Case Report

A case of autoimmune hypothyroidism presented as overlap syndrome of mixed connective tissue disorder

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INTRODUCTION

Mixed connective tissue disease (MCTD) is an autoimmune disorder which is characterized by features of other connective tissue diseases such as systemic sclerosis, systemic lupus, and polymyositis along with higher levels of anti U1-ribonucleoprotein (anti-U1RNP) antibody and antinuclear antibody (ANA) positive with speckled pattern being common.\(^1\) It was more prevalent in women than men and the mean age at diagnosis was 37.9 years. The most common organ systems to be involved were musculoskeletal system, skin and mucosa, gastrointestinal and hepatobiliary systems. Pulmonary artery hypertension (PAH) was found to be major cause of mortality in MCTD and prognosis becomes poor. Early diagnosis and treatment is necessary to prevent pulmonary complications.

CASE REPORT

A 39 year old female presented to medicine outpatient (OPD) with complaints of multiple joint pains involving both wrist, ankles, phalanges since 2 years. It was associated with joint swelling and morning stiffness of fingers. She also had dryness of skin, loss of appetite, constipation, difficulty in swallowing and dyspnea on exertion since last 2 months. Considering the joint pains an antinuclear antibody (ANA) was sent. She turned out to be RNP, Sm, Ro 52, Mi-2 positive. Anti-CCP, rheumatoid factors (RA), Raynaud’s phenomenon all were positive. Rheumatologist opinion was taken and she was diagnosed as mixed connective tissue disorder with hypothyroidism. Patient was successfully treated with immunosuppressants and supportive measures and responded well to tablet methotrexate, prednisone, nifedipine and hydroxychloroquine. Our patient had one major and 3 minor criteria: anti RNP antibody positive, Raynaud’s phenomenon, swollen fingers and synovitis. Thus, diagnosed as mixed connective tissue disease.

Keywords: Mixed connective tissue disorder, Anti RNP antibody, Raynaud’s phenomenon
presentations were initially attributed to hypothyroidism but thyroid function was later found to be under control and patient was reviewed. Patient was found to have positive Raynaud’s phenomenon. Systemic examination revealed no abnormality. Routine lab investigations were normal. C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and rheumatoid arthritis (RA) was positive. Anti-cyclic citrullinated peptide (anti-CCP) was positive and ANA blot was also positive for ribonucleoprotein (RNP), Smith (Sm), Ro 52, and Mi-2 antibodies. Chest x ray and x ray of hand was normal.

Figure 1: Raynaud’s phenomenon.

Figure 2: Swollen joints.

Figure 3: Barium swallow showing minimal persistent dilatation with impaired peristaltic wave seen in thoracic oesophagus.

Barium swallow was done suggestive of minimal persistent dilatation with impaired peristaltic wave seen in thoracic oesophagus. High resolution computed tomography (HRCT) thorax showed multiple prominent pre tracheal, para tracheal, pre vascular and subcarinal lymph nodes largest measuring 17×14 mm, multiple prominent bilateral axillary lymph nodes (LN) largest measuring 22×18 mm. Rheumatologist opinion was taken and patient diagnosed as a case of MCTD. The patient was treated with tablet methotrexate 15 mg, Tablet folic acid 5 mg, tablet prednisone 5 mg, tablet nifedipine 10 mg, tablet etoricoxib 90 mg and tablet hydroxychloroquine 200 mg and was discharged with regular follow up.

Figure 4: HRCT thorax showed multiple prominent pre tracheal, para tracheal, pre vascular and subcarinal lymph nodes largest measuring 17×14 mm, multiple prominent bilateral axillary LN largest measuring 22×18 mm.

DISCUSSION

MCTD was initially described by Sharp et al. It was explained as a chronic immune-mediated disorder which had overlapping features of systemic lupus erythematosus (SLE), scleroderma, and polymyositis. Cutaneous manifestations of MCTD may be the presentation of the disease. MCTD is now considered as a separate entity the characteristic feature of which is the presence of higher levels of antibodies against U1 RNP complex. The U1 snRNP is a target of autoreactive B and T cells in MCTD. Patients with MCTD have been found to have a higher incidence of Raynaud’s phenomenon and pulmonary hypertension with less severe involvement of kidney’s which include membranous or mesangioproliferative glomerulonephritis and have a better overall prognosis.

Individuals who express human leukocyte antigen (HLAs), HLA-DR4 or HLA-DQB1, are genetically predisposed. Specific nature of HLA associations that occur in relationship with MCTD differ with the ethnicity of populations studied and it may account in part to the variability of cutaneous features. MCTD more common among woman. The most common symptoms were arthritis and Raynaud’s phenomenon.

Raynaud’s phenomenon involves intermittent blanching followed by cyanosis and rubor on exposure to cold and often characterizes as earliest manifestations of MCTD. Nedumaran et al documented all patients of MCTD suffering from this phenomenon in their study.

Patients with MCTD can have other cutaneous features such as photosensitivity, livedoid vasculitis and
In the study by Furst et al administration of HCQ was associated with best clinical response. Our patient responded well with prednisolone, methotrexate and hydroxychloroquine.

CONCLUSION

We diagnosed MCTD in patient with pre-existing hypothyroidism on the basis of 1 major and 3 minor criteria of presence of anti RNP antibody, synovitis, Raynaud’s phenomenon and swollen hands respectively. Patient responded to methotrexate, prednisolone and hydroxychloroquine and is on regular follow up.

Recommendations

MCTD has to be looked up in patients with multi-systemic involvement along with rheumatological diseases where clinical features may overlap. Every patients with hypothyroidism always have a look for other autoimmune associations. Though MCTD is rare autoimmune disorder delayed diagnosis may be lead to pulmonary complications such as pulmonary artery hypertension.

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REFERENCES

1. John KJ, Sadiq M, George T, Gunasekaran K, Francis N, Rajadurai E, et al. Clinical and Immunological Profile of Mixed Connective Tissue Disease and a Comparison of Four Diagnostic Criteria. Hindawi Int J Rheumatol. 2020;9692030.

2. Sharp GC, Irvin WS, Tan EM. 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.

3. 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(2):148-59.

4. Bennett RM, O’Connell DJ. Mixed connective tissue disease: a clinicopathologic study of 20 cases. Sem Arthr Rheumat. 1980;10(1):25-51.

5. Kattah NH, Kattah MG, Utz PJ. The U1-snRNP complex: Structural properties relating to autoimmune pathogenesis in rheumatic diseases. Immunol Rev. 2010;233:126-45.

6. Bull TM, Fagan KA, Badesch DB. Pulmonary vascular manifestations of mixed connective tissue disease. Rheumat Dis Clin North Am. 2005;31(3):451-64.

7. Hajas A, Szodoray P, Nakken B. Clinical course, prognosis, and causes of death in mixed connective tissue disease. J Rheumatol. 2013;40(7):1134-42.

8. Kitridou RC, Akmal M, Turkel SB, Ehresmann GR, Quismorio FP, Massry SG. Renal involvement in mixed connective tissue disease: a longitudinal clinicopathologic study. Sem Arth Rheum. 1986;16(2):135-45.

9. Sen S, Sinhamahapatra P, Choudhury S, Gangopadhyay A, Bala S, Sircar G, et al. Cutaneous Manifestations of Mixed Connective Tissue Disease: Study from a Tertiary Care Hospital in Eastern India. Indian J Dermatol. 2014;59(1):35-40.

10. Swartz RA. Hematologic manifestations of mixed connective tissue disease. Available at: http://emedicine.medscape.com. Accessed on: 26 August 2020.

11. Grader-Beck T, Wigley FM. Raynaud's phenomenon in mixed connective tissue disease. Rheum Dis Clin North Am. 2005;31:465-81.

12. Burdt MA, Hoffman RW, Deutscher SL, Wang GS, Johnson JC, Sharp GC. Long-term outcome in mixed connective tissue disease: Longitudinal clinical and serologic findings. Arthritis Rheum. 1999;42:899-909.

13. Pope JE. Other manifestations of mixed connective tissue disease. Rheum Dis Clin North Am. 2005;31:519-33.

14. Ciang NC, Pereira N, Isenberg DA. Mixed connective tissue disease-enigma variations? Rheumatology (Oxford). 2017;56(3):326-33.
15. Aringer M, Smolen JS. Mixed connective tissue disease: what is behind the curtain? Best Pract Res Clin Rheumatol. 2007;21:103749.

16. Kasukawa R, Tojo T, Miyawaki S. Preliminary diagnostic criteria for classification of mixed connective tissue disease. Mixed connective tissue disease and antinuclear antibodies. Amsterdam: Elsevier. 1987:4147.

17. Gendi NS, Welsh KI, Van Venrooij WJ, Vancheeswaran R, Gilroy J, Black CM. HLA type as a predictor of mixed connective tissue disease differentiation. Ten-year clinical and immunogenetic followup of 46 patients. Arthritis Rheum. 1995;38:259-66.

18. Sharp GC. Diagnostic criteria for classification of MCTD. Mixed connective tissue disease and antinuclear antibodies. Amsterdam: Elsevier. 1987:2332.

19. Alarco´n-Segovia D, Villareal M. Classification and diagnostic criteria for mixed connective tissue disease. Mixed connective tissue disease and antinuclear antibodies. Amsterdam: Elsevier. 1987:3340.

20. Kahn MF, Appeboom T. Syndrome de Sharp. Les Maladies Systemiques. Paris: Flammarion. 1991:3:54556.

21. Narsimulu G, Vara PIR. Mixed connective tissue disease and overlap syndromes. API textbook of medicine. 9th edition. 2003;1877.

22. Amoura Z, Arnaud L. Mixed connective tissue disease. Orphanet. 2009. Available at: http://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=EN&Expert=809. Accessed on: 27 July 2020.

23. Lundberg IE. The prognosis of mixed connective tissue disease. Rheum Dis Clin N Am. 2005;31:53547.

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