A Rare case report on Mixed Connective Tissue Disease with Co-morbidities.

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INTRODUCTION:

Mixed connective tissue disease (MCTD) is a rare autoimmune disease diagnosed with a presence of anti-U1-ribonucleoprotein and there are features of at least two connective tissue diseases, including systemic lupus erythematosus, systemic sclerosis, polymyositis, dermatomyositis, and rheumatoid arthritis[1]. MCTD was recognised as a subtype of sclerosis but recently it is recognised as an independent disease entity due to presence of conditions such as pulmonary arterial hypertension, aseptic meningitis and trigeminal neuropathy [2]. The incidence of MCTD in United States of America (USA) was found to be 1.9 per 1, 00,000 adults per year [1] making it a rare occurrence. The exact cause of MCTD is not known. MCTD is characterised by overlapping of clinical features such as systemic lupus erythematous (SLE), progressive systemic sclerosis (PSS), polymyositis (PM) but presence with idiopathic portal hypertension has been rare in MCTD patients [3]. MCTD is commonly seen in females than in males within the age group 40-68 years. Diagnosis is complicated due to presence of variable and diverse symptoms upon presentation and changes in symptoms over time. However, MCTD can be confirmed by the presence of anti-U1-ribonucleoprotein (antibody to extractable nuclear antigen) [1]. Here, we present a case of MCTD with other co-morbidities such as pancytopenia, portal hypertension, massive splenomegaly and complex ovarian cyst.

Case Presentation:

A 33-year-old woman was admitted in Gandhi Hospital Hyderabad with an already existing diagnosis of cirrhosis of liver, portal hypertension and splenomegaly. She had complaints of abdominal pain since 20 days (insidious in onset, intermittent type with dragging sensation and heaviness in the left side of abdomen) and was found to be anorexic with early satiety. The patient had a history of jaundice ten years ago. No history of herbal medications use was reported. Menstrual history was found to be regular and obstetric history was P1L1 with no previous abortions. On examination she was found to be pallor, chloasma (brown patches form on the skin), Blood pressure-90/50 mmHg, Pulse Rate -85beats/min and abdomen was found to be soft, with tenderness in the left hypochondrium region.

Laboratory Findings: The various laboratory test results done are shown in **Table 1**.The complete blood picture (CBP) showed the clinical findings such as: red blood cells (RBCs) with microcytic, hypochromic, moderate anisopoikilocytosis, few macrocytes and ovalocytes, white blood cells (WBCs) with leukopenia and thrombocytopenia. Although the prothrombin time was 16.3 seconds, there were no signs of bleeding problems seen in the patient.

Table-1: Laboratory findings of CBP and biochemical analysis:

Laboratory findings	Values
1.W.B.C	2.12 [10^3/UL]
2.R.B.C	2.46 [10^6/UL]
3.Platelets	83000 [10^3/UL]
4.Hemoglobin	4.3 g/dl
5.Reticulocyte count	0.192%
6.Urea	18mg/dl
7.Creatinine	0.43 mg/dl
8.Total bilirubin	2.26
9.Albumin	2.93
10.Globulin	3.91
11.AST	15 IU/L
12.ALT	20 IU/L
13.Alkaline phosphatase	94 KAU/100ml
14.Prothrombin time/INR	16.3 sec/1.3

Ultrasound scan of abdomen was performed which showed cholelithiasis, gross splenomegaly with dilated splenic vein. The uterus was normal size, anteverted and poor window ovaries (reduction in quantity of ovarian follicles) were observed. Raised PSV (peak systolic velocity) in hepatic artery, dilated portal vein and massive splenomegaly with perisplenic and peripancreatic collaterals was also reported. Therefore, based on laboratory findings and physical examination she was diagnosed with severe anaemia, cirrhosis of liver with portal hypertension and massive splenomegaly. After 5 days of admission the antinuclear antibodies (ANA) test was advised and the results reported mixed pattern showing speckled (+) and cytoplasmic 2+ patterns with titre of 1:100 dilution. Also high titre value of anti-U1-RNP antibody was reported. From these tests results the patient was reported to be suffering from MCTD also. The bone marrow biopsy was done which showed impression of hyper cellular marrow with erythroid hyperplasia as shown in **Figure 1.** The test reported hypercellular marrow with normal in number and few immature forms of megakaryocytes and platelets. Erythroid myeloid ratio of 3:1.Erythroid hyperplasia with predominantly micro-normoblastic maturation and focal megaloblastic maturation.

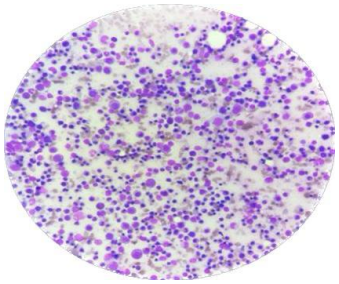

Figure 1: Impression of bone marrow biopsy report.

The treatment given to the patient was as follows.

On the day of admission the treatment was given for cirrhosis of liver with portal hypertension which included Tab. Propranolol 20 mg BD, Tab. Rifaximin 550 mg BD, Injection(Inj.) Pantoprazole 40 mg OD, Inj. Hyoscine butyl bromide 1amp SOS and Tab. Ursodeoxycholic acid (udiliv) 300 mg BD. Further continuing her hospital stay for 20 days, she was prescribed for Tab. Carvedilol 3.125 mg BD for portal hypertension and Tab. Rifaximin 550mg BD for 10 days duration followed by Tab. udiliv for 5 days.Meanwhile 2 packets of plasma concentrate (PC) and 4 packets of Random Donor Platelets (RDP) was planned and transfused due to severe anaemia condition. As an immune booster and to improve her over all well-being she was prescribed with oral supplementations such as Tab. B complex OD, Tab. Calcium + Vitamin D3 OD, Tab. Iron folic acid 335mg BD, Tab. Vitamin C 500 mg OD in her total length of stay at the hospital. After 15 days corticosteroid therapy (Inj. Methyl prednisolone 1gm in 100 ml NS IV OD) had been started due to the confirmation of MCTD which is an autoimmune disorder. The patient's health had stabilised and on the day of discharge she was prescribed Tab. Prednisolone 20 mg BD, Tab. Hydroxychloroquine 200 mg OD (to help prevent flare ups) and Tab. Amoxicillin + clavulanate 625 mg BD for 10 days together with oral vitamin and mineral supplements.

DISCUSSION:

Recent data have suggested that multiple organ complications have been observed with MCTD such as pulmonary arterial hypertension (PAH), glomerulonephritis (GNF), vasculitis, gastrointestinal bleeding and severe central nervous abnormalities [4]. However, in this case the patient experiencing portal hypertension was found to be a rare complication studied form previous literatures. From the previous studies it was also observed that PAH was the primary cause of death in MCTD patients and in patients with lung complications, but in this patient no lung related problems were observed. The patient was advised by the physician to do regular echocardiogram (ECG) and gammaglobulin tests for any life threatening complications as MCTD patients could present with hypergammaglobulinemia[4]. The only diagnostic test for confirming MCTD was found to be the presence of speckled ANA and presence of anti-U1-RNP antibody which were both positive in this case confirming the above medical condition [5]. It has been observed that MCTD patients have abnormal blood cells leading to hypochromic anemia, leucopenia and thrombocytopenia as reported in a previous case report Thrombotic Thrombocytopenic Purpura Associated with MCTD patient which was similar to our case report which showed hypochromic, moderate anisopoikilocytosis [6]. Improved haemoglobin levels were observed with 2 packets of PC and 4 packets of RDP transfusions as follows: Haemoglobin- 8g/dl, Platelets-101[10^3/UL], RBC-3.1[10^6/UL],WBC-3.8[10^3/UL]. Physician had advised bone marrow biopsy as myelodysplastic

syndromes have been reported in patients with connective tissue diseases which could be a risk factor in this patient. [7]. Hence, the main goal of therapy for MCTD patients lies with the symptomatic relief, avoiding any organ complications and maintaining disease remission.

CONCLUSION:

MCTD involves multiple organ dysfunctions. So, creating awareness and educating the patient with disease and the complications associated with it is of primary importance in this medical case to prevent any multi-organ failure or life threatening conditions from arising. Life expectancy can be increased with early diagnosis and better treatment.

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