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Case Report

Mixed Connective Tissue Disease with Acute Gastroenteritis and Hypothyroidism: A Case Report

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Abstract:

Mixed Connective Tissue Disease (MCTD) is a rare systemic autoimmune disease and is the least common connective tissue disorder. The presence of high titers of serum anti-U1 small nuclear Ribonucleoprotein along with features of SLE, Systemic Sclerosis, Dermatomyositis and Rheumatoid Arthritis is typical of the disease. We present a case of a 38 year old female patient, a known case of hypothyroidism, who presented with symptoms indicative of gastroenteritis but on further evaluation with appropriate investigations and based on the diagnostic criteria was found to be suffering with MCTD and was treated accordingly. We discuss the prognosis and the importance of early diagnosis to reduce the morbidity and mortality associated with pulmonary arterial hypertension.

Keywords: Connective Tissue Disease, Scleroderma, Myositis

Introduction:

Mixed Connective Tissue Disease (MCTD) is a rare systemic autoimmune disease which was described by Sharp et al as a syndrome with a combination of features resembling SLE, Systemic Sclerosis, Dermatomyositis/Polymyositis and Rheumatoid Arthritis. [1]
It was the first overlap syndrome to be associated with high titers of a distinct auto-antibody which was later found to be anti-U1 snRNP antibody. Patient may initially present with non-specific symptoms of fatigue, arthralgia, myalgia, fever, Reynaud's phenomenon, in which case it is initially diagnosed as undifferentiated connective tissue disease which may overtime develop into MCTD. [2]
It is predominantly seen in females with female to male ratio of 16:1. [3]
Mean age of onset in adults is 35yrs and children is 10yrs, however it has a lower incidence when compared to individual connective tissue diseases. [3]
In spite of there being no generally accepted criteria for classification of MCTD, the presence of pulmonary disease is suggestive of a distinct disease entity. [4]

CASE REPORT:

A 38 year old female presented to the outpatient department with multiple episodes of loose stools, nausea, fever without chills and rigors and non productive cough since 3 days. She is a known case of hypothyroidism and is on medication with T. Levothyroxine 62.5 mcg once daily. On enquiry, patient revealed that she had a previous history of painful swelling and stiffness involving the elbows followed by wrist and MCP joints since 1 year. She also complained of dragging type of pain in both thighs since 1 year. She was unable to squat and get up and she could only walk for a short distance. On further enquiry, patient revealed that she had a history of tightening of the skin over her face, surrounding the mouth, chest, abdomen, upper and lower limbs with loss of hair, dryness of skin, difficulty in opening the mouth with no difficulty in swallowing. She had a decrease in appetite with progressive loss of weight since 1 year. Additionally she mentioned that she developed whitish discoloration with tingling sensation over fingertips on exposure to cold water which was relieved on rewarming since 1 year and pruritus since 1 year which resolved spontaneously 1 month ago. No history of breathlessness or chest pain and normal frequency of micturition. No history of dryness of the eyes or mouth. No family history of similar complaints.
On examination, the patient was thin built with an emaciated appearance with a BMI of 11.2 with a temperature of 37˚C, PR- 100 beats/minute; all the peripheral pulses were palpable with normal volume and character, BP- 100/60 mm of Hg.
Skin was smooth, shiny, dry and taut with diffuse alopecia. Skin over the face was fixed to the underlying tissue with loss of wrinkles and could not be pinched associated with flattening of the nasolabial folds (Figures 1). Mouth orifice was small with difficulty in opening the mouth but oral cavity was normal (Figures 2).There were areas of

pigmentation and depigmentation of the skin (figure 3). There were ulcerations over the elbow, wrist and PIP joints and diffuse wasting of muscles (Fig 4)

On examination of her central nervous system, power in the flexors and extensors of her right and left hips were ⅗, bilateral knees ⅘ and bilateral ankle joints 5/5. Power in both her upper limbs was normal. Higher mental functions, cranial nerves, tone, reflexes, sensory system and cerebellar functions were normal. Findings on examination of the abdominal, cardiovascular and respiratory systems were unremarkable.

Investigations showed that CBP was normal with Hb - 11.3 g/dl, PLT - 300000/microL, WBC Count - 5300 cells/ cu.mm, CUE was normal, RFT - normal. Serum LDH - 540 U/L, Serum Creatine Kinase- 939 U/L, ESR - 50 mm/hr. TSH - 5.89 micro IU/ml in October 2018 and TSH - 9.19 micro IU/ml with T3 - 1.35 ng/ml and T4 - 6.21 mcg/dl. CRP - positive - 2.4 mg/dl. Serological tests for HIV, Hepatitis B and C were non reactive.

Serum RA factor was 132.9 IU/ml, ANA panel showed the serum was strongly positive for U1 snRNP and negative for SCL 70, Jo 1, SSA (Ro) and SSB, SmD1, PCNA, dsDNA, Nucleosomes, Histones.

Qualitative test for Anti-nuclear antibody - IFA-HEP2 was positive with fine granular pattern and titer of 1:40. Anti-CCP and Anti-TPO antibody levels were negligible.

Two dimensional echocardiogram showed mild tricuspid regurgitation and mild pulmonary arterial hypertension with ejection fraction of 68%. X Ray Chest was unremarkable (Fig.11). Patient was unable to perform the pulmonary function test satisfactorily. Barium swallow (Figure 6) was normal.

Skin Biopsy revealed thinned out epidermis with pigment incontinence, dermis including papillary dermis showing sclerosis which is also surrounding the sweat glands and extending into the subcutaneous tissue with mild inflammatory infiltrate and pigment at places, with reduction in number of sweat and sebaceous glands (Figures 7, 8).

A diagnosis of Mixed Connective Tissue Disease was made with overlap syndromes of Systemic Sclerosis, Rheumatoid Arthritis and Myositis.

DISCUSSION:

The patient's initial complaints were suggestive of acute gastroenteritis. In spite of being a known case of hypothyroidism with elevated TSH levels which were being normalized on T. Levothyroxine, she still presented with progressive loss of weight and loss of appetite pointing to an underlying etiology. Her diet was monitored on a day to day basis with significant improvement in her appetite and gain in weight after treating for gastroenteritis.

The presence of previous history of arthritis, proximal myositis, Reynaud's phenomenon, microstomia and tightening of skin with chronic ulceration correlated with the physical findings of taut, shiny, dry skin with alopecia, limitation of movements, low power in the flexors and extensors of her hips and knees with stiffness of her joints points to overlap syndromes of Systemic Sclerosis, Myositis and Rheumatoid Arthritis collectively called Mixed Connective Tissue Disease.

The diagnosis of Mixed Connective Tissue Disease was made on the basis of Alarcon Segovia's Criteria with elevated Anti-U1snRNP antibodies and 4 of the 5 clinical criteria i.e. synovitis, myositis as proven by elevated serum creatine kinase- 939 U/L, Reynaud's phenomenon, sclerodactyly ; Kasukawa's Criteria with Reynaud's phenomenon, positive Anti-U1snRNP antibodies, polyarthritis, sclerodactyly, muscle weakness with elevated serum creatine kinase. Alarcon-Segovia Criteria is considered the most sensitive and specific, hence it is widely used.

MCTD is a constellation of clinical features which overlap a few autoimmune diseases along with elevated anti-U1snRNP levels indicating B cell and T cell response. Antibodies to U1snRNP interact with endothelial and mononuclear cells leading to endothelial damage, intimal hyperplasia, obliterated vasculopathy and PAH in MCTD. It has a high genetic association with HLA DR4 and DR1, where as SLE with HLA-DR2, PM/DM with HLA-DR3, and Systemic Sclerosis with HLA-DR5 signifying it as a distinct clinical entity (7). With low levels of immune complexes circulating in the blood as opposed to isolated SLE. [1]

In our case, the patient had severe limitation of activity due to muscle weakness as well as evidence of muscle damage with elevated CK levels which is generally limited to myopathy and mild muscle enzyme abnormalities in MCTD. The patient was asymptomatic in terms of pulmonary involvement with no evidence of abnormality on Chest X-Ray.

A peculiar finding in this case was the presence of chronic non healing ulcers over the sites of arthritis which was not a common trend with other case reports. [5]

In our case, the patient was treated with Inj. ceftriaxone 1 gm IV twice daily and Inj. metronidazole 500 mg IV thrice daily for 5 days after which her gastroenteritis resolved. She was continued on T. Levothyroxine 62.5 mcg once daily for her previous diagnosis of Hypothyroidism. She was started on T aceclofenac 50 mg twice daily for arthralgia and myalgia and T. prednisolone 10 mg once daily, T. Methotrexate 10 mg weekly once, T. Folic Acid 5mg once daily skipping on the day of methotrexate for her arthritis and to prevent the progression of scleroderma. T Nifedipine 10 mg twice daily was given for her Reynaud's phenomenon and mild pulmonary arterial hypertension, 2 weeks after starting treatment, her ulcers got healed

The course of the disease is benign with a better prognosis due to the absence of severe renal disease in MCTD as a result of the high Anti-U1 snRNP antibodies which may have a protective role against development of diffuse proliferative glomerulonephritis as compared to the individual diseases. As well as to prevent the complication of pulmonary arterial hypertension which may develop later in the disease course in some patients which has very high morbidity and mortality with a potentially fatal consequence? [3, 6, 7]

The absence of controlled trials in these cases limits the treatment modality to specific manifestations of Scleroderma, RA and myositis with NSAIDS and

antimalarials like hydroxychloroquine for arthralgia, short course of corticosteroids and immunosuppressive agents like methotrexate which should be used with caution due to potential lung toxicity. [3]

Long term prognosis can be improved by monitoring for the development of pulmonary arterial disease with chest X-Rays, 2D echocardiography and pulmonary function tests on further follow ups. [3]

CONCLUSION:

Early diagnosis of MCTD is important as the overlap syndrome which may be considered to be a separate disease entity as for many patients

REFERENCES:

1. Sharp GC, Irvin WS, Tan EM et al. 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
2. Pepmueller PH. Undifferentiated Connective Tissue Disease, Mixed Connective Tissue Disease, and Overlap Syndromes in Rheumatology. Mo Med 2016;113:136-40
3. Narsimulu G, Varaprasad IR. Mixed connective tissue disorders (MCTD) Med Update. 2010;20:841–5
4. Benjamin C, Carlo Alberto S, Rosaria T, et al. Mixed connective tissue disease: state of the art on clinical practice guidelines. RMD Open. 2018;4(Suppl 1):e000783
5. Faden A, Aljamili A, Aljamili A et al. Mixed connective tissue disease in young Saudi patient with recurrent dental abscess: A case report. International journal of health sciences 2018;12(6):65-68
6. Laitinen O, Piirainen H. On the prognosis of patients with mixed connective tissue disease [letter]. Arthritis Rheum 1984;27:596
7. Agnieszka Paradowska-Gorycka. U1-RNP and TLR receptors in the pathogenesis of mixed connective tissue disease. Rheumatologia 2015; 53, 3:143-151

Fig 1: Showing pursed lips, loss of wrinkles and tautness of the facial skin

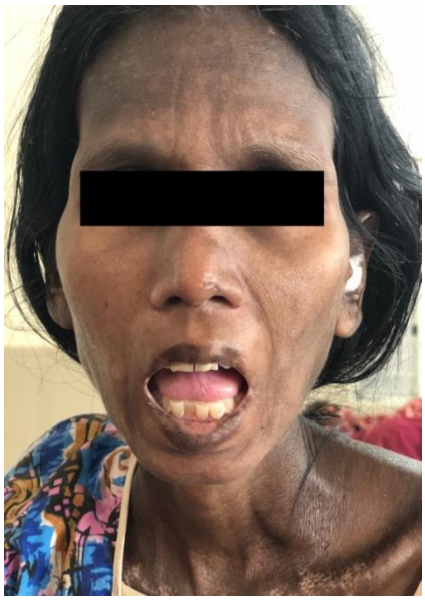

Fig 2: Showing microstomia and flattening of the nasolabial folds

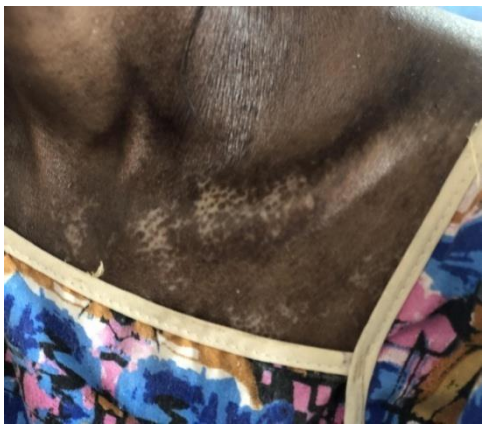

Fig.3. Showing areas of pigmentation and depigmentation (salt and pepper appearance)

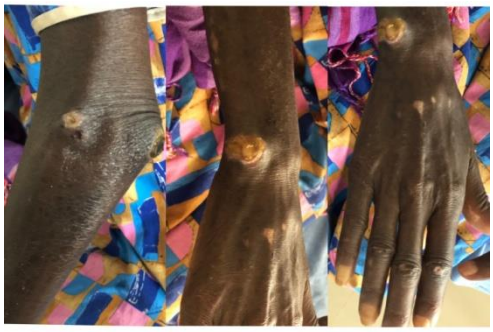

Fig 4: Showing ulceration over elbowShowing ulceration over elbow, wrist and proximal inter-phalangeal joints

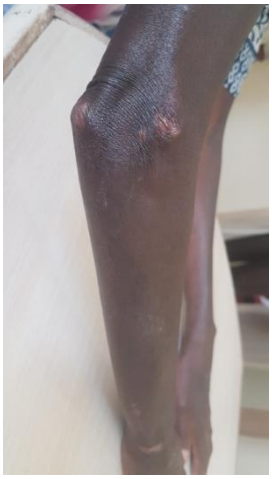

Fig 5: Showing healed ulceration over elbow, wrist and proximal interphalangeal joints

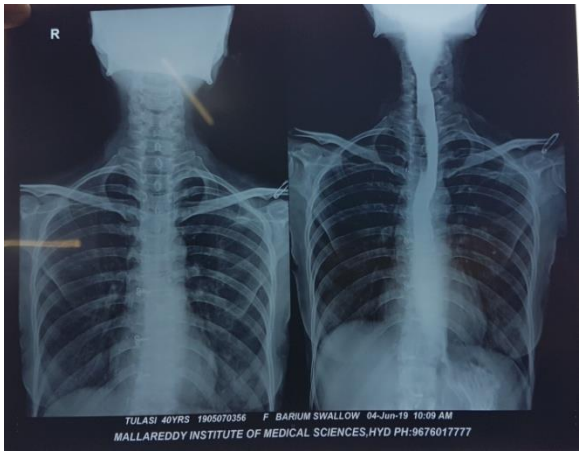

Fig 6: Barium Swallow – normal esophagus

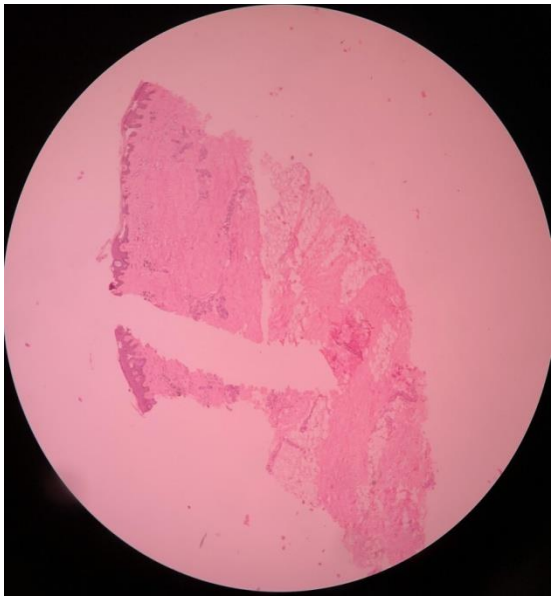

Fig.7. Skin biopsy- H & E stain -4X

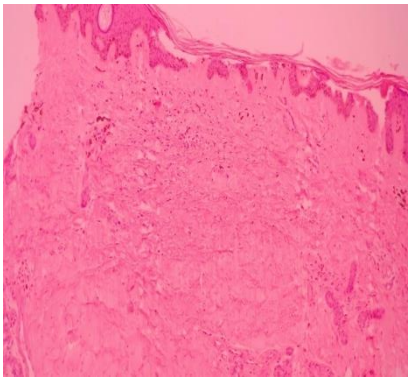

Fig.8. Skin Biopsy- H & E Stain - High Power Field (40X)

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