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# A CASE OF BILATERAL PLEURAL EFFUSION: AN ISOLATED PULMONARY MANIFESTATION OF MIXED CONNECTIVE TISSUE DISORDER

Pulmonary Medicine

**Preetam Goswami*** Post graduate resident, department of pulmonary medicine, Burdwan medical college, West Bengal. *Corresponding Author

**Anirban Das** Associate professor, department of pulmonary medicine. Burdwan medical college, West Bengal.

**Pronoy Sen** Post graduate resident, department of pulmonary medicine, Burdwan medical college, West Bengal.

## ABSTRACT

Pleural effusions can occur in a variety of conditions ranging from pulmonary to extrapulmonary. Pleural effusion in MCTD has an incidence of 50% with mean age of 31.9 years but most cases reported in literature have an additional parenchymal involvement present. Isolated pleural involvement is very rare in MCTD. This case reported here is of a 22-year-old female presenting with bilateral pleural effusion as the only manifestation of MCTD. In conclusion, mixed connective tissue disorder should be included in the differential diagnosis while suspecting a case of pleural effusion due to a connective tissue disorder.

## KEYWORDS

mixed connective tissue disease, bilateral pleural effusion, ribonucleoprotein, autoimmunity, autoantibody

## INTRODUCTION:

Mixed connective tissue disorder (MCTD) is a syndrome which is defined by a combination of symptoms similar to those of systemic lupus erythematosus (SLE), scleroderma, polymyositis and rheumatoid arthritis (RA) and high titers of circulating autoantibodies to ribonucleoprotein (RNP).[1] The diagnosis of MCTD is a challenging task because of the presence of overlapping symptoms of other connective tissue disorders.[2]

The mean age of presentation of MCTD is 31.9 years.[1] There is a marked imbalance in the prevalence of MCTD among sexes, with around 5 to 10 times as many women are affected as men.[3] Pulmonary manifestations occur in 20-80% of patients with MCTD.[4] Pulmonary manifestations include interstitial pneumonitis and fibrosis seen in 20–65% cases, pulmonary hypertension seen in 10–45% cases.[5] Pleural effusions in mixed connective tissue disorder are usually bilateral with an incidence of 50% and are mostly due to immunological lesions involving the pleura.[3]{6}

We report a case of bilateral pleural effusion in a 22-year-old female later diagnosed as MCTD.

## CASE REPORT:

A 22 years old female presented with acute shortness of breath on exertion (mMRC grade 3) and left sided chest pain for 15 days and multiple joint and muscle pains for past six months. The joint pains mostly involved the large joints (knee, ankle and elbow), was associated with redness and was asymmetrical in distribution. There is history of recurrent upper respiratory tract infections (URTI) in the past and also had history of Urinary tract infection (UTI) one month back. She had no other comorbidities. She also had history of colour change of the fingers during winters.

On physical examination, she was tachypnoeic. All other vitals were within normal limits. Pallor was present along with bilateral pedal oedema. There was swelling of hands, knee and ankle joints of both sides. Patient developed Raynaud's phenomenon on exposed to cold water. Skin examination showed hyper pigmented areas mostly on the face, neck and back and also there was marked alopecia. Chest signs were suggestive of a bilateral pleural effusion. All other system findings revealed no significant abnormality.

Laboratory investigations showed a pancytopenic picture with haemoglobin 6.7g% (ref: 12g/dl), white blood cell count 3100/cc (ref: 4000-11000/cc) with a normal differential and platelet count of 95,000/cc (ref: 1,50,000-4,00,000/cc). There was high Erythrocyte sedimentation rate (ESR) of 102 mm in the first hour (ref: less than 10mm) and high C-reactive protein (CRP) of 58.5 g/dl (ref: 6 g/dl). Renal function tests (RFT) and urine analysis were normal. Liver function tests (LFT) showed hypoalbuminemia. Peripheral blood smear showed anisocytic hypochromic anaemia with no abnormal morphology. Iron profile showed normal serum iron, high serum ferritin and Total iron binding capacity and low transferrin saturation. Thyroid function tests (TFT) were normal. Sputum was negative for Acid Fast Bacilli (AFB) and mycobacterial culture showed no growth. Sputum for cartridge-based amplification test (CBNAAT) detected no mycobacterium. Mantoux test was negative. Her serology (HIV & Hepatitis B&C) panel was normal.

**Table 1: Autoimmune Panel of the patient**

| *Investigation* | *Value (IU/ml)* | *Reference Value (IU/ml)* |
|---|---|---|
| Anti-Nuclear Antibody (ANA) | 95 (positive) | <25 |
| Anti-ds DNA | 55 (positive) | <30 |
| Anti U1 RNP | 55 (positive) | <26 |
| Creatinine Kinase (CK) | 256 (high) | 50-100 |
| RA factor | 6 | <14 |
| Scl 70 | Negative | |
| Anti-Ro/La | Negative | |
| Anti Jo-1 | 18 | <20 |

On chest roentgenography, she had a homogenous opacity in left middle and lower zone obliterating the left costophrenic angle and blunting of right costophrenic angle. Ultrasonography (USG) of thorax confirmed bilateral pleural effusion and chink of pericardial effusion. USG of whole abdomen showed mild hepatomegaly but no ascites. Contrast enhanced computed tomographic scan (CECT) of thorax showed left sided large pleural effusion but no obvious parenchymal involvement. Electrocardiogram (ECG) was normal and 2D-echocardiography showed mild pericardial effusion without any evidence of pulmonary arterial hypertension (PAH).

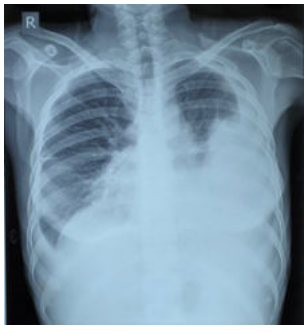

**Figure 1: Chest Xray showing homogenous opacity on left side and blunting of right costophrenic angle**

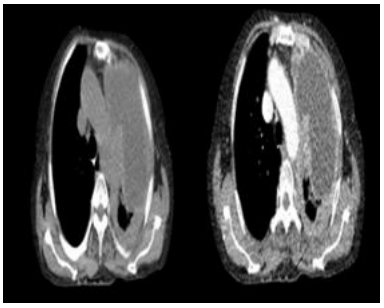

**Figure 2: Computed tomographic scan showing left sided pleural effusion (left- CT plain, Right- CT with contrast)**

Pleural fluid was clear straw coloured and pleural fluid analysis showed lymphocytic (90%) exudative (39g/L) pattern. Pleural fluid acid fast bacilli (AFB) smear was negative and pleural fluid mycobacterial cultures showed no growth. Adenosine deaminase (ADA) level was low. Pleural fluid cartridge based nucleic acid amplification test (CBNAAT) detected no mycobacteria. Pleural fluid cell block study was negative for malignancy. Pleural biopsy showed lymphocytic infiltrate without any obvious granuloma or malignancy.

She was started on oral prednisolone at 40mg/day and nonsteroidal anti-inflammatory drugs (NSAIDs) with partial resolution of pleural effusion and complete resolution of joint pains and gradual improvement of other symptoms. During hospital stay, she initially underwent therapeutic thoracentesis from left side of around 1.2 liters with immediate relief of her dyspnea. She was also transfused 2 units of packed red blood cells (PRBC) for the correction of her anaemia.

During follow up over next 8 months, with last follow up 1 month back, there was complete resolution of pleural effusion. The patient is asymptomatic without any joint swelling or muscle pain. The ESR also decreased to 34mm in first hour and Creatinine Kinase levels became normal (46U/L). Her pancytopenia also got corrected and ANA became normal.

## DISCUSSION:

The combination of high positive titers to U1-ribonucleoprotein along with combination of synovitis, chemical myositis and Raynaud's phenomenon has led us to the diagnosis of Mixed Connective Tissue Disorder (MCTD) as per Alarcon-Segovia and Villareal diagnostic criteria.[3] Tuberculosis has been excluded as sputum AFB, cultures and CBNAAT were negative and pleural fluid study also showed no evidence of AFB. Malignancy such as lymphoma or metastatic spread to pleura have been excluded as CECT of thorax was normal without any obvious mediastinal lymphadenopathy and pleural fluid cell block was negative for malignant cells.

**Table 2: Alarcon-Segovia and Villareal criteria for MCTD**

| *Diagnostic criteria*[3] |
|---|
| *Serologic criterion:*<br>Positive antibodies to U1 RNP antibodies at a titre ≥1:1600 |
| *Clinical criteria:*<br>1. Swollen hands<br>2. Synovitis<br>3. Myositis<br>4. Raynaud's phenomenon<br>5. Sclerodactyly |
| *Diagnosis Of MCTD:* Fulfilled serologic criterion and ≥3 of the clinical criteria (coexisting oedema of the hands, Raynaud phenomenon, and Sclerodactyly require an additional fulfilment of the criteria of either myositis or synovitis). |

Bilateral pleural effusion in our patient is an unusual presentation of MCTD. Pulmonary disease occurs in 20-80% of patients with MCTD.[4] 65% of these patients are asymptomatic while others may present with symptoms like dyspnea, chest pain, or cough.[1] 85% of patients with pulmonary disease due to MCTD show bilateral interstitial infiltrates.[1] These may occur as a result of alveolar cell hyperplasia and infiltration of the alveolar septa by the plasma cells and lymphocytes resulting in interstitial fibrosis which may be detected by the presence of diffuse lesions on the chest X-ray and marked impairment of lung function parameters.[7] Small pleural effusions were found in 6% of patients in one isolated series but all were accompanied by pulmonary infiltrates.[8] Pleural effusion due to connective tissue disorders may also be seen in systemic lupus erythematosus (30%), rheumatoid arthritis and scleroderma (3%).[3][9][10] In our case there was pleural effusion without any evidence of pulmonary interstitial infiltrates which is very uncommon. Another unusual feature of our case is that mean age of presentation of MCTD is 31.9 years [1], while our case was a 22 years old female. Pleural effusion in mixed connective tissue disorder may be possibly attributed to serositis or may also occur due to intercostal muscle inflammation.[1] In our case it is probably due to serositis as patient had pleural and pericardial effusion. Treatment with oral glucocorticoids showed improvement as the underlying disease is an autoimmune condition.

## CONCLUSION:

To conclude with, this is a case of bilateral pleural effusion which eventually came out to be mixed connective tissue disorder. This case report shows the importance of reaching a diagnosis for specific treatment and suggests that mixed connective tissue disorder should be included in the differential diagnosis while suspecting a case of pleural effusion due to a connective tissue disorder.

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