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Research Article

A CASE REPORT ON MIXED CONNECTIVE TISSUE DISORDER AND SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) WITH HYPOTHYROIDISM

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Abstract

Mixed connective tissue disease (MCTD) was first defined in 1972 as a condition characterized by features of systemic lupus erythematosus (SLE), systemic sclerosis (SSc), polymyositis/dermatomyositis, and rheumatoid arthritis (RA) as well as the presence of high-titer anti-U1small nuclear anti-ribonucleoprotein (anti-RNP) antibodies. A 32-year- old female housewife presented with a complaint of itching over whole body in the past 2 months, generalized weakness and Arthralgia (Joint pain) with difficulty in standing from sitting position in the last 1.5 years, generalized edema with a four-months. Particularly, in this case report systemic sclerosis, systemic lupus erythematosus and polymyositis suggests that patient is suffering from mixed connective tissue disorder. The patient was also diagnosed on the basis of clinical pattens. RA33-positive group showed major proportions of SLE- associated antibodies and low level of serum complement components. Generally, patients with MCTD are given NSAIDs to relieve symptoms and immunosuppressants to depress autoimmune reaction.

Keywords: Mixed connective tissue disorder (MCTD), systemic lupus erythematosus (SLE), rheumatic arthritis (RA), hypothyroidism.

INTRODUCTION

Mixed connective tissue disease (MCTD) was first defined in 1972 as a condition characterized by features of systemic lupus erythematosus (SLE), systemic sclerosis (SSc), polymyositis/ dermatomyositis (PM/DM), and rheumatoid arthritis (RA) as well as the presence of high-titer anti-U1small nuclear (sn) anti-ribonucleoprotein (anti-RNP) antibodies.[1]Raynaud's phenomenon, arthralgias, swollen joints, oesophageal dysfunction, muscle weakness, and sausage-like fingers are the most common clinical manifestations of mixed connective disease, along with the presence of anti-ribonucleoprotein (RNP) antibodies[2]. Systemic lupus erythematosus (SLE) is a prototypic autoimmune disease characterised by the production of antibodies against cell nucleus components in conjunction with a wide range of clinical manifestations[3]. Lupus can affect nearly every organ, most notably and fatally, the kidney and the central nervous system. Individual patients' severity can range from mild cutaneous involvement to severe organ damage, and the outcome can range from long-term remission to death[4].

CASE REPORT

A 32-year- old female housewife presented with a complaintof itching over whole body in the last 2 months, generalized weakness and Arthralgia (Joint pain)with difficulty in standing from sitting position in the last 1.5 years, generalized edema with a four-months. History of low-grade fever with chills and rigors x 4-5 days which was relieved on medication,Fatigue with a three-months, Productive whitish coughin the past 8-13 days and B/L ear itching for 8 days(ear discharge, ear bleeding, tinnitus, vertigo, facial palsy, nasal blockage, nasal discharge including throat pain.

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She also had decreased in appetite and Backache with a three-months, burningmicturition 1-2 weeks. She was bedridden since1 month. Otherwise, she had no family history of autoimmune disease.

Physical Examination

Upon Physical examination proximal muscle weakness noted, Vasculitis spots were observed, and non -scarring Alopecia was observed over scalp along with she had a hair loss since1.5 years, Oral cavity bluish telangiectasia noted. Generalized tenderness in B/L lower limb noted. The skin showed dryness, ulcers and lesion all over the body(ill-defined exfoliations positive B/L, U/L, L/L and buttocks). Severe pallor, mild icterus, changes in nails and pedal edema noted. On General Examination the patient has normal temperature, RS: AEBE clear with Harsh sound positive, CVS: S1S2 (Positive) with no murmur noted. ECG- T inversion in V1 along with QTc- 323

Vitals

Blood pressure (BP): 80/60 mm of HG, Respiratory Rate (RR): Normal; Pulse Rate (PR): 106 beats/ minute, RBS: 126 mg/dl; Oxygen Saturation (SpO2): 98%.

Patient's history of present illness

- Past History-Patient was asymptomatic before 1.5 years then she develops typhoid and it became worsened. She went to multiple private hospital where, she taken 6 PCV injection transfer 3 months back. MCTD (Mixed connective tissue disorder), Myositis on plus steroid therapy since 1.5 years. She also had diagnosed with hypothyroidism 20 days back and on medication Tab. THYROXIN (50 mcg).
- Family history-No family history of autoimmune disease.
- Diet history – Mixed diet.

Laboratory findings:

Table.1 Laboratory Table

Parameters	Obtained Value	Normal range	Interference
Hemoglobin	8.70 gm/dl	11.1-14.1 g/dl	Decreased
RBCs	2.99 x 10 ^6 /cmm	3.9-5.1 x10 ^6 /cmm	Decreased
PCV	27.20%	34-40%	Decreased
MCV	91.00 fL	75-87fL	Normal
MCH	29.10 pg	24-30pg	Normal
MCHC	32.00 gm/dl	29-37g/dl	Normal
RDWcv	18.90%	11.6 – 13.7 %	Increased
WBCs	8300 /cmm	4000-10000 / cmm	Normal
Platelets	299000 / cmm	150000- 410000 / cmm	Normal
Neutrophils	88.00%	40-80%	Neutrophilia
Lymphocytes	10.10%	20-40%	Lymphocytopenia
Monocytes	1.00%	2-10%	Monocytopenia
Eosinophils	1.00%	1-6%	Normal
ANC (Absolute Neutrophil Count)	8096.00 /cmm	1800-7800/ cmm	Increased
ANA (Anti-Nuclear Antibodies)	3.7	Positive: >1.5	Increased
S. Sodium (NA);	128.00 mEq/L	135-145mEq/L	Decreased
S. Potassium (K);	2.80 mEq/L	3.5-5mEq/L	Decreased
S. Urea	12.00 mg/dl	14-40 mg/dl	Decreased
LDH	105.00 U/L	230-460 U/L	Decreased
S.C Reactive Protein	32.70 mg/L	0-6 mg/ L	Increased
S.Total Protein(TP);	5.70 gm/dL	6-8 gm/dL	Decreased
S.Albumin (ALB);	2.40 gm/ dL	3.2-5 gm/ dL	Decreased
S.Globulin	3.30 gm/ dL	2.3-3.6 gm/ dL	Normal
S. A/G Ratio	0.73	1-2	Increased
S.Ferritin	1052.00 ng/ ml	10-120 ng/ml	Increased
S. Alkaline Phosphate (ALP);	191.00 U/L	28-111 U/L	Increased
T3	1.134 ng/ml	0.45-1.78	Normal
T4	6.325 ug/dl	4.60-12.23	Normal
TSH	16.14ug/ml	0.34-6.0	Increased
RA(Rheumatoid Factor)	26.0 IU/ml	Upto-20 IU/ml	Positive

Ana profile by immunoblot

Table.2 ANA Profile

Antigen	Quantitative result (RU/ ml)	Ratio	Quantitative result
RNP/Sm	11	1.0	Positive
Sm	4	0.4	0
Ro-52	1	0.1	0
SS-B	2	0.2	0
Sci-70	0	0.0	0
PM-Sci100	5	0.4	0
Centromere B	4	0.4	0
PCNA	2	0.1	0
Rib- P Protein autoantibodies	104	9.4	Positive+++
AMA-M2	4	0.4	0
Control(Co)	62	-	Positive+++

Table 3. Explanation

Quantitative result (RU/ ml)	Ratio	Quantitative result	Explanation
0-5	0.00-0.45	0	Negative
6-10	0.46-0.91	(+)	Borderline
11-25	0.92-2.27	+	Positive
26-50	2.28-4.55	++	Positive
51-265	4.56-23.27	+++	Strong Positive

Interpretation: ANA immunoblot is strong positive

Diagnostic tests

- C3 Complement – 62.65 mg/ dl decreased in level noted.
- C4 Complement – 16.28 mg/ dl was normal.
- Mild Anisocytosis, Mild Microcytic Hypochromic RBCs are seen.
- Chest X-ray PA view – Bilateral Bronchitis noted.
- ANA IFA: Cytoplasmic Patterns are seen.
- USG: ABDOMEN AND PELVIS: Mild hepato - splenomegaly noted.

Final diagnosis: K/C/O (MCTD) Mixed connective tissue disorder (Systemic Lupus Erythematosus)on Pulse Steroid therapy with Hypothyroidism

Plan of action:

Table 4. Supportive Management Chart

Sr.No.	Drug	Dose	Route	Frequency	days
1)	Inj. Optineuron +Normal saline	1 Ample + 500ml	IV	--	7 days
2)	Tab. Levocetrizne	5mg	PO	OD	5 days
3)	Tab. Folic acid	5mg	PO	OD	7 days
4)	Tab. Thyronorm	50mg	PO	1 ODBBF	
5)	Inj. Pantoprazole / Ondensteron	1 Ample	IV	12/8 hrly	7 days
6)	Tab. Calcium	500	IV	BD	
7)	Vitamin D3 Sachet	----	PO	Once a week	
8)	Tab. Prednisone	5mg	PO	9 tab. In morning with milk	
9)	Tab. Hydroxychloroquine (HCQ)	200 mg	PO	OD	
10)	Inj. Tramadol	1 Ample	IV	8 hrly (SOS)	3 days
11)	Syp. Citralkar (Disodium hydrogen citirate)	2TDS	PO	TDS	7 days
12)	Syp. Potclore (Potassium chloride)	2TDS	PO	TDS	7 days
13)	Inj. KCL + Normal Saline	2 Ample +100 ml	IV	10 cc/ hr	7 days
14)	Tab. Nitrofurantoin	100mg	PO	QID	7 days
15)	Syp. Laxose (Lactulose)	30 cc	PO	OD	7 days
16)	Neb. Duolin/ budecort		Nasal	8/12hrly	
17)	Inj. MPSS (methylprednisolone)	125mg	I V	OD	
18)	Cap. Augmentin	625mg	PO	TDS	7 days
19)	Inj. MGSO4 + Normal Saline	2Ample + 100ml	IV	--	
20)	Tab. MBSON	SL	PO	OD	7 days
21)	Tab. Paracetamol	500mg	PO	BD	5 days
22)	White soft Paraffin			LBAD	7 days
23)	Deboner Ear Drops	5ml		2-2-2-2	7 days

DISCUSSION

Systemic sclerosis, systemic lupus erythematosus (SLE), and polymyositis are all features of mixed connective tissue disease (MCTD), MCTD which became the first rheumatic disease syndrome with antibodies to RNAse sensitive extractable nuclear antigen. Raynaud's syndrome, swelling in hands, sclerodactyly, arthritis or arthralgia, oesophageal hypomobility, inflammatory polymyositis, and interstitial lung are all clinical manifestations that are frequently present.[5,6] When a patient exhibits symptom of SLE, arthralgia, and has positive RNP reactive antibodies, the diagnosis of MCTD would be considered to be probable.[7]We have described a rare case of a female Patient with MTCD with Hypothyroidism in our investigation. She was asymptomatic before 1.5 years then she develops typhoid and it became worsened. The Diagnosis was confirmed based on clinical patterns described that would apply to our patient as she has high titres of precipitating RNP reactive antibodies, positive Rib- P Protein autoantibodies, Lymphocytopenia, ANA positive and various clinical features of SLE such as non -scarring Alopecia, Oral cavity bluish telangiectasia, fever, decreased in appetite and Backache, and arthralgia. A study was conducted to examine the clinical relevance of anti-RA33 in CTDs, particularly systemic lupus erythematosus (SLE). The RA33-positive group showed greater proportions of SLE-associated antibodies, SLE patients with a high disease activity, and lower levels of serum complement components.[8]It would fit to our patient. She had higher percentages of SLE-related antibodies and had lower levels of serum complement components. For the treatment of MCTD, Symptom-relieving drugs like NSAIDS can relieve MCTD patients with inflammatory arthritis. In SLE, antimalarial drugs like hydroxychloroquine can be effective[9]. In this case report, Patient was given Tab. Hydroxychloroquine which suppressing activation of Toll- like receptors, these receptors play a significant role in autoimmune disease. Futhermore, Our patient was given Corticosteroids and Glucocorticosteriod such as prednisone and Inj. MPSS methylprednisonle which can reduce inflammation, aid in preventing the immune system from attacking healthy tissues and articular flare-ups.

The patient also received Thyronom (Levothyroxine), a synthetic Thyroid hormone used to treat hypothyroidism. Deboner Ear Drops, which treats bacterial and fungal ear infections, were also given to the patient. These drops are a combination of medications, Beclometasone (a corticosteroid), Clotrimazole (an antifungal), Lidocaine (a local anaesthetic), and Neomycin (an antibiotic).Upon Chest X-ray examination– Bilateral Bronchitis noted, patient was given nebulizer (Duolin Respules) is a combination of two medication Levosalbutamol is a bronchodilator while, Ipratropium is an anticholinergic and Inhalational Corticosteriod such Budesonide (Budecort)to treat Bronchitis.For burning micturition Tab. Nitrofurantoin, Tab. paracetamol for fever, various form of supportive therapy, including (MBSON) Methylcobalamin was also administered in order to treat and prevent vitamin B12 deficiency. Patients with MCTD frequently have inadequate levels of vitamin D.[10]

Conclusion

Mixed connective tissue disease (MCTD) is a rare systemic autoimmune disease. Particularly, in this case report systemic sclerosis, systemic lupus erythematosus and polymyositis suggests that patient is suffering from mixed connective tissue disorder. The patient was also diagnosed on the basis of clinical pattens. RA33- positive group showed major proportions of SLE- associated antibodies and low level of serum complement components. Generally, patients with MCTD are given NSAIDs to relieve symptoms and immunosuppressants to depress autoimmune reaction. The patient was given anti-malarial drug to suppress toll-like receptors and give effective result.

REFERENCES

1. Ortega-Hernandez OD, Shoenfeld Y. Mixed connective tissue disease: an overview of clinical manifestations, diagnosis and treatment. *Best Practice & Research Clinical Rheumatology.* 2012 Feb 1;26(1):61-72.
2. Tani C, Carli L, Vagnani S, Talarico R, Baldini C, Mosca M, Bombardieri S. The diagnosis and classification of mixed connective tissue disease. *Journal of autoimmunity.* 2014 Feb 1; 48:46-9.

3. Mok CC, Lau CS. Pathogenesis of systemic lupus erythematosus. *Journal of clinical pathology.* 2003 Jul 1;56(7):481-90.
4. Borchers AT, Naguwa SM, Shoenfeld Y, Gershwin ME. The geoepidemiology of systemic lupus erythematosus. *Autoimmunity reviews.* 2010 Mar 1;9(5):A277-87.
5. Venables PJ. Mixed connective tissue disease. Lupus. 2006;15(3):132-137. doi:10.1191/0961203306lu2283rr
6. Withrington RH, Seifert MH. Hypothyroidism associated with mixed connective tissue disease and its response to steroid therapy. *Ann Rheum Dis.* 1981 Jun; 40(3):315-6. doi: 10.1136/ard.40.3.315. PMID: 7247477PMCID: PMC1000771.
7. Liang R, Landry I, Saliaj M. Systemic Lupus Erythematosus vs. Mixed Connective Tissue Disease Disguised As Scabies. Cureus. 2022 Mar 29;14(3):e23621. doi: 10.7759/cureus.23621. PMID: 35505737; PMCID: PMC9053354.
8. Lu W-Y, Hong X-P, Xie J-Y, et al. Clinical significance of anti-rheumatoid arthritis 33 antibody in patients with systemic lupus erythematosus. *Journal of Investigative Medicine*. 2023;0(0). doi:10.1177/10815589221150643
9. Lozada CJ, Hoffman RW. Management of mixed connective tissue disease. *International Journal of Clinical Rheumatology.* 2008 Aug 1;3(4):357.
10. Agota Hajas; Janos Sandor; Laszlo Csathy; Istvan Csipo; Sandor Barath; Gyorgy Paragh; Ildiko Seres; Gyula Szegedi; Yehuda Shoenfeld; Edit Bodolay (2011). *Vitamin D insufficiency in a large MCTD population. , 10(6), 317–324.* doi:10.1016/j.autrev.2010.11.006

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