Sertraline Induced Systemic Lupus Erythematosus
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Citation

Abstract
Objective: To report the occurrence of drug induced Systemic lupus erythematosus (SLE) with multisystem manifestations in a patient who was initiated on treatment with sertraline.

Case Summary: A 48 year old female presented to the hospital with new onset malar rash, arthralgias and other systemic symptoms after being started on sertraline for management of her depressive symptoms. The work up of her case including history, physical examination and biochemical markers was consistent with the diagnosis of drug induced lupus(DIL). Besides supportive management for her multisystem manifestations, she was started on intravenous steroids for the treatment of the DIL.

Discussion: SLE is a well known multisystem autoimmune disorder. Testing patients' sera for antibodies against specific nuclear antigens along with the patient's history and physical examination help in differentiating the idiopathic form from DIL. Sertraline is a well known selective serotonin reuptake inhibitor and besides a single case report of a 'discoid lupus like' skin eruption, this drug so far had not been incriminated in the pathogenesis of SLE. An objective causality assessment using the Naranjo scale revealed a possible relationship between the development of SLE and sertraline therapy in this patient.

Conclusion: Sertraline can induce a full-blown picture of SLE with multisystem involvement. The use of this drug in patients with pre-existing lupus needs to be further investigated. DIL needs to be in one of the top differentials in mind while encountering a patient with new onset lupus, recently started on sertraline.

INTRODUCTION
Systemic lupus erythematosus (SLE) is a prevalent autoimmune disorder. When a patient presents with features suggestive of SLE, the presence of anti nuclear antibodies (ANA) in the patient's serum is usually used as a screening test. Further testing with antibodies against specific nuclear antigens along with the patient's history and physical examination help in differentiating the idiopathic form from drug induced lupus (DIL). Several drugs such as Hydralazine, Procainamide, Isoniazid and Phenytoin are linked to DIL. The presence of antibodies against double stranded DNA (anti ds-dna) confirms the diagnosis of idiopathic SLE. The presence of antibodies against the histone proteins (anti- histone antibodies) is characteristic for DIL and when accompanied by a history of a newly initiated drug, the presence of pleuro-pericardial manifestations and a normal serum complement level, is further evidence for the diagnosis of the latter. We discuss the case of a woman who presented with the above features and was diagnosed to have DIL secondary to sertraline.

CASE REPORT
The patient was a 48 year old white female with a past medical history significant for hypothyroidism and end stage liver disease secondary to Hepatitis C infection and alcoholism, who came into the emergency room with complaints of generalized weakness accompanied by the sudden appearance of a malar rash 4-5 days ago. On questioning she stated that her problems began after she was started on sertraline for her depressive symptoms about a week ago. She complained of intermittent joint pains over the last few days. She denied symptoms suggestive of focal neurological deficits, similar rash on any other part of her body, dysuria, fever and urethral or conjunctival discharge. Her review of systems was however positive for intermittent, non radiating, stabbing type of a retrosternal chest pain within the last few days unaccompanied by anginal equivalents.
The patient did not have any past medical or family history suggestive of a connective tissue disorder and the rash on her face was new. Her home medications included Furosemide, Spironolactone, Nadolol, Lansoprazole, Levotyroxine and Multivitamin supplements; which she had been on for several years and none of them have been implicated in the development of SLE.

On examination the patient had stable vital signs. There was an erythematous, confluent, macular, malar rash with telangectasia and a fine scale sparing the nasolabial fold, extending across the bridge of her nose. There was no visible oozing or discharge from the region. The rash was non-tender; there was no local rise of temperature and the rash did not blanch with pressure. Her oral cavity was clear to inspection. Her chest was clear to auscultation and there were no cardiac murmurs, rubs or gallops. The rest of her physical examination was normal except for gross hematuria noted in the bedside pan.

Her diagnostics revealed a platelet count of 16,000/cu mm (n = 150,000 to 400,000/cu mm), as compared to her baseline of about 60,000 –70,000/cu mm about 6 months ago; a hemoglobin of 10.4 g/dl (n =12 to 16 g/dl) and a white blood cell count of 5,300/cu mm (n = 4,300 to 10,800 /cu mm). Her basic metabolic panel revealed a serum creatinine of 1.7mg/dL (n = 0.8 to 1.4 mg/dl) as compared to her baseline of 0.9mg/dL. Her ESR was elevated at 97mm/hr (n = 0 to 20mm/hr) by the Westergren's method. Her urine analysis showed evidence of proteinuria and numerous red blood cells. Her serum revealed the presence of ANA in a homogenous pattern with a titer of 1:320, anti histone antibodies with a titer of 41 Units (n = negative) but a negative test for anti DNA antibodies. A direct Coomb's test was found to be positive but eluate studies were found to be negative ,which indicated a drug induced reaction. Patients with drug induced lupus usually present with systemic complaints and have arthralgias, pleuropericarditis, thrombocytopenia and acute renal failure. She presented with these features after initiation of treatment with sertraline. Her platelet count fell remarkably below her baseline and her renal failure was accompanied by the presence of proteinuria and hematuria. The positive direct Coomb's test with negative eluate studies indicated the presence of a drug induced reaction. Patients with drug induced lupus usually present with systemic complaints and have arthralgias and pleuropericarditis in 25-50% of the cases, as did our patient. Her history of recent chest pain in lieu of her EKG findings was suggestive of resolving pericarditis. All of the above features with the presence of ANA and anti Histone antibodies in her serum, the absence of antibodies to ds DNA and a normal serum complement level confirmed the diagnosis of drug induced SLE. An objective causality assessment using the Naranjo scale revealed a possible relationship between the

DISCUSSION

Our patient satisfied the criteria for the diagnosis and classification of SLE as per the guidelines of the American Rheumatism Association. [Table 1].

Figure 1

Table 1: The 1982 Revised ARA Criteria for Classification of Systemic Lupus Erythematosus

<table>
<thead>
<tr>
<th>1. Malar Rash</th>
<th>7. Renal Disorder</th>
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<tr>
<td>2. Discoid Rash</td>
<td>8. Hematological Disorder</td>
</tr>
<tr>
<td>4. Oral Ulcers</td>
<td>10. Immunological Disorder</td>
</tr>
<tr>
<td>5. Arthritis</td>
<td>11. Antinuclear Antibody</td>
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<tr>
<td>6. Serositis</td>
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A person is said to have systemic lupus erythematosus if any 4 or more of the 11 criteria are present, serially or simultaneously, during any interval of observation. Our patient had multisystem manifestations of SLE, namely the presence of the malar rash, arthralgias, hemolytic anemia, pericarditis, thrombocytopenia and acute renal failure. She presented with these features after initiation of treatment with sertraline. Her platelet count fell remarkably below her baseline and her renal failure was accompanied by the presence of proteinuria and hematuria. The positive direct Coomb's test with negative eluate studies indicated the presence of a drug induced reaction. Patients with drug induced lupus usually present with systemic complaints and have arthralgias and pleuropericarditis in 25-50% of the cases, as did our patient. Her history of recent chest pain in lieu of her EKG findings was suggestive of resolving pericarditis. All of the above features with the presence of ANA and anti Histone antibodies in her serum, the absence of antibodies to ds DNA and a normal serum complement level confirmed the diagnosis of drug induced SLE. An objective causality assessment using the Naranjo scale revealed a possible relationship between the
development of SLE and sertraline therapy in this patient.\textsuperscript{17}

The onset of symptoms in DIL may be fairly abrupt with the development of musculoskeletal symptoms or serositis but may appear several months after the initiation of the offending drug. It may be noted that there appears to be a genetic predisposition to DIL determined by drug acetylation rates,\textsuperscript{18, 19} which might have been a predisposing factor in our patient secondary to her advanced liver disease.

**CONCLUSION**

There had been a single case report indicating that sertraline had caused a 'discoid lupus like' skin eruption\textsuperscript{20} but it can be fairly concluded from the above presentation that sertraline can induce a full-blown picture of SLE with multisystem involvement. The use of this drug in patients with pre-existing Lupus needs to be further investigated.

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**References**

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