

# A Filipino with Systemic Lupus Erythematosus-Scleroderma Overlap Syndrome

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## Abstract

**Background:** Overlap syndrome is a large group of condition that manifests with symptoms from two or more autoimmune conditions and satisfies the diagnostic criteria of at least two connective tissue diseases in the same patient. This condition might be unrecognized by the primary care physician and underreported.

**Case:** A 30-year-old female had a 10-week history of non-pruritic erythematous macules on her face that gradually spread to her trunk, and upper extremities which progressed to hyperpigmented macules and tightening of the skin. There was note of hair loss, anemia, ulcerating wounds on distal extremities and finger tips. She then developed generalized body weakness and easy fatigability. Physical and laboratory examinations were consistent with SLE and scleroderma. 2D-echocardiogram

showed a large pericardial effusion and pulmonary hypertension. She was treated with prednisone and azathioprine which in less than a week, diminished significantly the pericardial effusion. Patient also complained of a few day history of unilateral blurring of vision which turned out to be central retinal artery occlusion.

**Conclusion:** Overlap syndrome is a disease entity to consider in patients with multiple symptoms that cannot be classified into one connective tissue disease. Treatment of this disease should be individualized and based on the connective tissue diseases involved.

**Keywords:** Systemic sclerosis, scleroderma, systemic lupus erythematosus, SLE, overlap syndrome

## Introduction

Overlap syndrome is a large group of condition that manifests with symptoms from two or more autoimmune conditions and satisfies the diagnostic criteria of at least two connective tissue diseases in the same patient.<sup>1,2</sup> This condition might be unrecognized by the primary care physician and its prevalence still not defined locally. We describe here a patient presenting with generalized body weakness and eventually being diagnosed and treated as SLE-scleroderma overlap.

## Case Report

A 30-year-old female, presented with generalized body weakness. There was a 10-week history of non-pruritic erythematous macules on her face that gradually spread to her trunk, and upper extremities in days. No fever, joint pain, decrease in appetite,

or abdominal pain were noted. Over the next two weeks, she noted darkening of her skin and transformation of the generalized erythematous macules to hyperpigmented macules. She started to have ulcerating wounds on her left malleolar area and distal fingers (Figure 1), even with no trauma. Her hair became brittle and would fall easily. This time, relatives noted that the patient had weight loss and pallor. She consulted a private physician who requested for complete blood count revealing low hemoglobin and was prescribed with ferrous sulfate twice a day. Interval history showed persistence of symptoms. She claimed that the hyperpigmented macules increased in number, her complexion further darkened and skin tightened (Figure 2), her hair became scanty and thin with areas devoid of hair, her wounds would dry up but would recur again, but deeper and sometimes with yellowish discharge (Figure 3). Four weeks prior to admission, still with persistence of symptoms, now accompanied by joint pains particularly on the knees and hands, blurring of vision, decrease in appetite, progressive weight loss, generalized body weakness and shortness of breath. She denied fever, cough, headache, vomiting, and chest pain at this time. These symptoms persisted for two weeks, prompting consult in a local hospital in Samar where CBC showed anemia. She was advised further work up. Four days prior to admission, the

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patient decided to go to Manila for work-up. At this time, there was an increase in shortness of breath accompanied by generalized body weakness. She was brought to Cardinal Santos Medical Center and was subsequently admitted. On review of systems, there were no melena, hematochezia or bleeding episodes. Her past medical history was unremarkable and she denied of any vices, or history of illicit drug use.



**Figure 1: Ulceration on the distal fingers**



**Figure 2: Hyperpigmented macules with darkening of the skin, and hair thinning**



**Figure 3: Ulceration on left medial malleolus**

Upon admission, the patient was weak looking, with warm, dry, taut skin and diffuse hyperpigmented

macules. She had scanty, thin and brittle hair, dry lips with fissures on the lateral commissures. Her anterior chest showed hyperpigmented macules (salt and pepper rash). Cardiac examination showed a dynamic precordium with distinct heart sounds and S3 gallop. She had bilateral sclerodactyly and had an ulcerating wound on the left malleolar area, healing wounds on the tip of the fingers. Complete blood count and peripheral blood smear showed anemia, mostly normocytic normochromic RBCs. Reticulocyte count, total and indirect bilirubin were noted to be high. C-Reactive Protein (CRP) was also elevated. 12-lead ECG showed sinus tachycardia, with low voltage QRS in precordial/limb leads. Chest x-ray showed blunting of posterior gutters and cardiomegaly rule out pericardial effusion (Figure 4), hence, a 2D-echocardiogram was requested for further evaluation. This confirmed the presence of a large pericardial effusion with note of pulmonary hypertension.

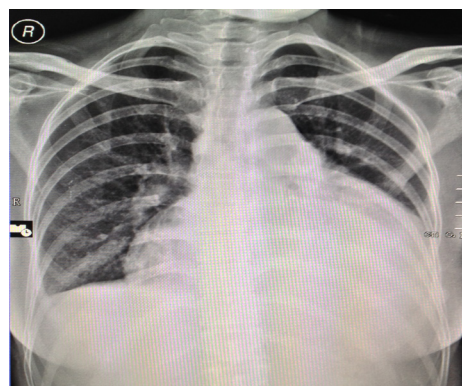


**Figure 4: Chest x-ray showing blunting of posterior gutters and cardiomegaly rule out pericardial effusion**

She was started on prednisone 20mg/tab one tablet twice a day and azathioprine 50mg/tab one tablet daily and was transfused with packed RBC. Despite correction of anemia, the patient had persistent shortness of breath. She was advised pericardiocentesis to relieve the symptom, however, on the sixth hospital day, a repeat 2D-echocardiogram showed significant diminution of pericardial effusion, hence was deferred. Her easy fatigability and shortness of breath gradually improved.

Skin biopsy was performed, and revealed findings consistent with scleroderma (Figure 5). Lupus panel was obtained and the result showed positive results for ANA, anti-SM and anti-Scl70 while anti-SSA, anti-SSB, anti-Jo1, anti-RNP and RF were all negative. Dilated fundus exam showed hypopigmented patches on the macula (Figure 6) hence fluorescein angiography was done revealing central retinal artery occlusion (Figure 7). Patient was discharged on the thirteenth hospital day with prednisone and azathioprine as she went

back home to Iloilo.

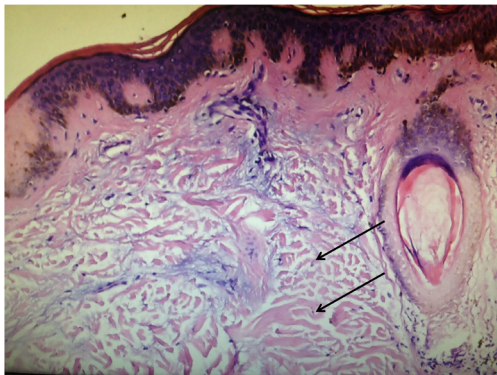


**Figure 5: Histopathology of skin showing excessive deposition of collagen**

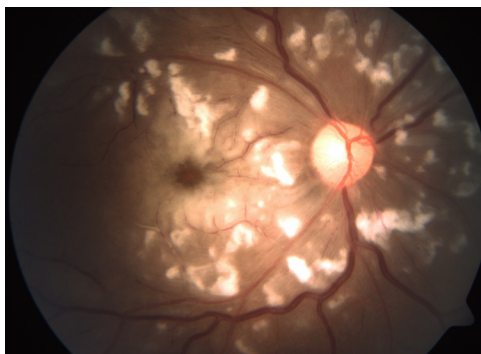


**Figure 6: Dilated fundal examination showing disc neovascularization, multiple cotton wool spots, and marked venous tortuosity**



**Figure 7: Fluorescein angiography showing marked capillary closure, disc neovascularization, and left macular ischemia**

## Discussion

The presence of autoimmune rheumatic diseases may be affected by the interplay of genetic and environmental factors leading to the presence of autoimmune disease and/or their autoantibodies in families, which is the concept of "shared autoimmunity".<sup>2</sup> Hence, the idea of shared

autoimmunity may explain the definition of overlap syndrome.

We are presented with a 30-year old female presenting initially with generalized body weakness, skin tightening, sclerodactyly, ulcerations on the finger tips and pulmonary hypertension on 2D echocardiogram with a positive anti-Scl70 showing a score of 11. The criteria for the diagnosis of scleroderma is shown on (Table II) and a score of >9.0 is definitive of scleroderma.<sup>4</sup> In patients with scleroderma, an abnormal accumulation of extracellular matrix constituents, most notably collagen types I and III, is the most prominent pathological manifestation of the disease in skin. Two stages are recognizable: an early cellular stage and a later fibrotic stage.<sup>3</sup> On the other hand, the patient had hair loss, hemolytic anemia with reticulocytosis, serositis presenting as pericardial effusion, positive ANA and anti-Sm suggestive of SLE.<sup>5</sup> The combination of these signs and symptoms cannot be totally explained by one connective tissue disease. Our patient satisfied the criteria for both the 2013 ACR/EULAR Classification Criteria for Scleroderma and the 1997 American College of Rheumatology revised criteria for SLE<sup>4,5</sup> showing a diagnosis of overlap syndrome rather than a mixed connective tissue disease.

**Table I: 2013 ACR/EULAR criteria for the classification of Systemic Sclerosis (Scleroderma)<sup>4</sup>**

|                                                                                                                          |                                                                                                                        |   |
|--------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|---|
| Skin thickening of the fingers of both hands extending proximal to the metacarpophalangeal joints (sufficient criterion) | -                                                                                                                      | 9 |
| Skin thickening of the fingers                                                                                           | Puffy fingers                                                                                                          | 2 |
|                                                                                                                          | Sclerodactyly of the fingers (distal to the metacarpophalangeal joints but proximal to the proximal phalangeal joints) | 4 |
| Finger tip lesions                                                                                                       | Digital tip ulcers                                                                                                     | 2 |
|                                                                                                                          | Fingertip pitting scars                                                                                                | 2 |
| Telangiectasia                                                                                                           | -                                                                                                                      | 2 |
| Abnormal nailfold capillaries                                                                                            | -                                                                                                                      | 2 |
| Pulmonary hypertension and/or interstitial lung disease                                                                  | Pulmonary arterial hypertension                                                                                        | 2 |
|                                                                                                                          | Interstitial lung disease                                                                                              | 2 |
| Raynaud's phenomenon                                                                                                     | -                                                                                                                      | 3 |
| SSc-related autoantibodies [anti-centromere, anti-topoisomerase I (anti-Scl70), anti-RNA polymerase III]                 | Anticentromere 3<br>Anti-topoisomerase I<br>Anti-RNA polymerase III                                                    | 3 |

We should also investigate all the symptoms of the patient. Here, we are also presented with unilateral blurring of vision which on work-up showed central retinal artery occlusion which is a rare but guarded complication of systemic sclerosis.<sup>6</sup>

Prevalence of SLE-scleroderma overlap is only

1.2% among scleroderma patients and 5.0% among overlap syndromes. SLE-scleroderma combination often has an uncontrolled course and even a fatal outcome.<sup>7</sup> The rational management of overlap connective tissue disease is confounded by the absence of controlled trials. Recommendations for management are based on conventional treatments for each connective tissue disease.<sup>8</sup> For our patient, the patient was very responsive to prednisone and azathioprine which significantly diminished the amount of pericardial effusion.

**Table II: 1997 Update of the 1982 American College of Rheumatology revised criteria for classification of Systemic Lupus Erythematosus<sup>5</sup>**

|                        |                                                                                                                                         |
|------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| Malar rash             | Fixed erythema, flat or raised, over the malar eminences                                                                                |
| Discoid rash           | Erythematous circular raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur               |
| Photosensitivity       | Exposure to ultraviolet light causes rash                                                                                               |
| Oral ulcers            | Includes oral and nasopharyngeal ulcers, observed by physician                                                                          |
| Nonerosive arthritis   | Nonerosive arthritis of two or more peripheral joints, with tenderness, swelling, or effusion                                           |
| Serositis              | Pleuritis or pericarditis documented by ECG or rub or evidence of effusion                                                              |
| Renal disorder         | Proteinuria >0.5 g/d or ≥3+, or cellular casts                                                                                          |
| Neurologic disorder    | Seizures or psychosis without other causes                                                                                              |
| Hematologic disorder   | Hemolytic anemia or leukopenia (<4000/uL) or lymphopenia (<1500/uL) or thrombocytopenia (<100,000/uL) in the absence of offending drugs |
| Immunologic disorder   | Anti-dsDNA, anti-Sm, and/or antiphospholipid                                                                                            |
| Antinuclear antibodies | An abnormal titer of ANA by immunofluorescence or an equivalent assay at any point in time in the absence of drugs known to induce ANAs |

## Conclusion

Overlap syndrome is a disease entity to consider in patients with multiple symptoms not classified into one connective tissue disease. This case shows that SLE-scleroderma overlap is a possible combination and presentation could be different due to clinical diversity. Treatment of this syndrome should be individualized and based on the connective tissue diseases involved.

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