major problems in clinical practice. Editors: A. J. Schaeffer, M. Markowitz, W. B. Saunders Co. Ltd., Philadelphia, London. 1978;16:202.
3. Lorber M, Gershwin ME, Shoenfeld Y. The coexistence of systemic lupus erythematosus with other autoimmune diseases: the kaleidoscope of autoimmunity. *Semin Arthritis Rheum.* 1994;24:105-13.
4. Jury EC, D'Cruz D, Morrow WJ. Autoantibodies and overlap syndromes in autoimmune rheumatic disease. *J Clin Pathol.* 2001;54:340-7.
5. Sharp GC, Irvin WS, Tan EM, Gould RG, Holman HR. Mixed connective tissue disease an apparently distinct rheumatic disease syndrome associated with a specific antibody to an extractable nuclear antigen (ENA). *Am J Med.* 1972;52:148-59.
6. Mercado U. Mixed connective tissue disease, or should it be Sharp's syndrome? Comment on the article by Farhey and Hess. *Arthritis Care Res.* 1999;12:227.

8. Venables PJ. Mixed connective tissue disease. *Lupus*. 2006;15:132-7.
9. Maddison PJ. Mixed connective tissue disease: overlap syndromes. *Baillieres Best Pract Res ClinRheu- matol*. 2000;14:111-24.

Cite this article as: Shah VK, Dave D, Parikh R, Lala D, Nabar ST, Bhate A. Mixed connective tissue disease presenting with isolated pulmonary hypertension, and limited cutaneous sclerosis. *Int J Res Med Sci* 2016;4:4226-9.