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Case Report

Rhupus Syndrome: Overlap of Rheumatoid Arthritis and Systemic Lupus Erythematosus

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Abstract

Rhupus syndrome is a rare and incompletely described autoimmune entity in which the same patient sequentially develops symptoms both of Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE). Both diseases have different diagnostic criteria and laboratory investigations but have mixed clinical presentation so can easily miss the rhupus syndrome. Overlap phenomenon is common in various autoimmune diseases which otherwise differ in presentation, treatment response and prognosis. RA and SLE overlap is very rarely reported and no rational criteria for its diagnosis and treatment strategy are finalized yet. In most of the reported cases of Rhupus syndrome, RA appeared first and SLE developed later while in a small number of cases SLE appeared first which later evolved to RA and in a few cases symptoms of both diseases appeared simultaneously. A 55-years old female patient was diagnosed with RA four years back and recently developed oral ulcers, anemia, leucopenia and thrombocytopenia. After complete history, general physical examination, laboratory investigations and fulfillment of SLE (SLICC criteria 2012) and (ACR criteria 2010) for RA, a final diagnosis of Rhupus syndrome was established.

Keywords: Autoimmunity; Overlap; Systemic lupus erythematosus; Rheumatoid arthritis

Introduction

Overlap of autoimmune diseases is a common phenomenon and coexistence of SLE and RA was first reported in 1960 while the term Rhupus syndrome was first coined by peter Schur in 1971. Rhupus syndrome is a rare, neglected autoimmune entity which has features of both RA and SLE which mostly appear sequentially. SLE related features are usually mild and include hematological, mucosal and skin involvement [1]. Diagnostic criteria and treatment strategies for Rhupus syndrome do not exist but common criteria used for SLE is SLICC-2012 and that for RA is ACR/EULAR-2010. These criteria's along with articular erosions, high titre of RA factor, anti CCP, ANA and anti dsDNA are used for the diagnosis of Rhupus syndrome [2]. Females are affected most with Rhupus. In 70% of the cases RA is diagnosed first with later development of SLE while in 20% of the cases SLE developed first followed by appearance of RA features. Few cases have also been reported with simultaneous appearance of symptoms of both SLE and RA2. Patients have more chances to evolve into Rhupus if they develop RA at a young age or develop SLE in old age and female patients are more susceptible during the post-partum period and around menopause [3]. The prevalence of patients with RA and SLE proceed to Rhupus syndrome varies from 0.09% to 9.7% in different population [4]. Rhupus syndrome mostly presents with symmetric erosive polyarthritis mainly affecting the hands, hematological manifestations, skin lesions, oral ulcers, serositis, renal involvement, less frequently organ and neurological involvement [5]. Patients with Rhupus syndrome also have high titres of RA factor, anti-CCP, ANA and anti dsDNA antibodies. The exact triggers of Rhupus are not known but combined role of immunological, hormonal, genetical and environmental factors may play a role [6].

Case Presentation

A 55 years old female with medium built was diagnosed with RA four years back when she visited the medical specialist with complains of polyarthritis involving multiple small and large joints, morning stiffness in the joints of hands and feet. RA factor and anti-CCP were positive on laboratory investigations. She was started on NSAIDs, Methotrexate and corticosteroids which she took for one year only and did not visit for follow up. Then she took homeopathic medicines and traditional treatment on and off. Her symptoms worsened and she developed swan neck deformity of hands, with weakness and lethargy. Her laboratory workup showed anemia, leucopenia and thrombocytopenia with raised ESR & CRP. Bone marrow aspiration was performed which was suggestive of mixed deficiency anemia. X-rays showed erosions of proximal interphalangeal and metacarpophalangeal joints and knee joints respectively. Few weeks later patient developed oral ulcers. She was referred to Immunology department Armed Forces Institute of Pathology for workup of mixed connective tissue disorder and Felty's syndrome. After complete history and general physical examination autoimmune workup was advised. Blood CP showed Hb 8.2g/dl, TLC $2.6x10^9$/L, Platelets $65x10^9$/L , ESR 81mm at 1st hour and CRP 38.3mg/L, RA factor (>256IU/ml), Anti-CCP (>80AU/ml), ANA (titer 160, peripheral pattern) and anti dsDNA (titer 160), C3 0.5g/l (0.7-1.7 g/l) and C4 0.05 g/l (0.2-0.5 g/l), ENA positive for anti-nucleosome antibodies whereas anti-Sm, anti-SSA, anti-SSB and anti-RNP were absent, LFTs and RFTs were within normal limits. Abdominal ultrasound ruled out splenomegaly and thus Felty's syndrome. Based on history, physical examination and SLE SLICC criteria 2012 and ACR criteria 2010 for RA, final diagnosis of Rhupus syndrome was established.

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Discussion

Rhupus syndrome is a rare overlap entity of autoimmunity. Its diagnostic criteria and treatment strategy do not exist at the moment. The coexistence of RA and SLE was reported for the first time by toone et al. in 1960 [1]. Many studies concluded that Rhupus patients have more severe arthritis, morning stiffness, joint deformity, joint erosions, inflammatory changes, less organ and neurological involvement [1]. The treatment of Rhupus includes Corticosteroids and DMARDs as commonly used in RA and SLE but few studies also suggested the use of immunosuppressant's and biologics when organ involvement is present [1]. In our patient, severe joint pain, significant morning stiffness, joint deformity and erosion were present. Most patients with Rhupus have mild SLE features which mainly include hematological manifestations, mucosal and skin involvement [1] and our patient had anemia, leucopenia, thrombocytopenia and oral ulcers. Patients with Rhupus have more pronounced CRP and ESR [6] and our patients had raised CRP and ESR. Rhupus patients have high titer of RA factor and anti-CCP [7] which were present in our patient. Rhupus patients also have high titer of ANA and anti dsDNA antibodies which were also present in high titre in our patient. 50% of Rhupus syndrome patients have low complements C3 and C4 levels [7] which were also significantly reduced in our patient. A case report in India mentioned malar rash and discoid rash on back of chest with [8] which were absent in our patient and laboratory investigations revealed anemia, leucopenia, thrombocytopenia, raised ESR & CRP, with normal C3, C4 which was similar to our patient except low C3 and C4.

The diagnosis is based primarily on history, general physical examination, SLE SLICC criteria 2012, ACR criteria 2010 for RA and various immunological investigations. On the basis of high titer of RA factor, anti-CCP, ANA and anti dsDNA antibodies, ENA, raised CRP & ESR, severe erosion of joints with clinical features of both RA and SLE, a final diagnosis of Rhupus syndrome was established. This is one of the rare case of autoimmunity in which the incidence of hand arthritis, polyarthritis, morning stiffness, joint swelling, rheumatoid nodules and erosions is significantly higher. This syndrome can easily be overlooked because of mixed clinical presentation in the presence of an already diagnosed autoimmune disease. Patients with RA and SLE are recommended to get their various immunological investigations such as ANA, anti dsDNA, ENA, RA factor and anti-CCP checked on a regular basis. Joint erosions in RA and SLE must also be ruled out for Rhupus syndrome. This case of Rhupus syndrome is being reported for the first time in Pakistan.

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