International Journal of Multidisciplinary Research and Development
Online ISSN: 2349-4182 Print ISSN: 2349-5979
www.allsubjectjournal.com
Volume 3; Issue 1; January 2016; Page No. 32-33

Rare case of fever of unknown origin (mixed connective tissue disease)

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Abstract
Mixed connective disease a group of patients with overlapping clinical features of systemic lupus erythematosus (SLE), scleroderma, polymyositis and rheumatoid arthritis with presence of a distinctive antibody against what now is known to be U1-Ribonucleoprotein (RNP) [1].

Keywords: Mixed connective tissue disase, Fever of unknown origin.

Introduction
Mixed connective tissue disease (MCTD) was first recognized by Sharp and colleagues (1972).autoimmunity to components of the U1-70 kd sn RNP are a hallmark of disease. Anti-RNP antibodies can precede overt clinical manifestations of MCTD, but overt disease generally develops within 1 year of anti -RNP antibody induction. The loss of T-lymphocyte and B-lymphocyte tolerance due to cryptic self antigens abnormalities of apoptosis or molecular mimicry by infectious agents and driven by U1-RNP induced innate immune responses are proposed current theories of pathogenesis. The cause of MCTD is unknown. This is the first case report of MCTD from Osmania General Hospital.

Case Study
14 year old female patient came with chief complaints of fever since 2months, joint pains since 2 months and bilateral periorbital swelling since15 days.

Past history: no similar complaints in the past. No history of other comorbidities.

Family history: Not significant.

Personal history: mixed diet, normal appetite, bowel and bladder regular.

Menstrual history: She attained menarche at the age of 13 years. Her menstrual cycles are regular.

General examination: patient conscious, coherent, no pallor cyanosis clubbing edema lymphadenopathy and revealed bilateral periorbital swellings.

Vitals: normal

Systemic examination: CVS Respiratory system GIT and CNS normal.

Investigations: Complete blood picture revealed anemia. Her renal function tests, liver function tests were unremarkable.24 hour urine examination revealed proteinuria (432 mg/24 hours). ASO titres were elevated (>200). ANA profile revealed ANA strong positive and U1RNP strong positive. Ultrasonography of abdomen, Chest radiography, 2D Echocardiography were unremarkable.

Case discussion
Mixed connective tissue disease (MCTD) was first recognized by sharp and colleagues 1972 as a connective tissue disorder characterized by the presence of high titers of a distinctive autoantibody, now called anti-U1 ribonucleoprotein (RNP) (previously termed antibody to extractable nuclear antigens [anti-ENA]) [1]. The central premise of the MCTD concept is that of an overlap syndrome associated with anti-U1 RNP antibodies that incorporates selected clinical features of systemic lupus erythematosus (SLE), systemic sclerosis (scleroderma [SSc]), and polymyositis (PM) [2]. The definitive diagnosis of MCTD is often complicated by the fact that the overlapping features tend to occur sequentially [3]. This confusion arises due to the overlap of the various diffuse connective tissue diseases (DCTD), as well as to changes in the underlying pathology of the illness.

Diagnostic criteria: Several attempts have been made to standardize the diagnostic criteria for MCTD [4]. One study reviewed four sets of diagnostic criteria (Sharp, Alarcon-Segovia, Kasukawa, and Kahn) and concluded that those of Alarcon-Segovia and Kahn were “best”. The criteria utilized by Alarcon-Segovia had a sensitivity and specificity of 63 and 86 percent, respectively; this accuracy is comparable to that found with the criteria utilized by Kahn

Alarcon-Segovia Diagnostic Criteria for Mixed Connective Tissue Disease (MCTD) [5]

1. Serological criteria: Positive anti U1 RNP at haemagglutination titer >1:1600.

2. Clinical criteria: a. Oedema ofhands b. Synovitis c. Myositis d. Raynaud´s e. Acrosclerosis

Requirements: a. Serological b. Atleast 3 clinical features c. Association of hand oedema, Raynaud´s and acrosclerosis requires atleastone other feature

Kusukawa Diagnostic Criteria for Mixed Connective Tissue Disease (MCTD)

Common Symptoms

1. Raynaud´s Phenomenon.
2. Swollen fingers or hands Presence of Anti U1 RNP.

Mixed findings

A. Systemic lupus erythematosus (SLE) like Polyarthritis, Pericarditis/pleuritis, Lymphadenopathy, Facial erythema, Leucopenia/thrombocytopenia.
B. Scleroderma like Sclerodactyly, Pulmonary fibrosis, Esophageal dysmotility.
C. Polymyositis like Muscle weakness, High creatine phosphokinase (CPK), Myopathic electromyogram (EMG).

Requirement for diagnosis: Atleast one common symptom, with positive U1 RNP antibodies and one or more findings in at least two of the three categories A, B, and C.

In the early stages, most patients destined to develop MCTD cannot be differentiated from the other classical DCTDs. The early simultaneous presence of overlap features usually seen in systemic lupus erythematosus (SLE), systemic sclerosis (scleroderma [SSc]), and polymyositis (PM) is seldom seen. More commonly, the overlapping features occur sequentially over several years. Prominent early symptoms are easy fatigability, poorly defined myalgias, arthralgias, and the Raynaud phenomenon.

The major reason to consider MCTD a distinct clinical entity is that the presence of high titers of anti-U1 RNP antibodies is associated with several distinctive clinical characteristics. Characteristic clinical symptoms of MCTD eventually emerge, including the Raynaud phenomenon, hand edema, puffy fingers, and/or prominent synovitis. Overlapping clinical features include inflammatory muscle disease and sclerodactyly. Affected patients are prone to develop pulmonary hypertension and a scleroderma-like vasculopathy, but serious renal or central nervous system (CNS) disease is uncommon.

Nevertheless, anti-U1 RNP antibodies alone do not guarantee that a patient either has MCTD or will continue to display the MCTD phenotype. As an example, the first clue to the diagnosis of MCTD is often the presence of a positive ANA with a high titer speckled pattern (commonly >1:1000 and often >1:10,000). However, antibodies to U1 RNP, Sm, Ro, and La all produce a speckled pattern, and antibodies to double-stranded deoxyribonucleic acid (dsDNA), Sm, and Ro are occasionally seen transiently in patients with MCTD. If dsDNA, Sm, or Ro are the dominant and persistent autoantibody system, then the patient is more likely to develop a connective tissue illness other than MCTD. If, on the other hand, antibodies to U1 RNP remain dominant, then the patient is likely to continue to have the clinical characteristics of MCTD.

Treatment

MCTD is a steroid responsive disease with a good prognosis. Among patients requiring long-term glucocorticoids, the use of antimalarials (400 mg of hydroxychloroquine per day) or methotrexate (7.5 to 15 mg/week) may be reasonable in an attempt to minimize the cumulative steroid burden. Unless contraindicated, all steroid-treated patients should take calcium and vitamin D supplements.

Conclusion

Our patient was put on steroids and calcium and vitamin D supplementation and is referred to NIMS for rheumatologist consultation. She was advised to follow up under nephrologist as she had sub nephrotic proteinuria at the time of presentation.

Bilateral Periorbital Edemas

References

1. Mixed connective tissue disease--an apparently distinct rheumatic disease syndrome associated with a specific antibody to an extractable nuclear antigen (ENA). Sharp GC, Irvin WS, Tan EM, Gould RG, Holman HR Am J Med. 1972; 52(2):148.
2. Mixed connective tisssue disease: a clinicopathologic study of 20 cases. Bennett RM, O'Connell DJ Semin Arthritis Rheum. 1980; 10(1):25.
3. Bennett RM. Overlap Syndromes. Textbook of Rheumatology, 8th, WB Saunders Co, Philadelphia 2009, 1381.
4. Alarcon-Segovia D, Cardiel MH. Comparison between 3 diagnostic criteria for mixed connective tissue disease. Study of 593 patients. J Rheumatol. 1989; 16(3):328-34.
5. Alarcon-Segovia D. Mixed connective tissue disease and overlap syndromes. Clin Dermatol. 1994; 12(2):309-16.