

Overlap Syndrome in a 13- Year- Old Girl:A Case Report

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Abstract:

The “Overlap Syndrome” is a rare condition which comprises two or more connective tissue disease in a same patient. Among them, some are associated with specific autoantibody profile and some are not. Here, we reported a case of overlap syndrome who presented with seizures and features of systemic lupus erythematosus, systemic sclerosis with the presence of strongly positive ANA, Anti snRNP, Anti Scl-70 antibody and weakly positive Anti Sm antibody.

Keywords: *Overlap Syndrome; Systemic Lupus Erythomatosus; Systemic Sclerosis; Morphea; ANA; Anti snRNP antibody; Anti Scl-70 antibody; Anti Sm antibody; Cerebral Vasculitis;*

Introduction:

The concept of overlap syndrome in rheumatology field is very recent. When two or more connective tissue disorder, may fulfill the diagnostic criteria independently or not with or without specific antibodies, is identified in the same patient and cannot assign with a single disease entity, the term ‘Overlap Syndrome’ is used to describe that case. Sometimes, the presentation is so peculiar that the precise diagnosis is very difficult clinically and the specific treatment is not possible initially. A fatal outcome may also occur before reaching a diagnosis. Here, we discussed about a case of overlapping features of systemic lupus erythematosus, systemic sclerosis.

Case Report:

A 13-year-old young girl from Dhaka admitted to Dhaka Medical College Hospital on 17th February, 2013 with the complaints of low grade fever, alopecia, arthralgia, oral ulcers, muscle pain, scaly eruptive lesion on different parts of body for last two months, difficulties in swallowing for

last fifteenth days, history of convulsion single episode one day back. Her general health was deteriorated with fever development. It was low grade, maximum temperature 101 degree F, not came with chills and rigor and subsided after taking antipyretic drugs. With fever, diffuse alopecia and multiple joint pain including knee joint, ankle joint, elbow joint, wrist joint, proximal and distal interphalangeal joint pain developed simultaneously. Sometimes it was so painful that she did not able to move her joint at early morning. Recurrent painful oral ulcers also developed. She also felt muscle pain in both thighs, mild in severity. Initially she was able to do her daily activities but later she felt difficulties in standing from a chair and lifting a heavy item by hands. Time to time, it progressed and one and half months later, she was completely unable to arise from bed. In this time, in some parts of body, mild itchy, eruptive lesion was also developed over lower back, forearms and legs. She also felt difficulties in swallowing for last 15 days, mostly of solid food without pain. There was no history of difficulty speaking, altered sense of taste. Patient party also gave a history of single episode of convulsion, which was generalized, persisted more than three minutes followed by urinary incontinence and confusion for around fifteen minutes. On enquiry, she had no history of photosensitivity, leg swelling, purpuric rash, and digital painful ulceration or colour changes on exposure to cold. She was properly examined and found mild anaemia, normal blood pressure with tachycardia (130 beats/min), diffuse non scarring alopecia, a red –blackish well defined flat rash over the checks sparing naso- labial fold, a circumscribed raised shiny hypopigmented firm skin around 4 x 4 cm² over the nape of neck just above the hair line covered with scalp hair (figure 1), bilateral symmetrical scaly eruptive lesion with multiple shiny hypopigmentation over lower back, extensor surface of forearm (figure 3) and extensor surface of both lower leg just over the lower part of knee,

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two small shiny hypopigmented area over dorsum of right hands (figure 2). There was a tongue ulcer on right lateral border and a buccal ulcer on left site of buccal mucosa, less than 0.25 x 0.25 cm², with erythematous halos, circumscribed margin and gray- whitish floor. Bilateral mild basal creps was also noted with vesicular breath sound. No organomegaly was found in abdomen. There were no signs of meningeal irritation with intact sensory and motor systems. No cardiac abnormality was noted. After admission, only two episodes of seizures developed. In both times, we managed with diazepam immediately and did RBS by glucometer and serum electrolytes that were



Fig.-1 : Possible Circumscribed Morphea over nape of the neck with diffuse non scarring alopecia.



Fig.-2 : Shiny hypopigmented area over the dorsal surface of right hand

normal. With high suspicion of rheumatological disorders, we investigated and found 10.1 gmHb%, 60 mm ESR in 1st hour, $8 \times 10^9/l$ WBC, 74% neutrophils and 23% lymphocytes, normal platelet count. CRP, Serum electrolytes and serum creatinine were normal. Urine routine microscopic examination revealed trace amount proteinuria, no RBC and 0-2 /HPF pus cell. 24 hours UTP was 0.37 gm/ day. There were strongly positive ANA (ELISA; 120 IU/ml), weakly positive Anti SmAb, strongly positive Anti snRNPA, strongly positive Anti Scl-70 Ab, Negative Anti SSAAb, Anti SSBAb, Anti Jo-1 Ab, anti – phospholipid antibody IgM&IgG, Anti- dsDNA (ELISA) (200 IU/ml; suspicious: > 200 IU/ml). CPK was raised 964 U/l (N: 30 – 135 U/L); C3 & C4 level was 0.539 g/l (N: 0.9 – 1.8 g/l) & 0.12 gm/l (N: 0.1 – 0.4 g/l) successively. CT scan of brain, ECG & echocardiography was normal.



Fig.-3 : Scaly eruptive lesion with multiple shiny hypopigmentation over extensor surface of right forearm

Discussion:

In 1972, Sharp and his colleagues recognized overlapping clinical features of systemic lupus erythematosus, scleroderma and myositis among a group of patients with the presence of a distinctive antibody against snRNP.¹ The difficulty to assign this type of disease presentation to a single disease category led to the concept of “Overlap Syndrome” where symptoms of two or more autoimmune conditions are identified in the same patient. The identification of overlap syndrome (OS) is useful in order to clarify the disease prognosis and facilitate management. To categorizing such condition two approaches suggested - 1) by the detection of a specific antibody marker combined with peculiar clinical findings 2) by the identification of a pattern of clinical features without a specific serologic marker.

Table-I*Overlap Syndromes: Classification²*

Associated with specific autoantibody profile
Mixed Connective Tissue Disease (Anti-U1 snRNP)
Anti- Synthetase Syndrome (Anti-tRNASynthetase)
Polymyositis And Scleroderma (Anti-PM/Scl)
Systemic Lupus Erythematosus and Sjögren Syndrome (Anti- La/ SSB)
Not associated with specific autoantibody profile
Rhupus Syndrome
Systemic Sclerosis and Sjögren Syndrome
Systemic Sclerosis and Rheumatoid Arthritis
Systemic Lupus Erythematosus and Systemic Sclerosis
Rheumatoid Arthritis and Sjögren Syndrome
Polymyositis and Sjögren Syndrome

This patient having recurrent oral ulcers, malar rash sparing the naso labial fold, convulsion in the absence of any precipitating factors, strongly positive ANA by ELISA, weakly positive Sm antibody made a diagnosis of SLE according to 1997 update of the 1982 American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus.³ These symptoms developed only at 13 years of age, 5 months after menarche suggested the role of hormone in the pathogenesis of this disease. Though along with these features, in early age onset SLE, others features such as renal involvement including proteinuria (>500 mg/day), cellular cast, thrombocytopenia, hemolytic anaemia, lymphadenopathy are common⁴, we did not find any other involvement except mild proteinuria that did not fulfill the criteria for diagnosing SLE. The presence of strongly positive anti snRNP may play a role for that in this case as this antibody has been associated with mild renal involvement and a lower prevalence of Raynaud's phenomenon though no history of Raynaud's phenomenon were given.⁵ Elevated Anti snRNP was reported in only 38 - 45% cases of SLE.⁶ Recently reviewed by Mahler et al., low level of anti scl-70 antibody positive in all cases of SLE but strongly positive anti Scl-70 antibodies were reported in 23.2% of 531 systemic sclerosis (SSc) cases and in 4.1% of 2366 SLE patients.⁷ Strongly positive anti scl-70 antibody can help to differentiate systemic sclerosis (SSc) from SLE. In this case, the presence of strongly positive anti Scl-70 antibody in SLE patient with some features of systemic sclerosis make a diagnosis of SSc / SLE overlap syndrome. Hietarinta et al. identified that 73% of eleven patients of systemic sclerosis (SSc) with neurological involvement had either anti RNP or anti Scl-70 antibodies in their serum.⁸ As this patient having seizures and strongly positive anti RNP

and anti scl-70 antibodies, there is a probability of developing this neurological manifestation due to systemic sclerosis. But Joseph et al identified that primary neurological presentation of SLE was more common than anticipated. In 27% cases, a seizure was an early manifestation and in 10% cases, it was the first SLE symptom.⁹ It may result from cerebral vasculitis, cardiac embolism, opportunistic infection, drug intoxication or associated metabolic derangements. After 1st episode of seizure, we started methylprednisolone. There was no convulsion after 2nd dose of methylprednisolone of 2nd day of hospitalization. Though there was no neurological sequel including headache, memory impairment, hemiplegia or hemiparesis, we did CT scan of brain that was normal in this case. Joseph et al. also reported that only 35% CT scan and 65% of MRI was abnormal in CNS lupus. CT scan remains valuable in identifying hemorrhage and large infarction in patient of CNS lupus.⁹ Whereas systemic sclerosis related cerebral vasculopathy was identified by CT scan of brain in 42% cases and MRI of brain in 73% cases out of 52 cases according to Terrier et al.¹⁰ Whatever the main etiology either SLE or SSc, both can cause cerebral vasculitis what we considered in this case. Cerebral vasculitis can only be detected by conventional contrast MR angiography. However, in MR angiography, the predominantly small vessels involvement of lupus vasculopathy is often missed. In this case, circumscribed raised shiny hypopigmented firm skin over the nape of neck just above the hair line covered with scalp hair was described. It may be a circumscribed morphea. To the best of our knowledge, there was an only one case of morphea overlapping with SLE reported previously.¹¹ ANA are present in approximately 20-80% of morphea patients, typically with a homogeneous, speckled, or nucleolar pattern,¹² and anti Scl-70 antibodies are present in less than 5% of patient¹³ though we did not know the staining pattern of ANA in indirect immunofluorescent method in this case. We also found bilateral symmetrical mildly pruritic scaly eruptive lesion followed by development of multiple shiny hypopigmentation over lower back, extensor surface of forearm and extensor surface of both lower leg just over the lower part of knee. We observed that it was only involved in that area most commonly involved with friction and pressure. This skin manifestation associated with diffuse hair loss, malar rash, mild eruptive red- blackish discoloration over anterior chest, proximal myopathy with muscle pain and raised serum creatinine kinase suggestive of myositis gave an impression of dermatomyositis. There was a probability that the presence of this myositis was not only due to dermatomyositis but also due to lupus vasculitis of the small vessels feeding that muscle or presence of scleromyositis. Low grade muscle involvement was reported

around 50 – 80% of scleroderma patient.¹⁴ Anti Mi-2 antibodies, anti Jo-1 (antihistidyl transfer RNA [t-RNA] synthetase), anti Signal Recognition Protein (anti SRP), anti PM-Scl and anti Ku antibodies can be present in myositis.¹⁵ Anti Mi-2 antibodies have high specificity but low sensitivity for dermatomyositis. Anti Jo-1 antibody is more common in polymyositis. With severe polymyositis, anti SRP was also found. Anti PM-Scl& anti Ku antibodies are associated with scleromyositis. Out of 5 antibodies commonly related to myositis, we only did anti- Jo-1 antibody that was negative. Other antibody tests were not available in Bangladesh.

A muscle biopsy can solve all questions arising in this article whether this skin lesion was due to lupus dermatitis or dermatomyositis or polymyositis or scleromyositis. But patient party refused to do that.

Conclusion:

As SLE/SSc overlap syndrome is very uncommon disorder without a specific serologic marker, all the clinical features should be evaluated on clinical context and ENA profile should be done on background of high titre of ANA in ELISA or staining pattern other than rim and homogenous staining pattern of ANA in indirect immunofluorescent method.

Conflict of Interest : None

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