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Title
Overlap syndrome of systemic sclerosis and systemic lupus erythematosus with renal involvement: Case Report

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Author contributions
RS & SP: data collection, preparation of manuscript; SD: preparation of renal biopsy images and preparation of manuscript, MN: preparation of manuscript

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Abstract
Overlap syndrome between systemic sclerosis and systemic lupus erythematosus with renal involvement poses a diagnostic and management dilemma. The delineation between lupus nephritis and scleroderma renal crisis is critical to administer prompt and appropriate treatment. The presence of anti RNA III polymerase antibodies may suggest underlying scleroderma renal crisis. However, it is only on diagnostic renal biopsy that an accurate assessment of the underlying disease process can be made. This case demonstrates the utility of a renal biopsy in an undifferentiated case of overlap syndrome with renal involvement and positive RNA III polymerase antibodies.

Key words
Overlap syndromes, Systemic Lupus Erythematosus, Systemic sclerosis, Lupus nephritis

Background
Overlap syndrome is defined as an entity that satisfies classification criteria for at least two connective tissue diseases (CTDs). Many clinical and serologic markers lack specificity and may be present across several CTDs. The overlap syndrome between systemic sclerosis (SSc) and systemic lupus erythematosus (SLE) is uncommon; however, early recognition allows for the prompt initiation of appropriate management.

Clinical Case

A 55-year-old Malaysian female was referred to hospital by her general practitioner for investigation of anaemia (Hb 70g/L) and a pericardial effusion demonstrated on echocardiogram. She had no significant past medical history and did not take any regular medications. She reported a several month history of peripheral oedema, dyspnoea, skin thickening affecting her hands and feet, as well as Raynaud phenomenon. On examination, there was evidence of sclerodactyly affecting her fingers and toes, not extending beyond her wrists or ankles, with associated fixed flexion deformities. She was hypertensive with a blood pressure of 155/65mmHg.

Her initial presentation was concerning for a scleroderma renal crisis (SRC) and she was promptly commenced on 2.5mg of perindopril. The autoimmune screen revealed a positive ANA, positive U1-RNP antibodies, positive anti-Smith antibodies, raised dsDNA antibody titres, low complement, and positive RNA-polymerase-III antibody (RNAP) (results summarised in table 1). Urine protein/creatinine ratio was elevated at 156 mg/mmol. Renal function was preserved with a creatinine of 44umol/L and GFR>90mL/min/1.73m². A repeat echocardiogram demonstrated a large pericardial effusion without tamponade, and an elevated right ventricular systolic pressure of 60mmHg. A right heart catheter study was performed and was not diagnostic of pulmonary arterial hypertension with a mean pulmonary artery pressure of 22mmHg and pulmonary vascular resistance of 2.02 Woods units.

The combination of clinical signs and positive autoantibodies raised speculation regarding the etiology of the patient’s renal dysfunction. Further treatment of her renal disease was limited by lack of delineation between lupus nephritis (LN) and SRC. The patient proceeded to renal biopsy which demonstrated class II LN. She was subsequently commenced on prednisolone, mycophenolate and hydroxychloroquine. Her blood pressure was closely monitored to ensure evolving SRC was not missed. The patient’s anemia, proteinuria, pericardial effusion and peripheral oedema improved with immunosuppression.

Figure 1 – Renal Biopsy
Renal biopsy (PAS stain at 400x magnification) showing mesangial hypercellularity. This finding along with a full house pattern of immunofluorescence staining are consistent with Class II lupus nephritis

Discussion

In patients with an overlap syndrome of SSc and SLE, with associated renal dysfunction and/or hypertension, it is important to distinguish between LN and SRC. The treatment of each of these manifestations is vastly different and the use of systemic corticosteroids in an attempt to treat suspected lupus renal disease or other systemic manifestations of lupus, may induce or exacerbate an underlying SRC [2]. Anti-RNAP antibodies are known to confer a higher risk of developing SRC [3]. It is uncommon to see a positive anti-RNAP antibody in an overlap syndrome with LN as the cause of renal dysfunction [4]. The wide array of autoantibodies seen in this patient is noteworthy and a known, albeit uncommon, phenomenon in certain cases of CTD with overlapping features [5].

Whilst there may be concern in relation to the potential risk of bleeding complications when biopsies are performed in SRC [6], our case of SSc and SLE overlap syndrome with renal involvement demonstrates the importance of performing a renal biopsy to accurately distinguish between the two possible aetiologies and ensure appropriate treatment is administered.

Table 1: Summary of Patient Blood Results
<table>
<thead>
<tr>
<th>Test</th>
<th>Patient Result</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>C Reactive Protein</td>
<td>25</td>
<td>&lt;5mg/L</td>
</tr>
<tr>
<td>Erythrocyte Sedimentation Rate</td>
<td>94</td>
<td>&lt;20mm/h</td>
</tr>
<tr>
<td>Anti-Nuclear Antibody Titre</td>
<td>&gt;2560 - homogenous</td>
<td>Titre &lt;80</td>
</tr>
<tr>
<td>Anti-Neutrophil Cytoplasmic Antibody (ANCA)</td>
<td>15 (Proteinase 3- ANCA)</td>
<td>&lt;5U/mL</td>
</tr>
<tr>
<td>Anti-double stranded DNA</td>
<td>271</td>
<td>&lt;100IU/mL</td>
</tr>
<tr>
<td>Anti U1 ribonucleoprotein</td>
<td>positive</td>
<td>negative</td>
</tr>
<tr>
<td>Anti-Smith</td>
<td>positive</td>
<td>negative</td>
</tr>
<tr>
<td>Anti Ro</td>
<td>weakly positive</td>
<td>negative</td>
</tr>
<tr>
<td>Anti La</td>
<td>negative</td>
<td>negative</td>
</tr>
<tr>
<td>Anti Scl 70 (topoisomerase)</td>
<td>positive</td>
<td>negative</td>
</tr>
<tr>
<td>Anti Jo</td>
<td>negative</td>
<td>negative</td>
</tr>
<tr>
<td>Anti RNA polymerase III</td>
<td>positive</td>
<td>negative</td>
</tr>
<tr>
<td>Rheumatoid Factor</td>
<td>14</td>
<td>&lt;14</td>
</tr>
<tr>
<td>Anti-Cardiolipin (IgG)</td>
<td>9</td>
<td>&lt;15U/mL</td>
</tr>
<tr>
<td>Anti B2 glycoprotein (IgG)</td>
<td>11</td>
<td>&lt;8U/mL</td>
</tr>
<tr>
<td>C3</td>
<td>0.28</td>
<td>0.90-1.80g/L</td>
</tr>
<tr>
<td>C4</td>
<td>0.03</td>
<td>0.16-0.47g/L</td>
</tr>
<tr>
<td>Anti-centromere A</td>
<td>positive</td>
<td>negative</td>
</tr>
<tr>
<td>Anti-centromere B</td>
<td>positive</td>
<td>negative</td>
</tr>
<tr>
<td>Anti RNA polymerase III (155kDa)</td>
<td>weakly positive</td>
<td>negative</td>
</tr>
<tr>
<td>Anti RNA polymerase III (11kDa)</td>
<td>negative</td>
<td>negative</td>
</tr>
<tr>
<td>Anti Ku</td>
<td>negative</td>
<td>negative</td>
</tr>
<tr>
<td>Anti PM Scl 100</td>
<td>negative</td>
<td>negative</td>
</tr>
<tr>
<td>Anti PM Scl 75</td>
<td>negative</td>
<td>negative</td>
</tr>
<tr>
<td>Anti-Fibrillarin</td>
<td>negative</td>
<td>negative</td>
</tr>
<tr>
<td>Anti NOR 90</td>
<td>negative</td>
<td>negative</td>
</tr>
<tr>
<td>Anti-tyrosine hydroxylase</td>
<td>negative</td>
<td>negative</td>
</tr>
<tr>
<td>Anti PDGFR</td>
<td>negative</td>
<td>negative</td>
</tr>
</tbody>
</table>

References


4) Satoh M, Vazquez-Del Mercado M, Chan EKL. Clinical interpretation of antinuclear antibody tests in systemic rheumatic diseases. *Mod Rheumatol* 2009 **19**: 219-228

5) Murakami K, Mimori T. Recent advances in research regarding autoantibodies in connective tissue diseases and related disorders. *Intern Med* 2019 **58**(1): 5-14


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