Seizures in Systemic Lupus Erythematosus Patients

May Azem, Kholoud Al-Khayer, Mandy Corrigan, and Steve Kravec.

**Introduction:** Seizures, generalized or focal, occur in up to 20% of patients with Systemic Lupus Erythematosus (SLE). Psychogenic nonepileptic seizures, known as pseudoseizure, are clinical convulsion without correlation on video recording or electroencephalography (EEG). The incidence of pseudoseizure in SLE has not been previously reported. Distinction between seizures and pseudoseizures in SLE patients is essential giving its potential implication on prognosis and management.

**Objective:** -To analyze the various epilepsy syndromes, including pseudoseizure, in patients with SLE. -To identify clinical or laboratory differences in patients with various epilepsy syndromes.

**Design:** Retrospective chart review.

**Methods:** IRB approval was obtained. Patients were recruited from the Epilepsy Unit at the Cleveland Clinic Foundation by their diagnosis code of epilepsy or pseudoseizure. One hundred and twenty medical records were retrospectively reviewed to include clinical, laboratory, and demographic data. Records were reviewed for SLE symptoms and signs including nephritis, end-stage renal disease (ESRD), presence of antiphospholipid antibodies (APLA), age at onset of seizure (SZ), age at onset of SLE, and seizure type. For the statistical analysis Chi-Square Test was used to compare percentages and testing associations. We considered p values of < 0.05 to be significant.

**Results:** Seventeen (14.2%) patients were diagnosed with pseudoseizure. Forty two out of ninety three patients had positive APLA (valid percent 45.2%) regardless the type of seizure. Thirteen of twenty four patients with focal SZ (88.4 %) had positive APLA compared to two of three patients with generalized SZ (80 %) (P = 0.65). Eleven out of nineteen (77%) with focal seizure had the onset of seizure after the diagnosis with SLE compared to none of three patients (0%) with generalized seizure (P= 0.006).

**Conclusion:** Pseudoseizures do occur in patients with SLE, with a frequency of 14.2%. The association of positive APLA in our patients with SLE and any type of seizure was (45.2%); however we did not find association of APLA with focal seizure. Seizures occurring after the diagnosis of SLE are more likely to be of focal type.
Introduction and Background:

Seizures, generalized or focal, occur in up to 20% of patients with Systemic Lupus Erythematosus (SLE). Seizures may be the first manifestation of lupus or develop during the course of the illness. The exact pathophysiology of seizures in these patients is still unclear but it is a marker for an overall poor prognosis. It may reflect an acute inflammatory episode or old central nervous system (CNS) damage with scarring. Other factors may also contribute including antiphospholipid antibodies (APLA), metabolic disturbances (such as uremia), hypertension, infections, tumors, head trauma, stroke, and medication withdrawal, vasculopathy, or drug toxicity. Seizures in these patients can be treated with a variety of medications depending on the type of seizure whether it is focal or general.

Psychogenic nonepileptic seizures, known as pseudoseizure, are clinical convulsion without correlation on video recording or electroencephalography (EEG). Pseudoseizures should not be treated with regular antiepileptic medications, simply because it won’t work, therefore patients who suffer from this kind of seizures are exposed to unnecessary treatments with potential major side effects. The incidence of pseudoseizure in SLE patients has never been previously reported. Distinction between seizures and pseudoseizures in SLE patients is essential giving its potential implication on prognosis and management.

Antiphospholipid antibodies (APLA) can be present in patients with SLE with even higher occurrence in ones suffering from seizures. It is not clear though whether having positive APLA would affect the type of seizure (focal or general) a patient is at risk of developing. Few previous reports mention that the presence of APLA is a risk for focal type seizure in this population that might imply arterial thrombosis of the affected areas. This is important to identify in these patients for possible prevention with certain medications such as aspirin and or warfarin.

It is also been suggested in the past that onset of seizures relative to the onset of SLE has a factor on the type of seizure. Saying that if seizures occur after the diagnosis of SLE it will be more likely to be the focal type, suggesting a local damage to the brain by the previously existing SLE.
Objectives:

As mentioned above, there are several gaps with unclear or unanswered questions in regards to SLE patients with seizures. Our objectives in this study, based on these gaps, are:

- To analyze the various epilepsy syndromes, including pseudoseizure, in patients with SLE.
- To identify clinical, laboratory or characteristic differences in patients with various epilepsy syndromes, and to test whether they can influence the type of seizure.
- To test whether positive antiphospholipid antibodies is associated more with focal type seizures than general or other types.
- To test if the type of seizure is dependent on whether the onset of seizure was before or after SLE.

Design: Retrospective chart review.

Methods:

Subjects and Definitions:

One hundred and forty four records of subjects with epilepsy (confirmed with video EEG) and pseudoseizure were recruited through the Epilepsy Unit at the Cleveland Clinic Foundation for retrospective review. All of these patients had a possible or definite diagnosis of SLE in their records. Twenty four patients had incomplete or unavailable records so we had one hundred and twenty patients included in the study.

Appropriate IRB approval was obtained from our local IRB office. Patients were recruited from the Epilepsy Unit at the Cleveland Clinic Foundation by their diagnosis code of epilepsy or pseudoseizure. One hundred and twenty medical records were retrospectively reviewed to include clinical, laboratory, and demographic data. Records were reviewed for SLE symptoms and signs including nephritis, end-stage renal disease (ESRD), presence of antiphospholipid antibodies (APLA), age at onset of seizure (SZ), age at onset of SLE, and seizure type.
We reinvestigated all subjects' diagnosis of SLE with the consensus of a senior rheumatologist and using as a guide the 1982 revised ACR criteria. (ACR= American College of Rheumatology) Patients were defined with “definite” SLE if they met at least four or more of the ACR criteria or if they were diagnosed by a rheumatologist as long as their clinical and serological manifestations were clearly described. Patients who did not fulfill the criteria but had symptoms or signs highly suggestive for SLE and still might have SLE in their future were labeled as probable SLE.

**Data Entry and Statistical Analysis:**
We used SPSS for data entry and for the analysis. All patients’ personal identifiers were removed for privacy. All our variables were categorical. For the statistical analysis we used Chi-Square Test to compare percentages and test associations. We also used a logistic regression model to check for important factors affecting the type of seizures, using the type of seizure as the dependent variable (focal or general) and the other patients’ characteristics as the independent variables in the model. We considered p values of < 0.05 to be significant.

**Results:**

**Patients’ Descriptive:**
We had in our studied group one hundred and six females (89.1%) and thirteen males (10.9%). Of them thirty (28%) were African American and sixty three (58.9%) were Caucasian. Mean age at diagnosis of seizure was 28.6 +/-15.9 (range 3-71) and mean age at diagnosis of SLE was 29.1 +/-13.4 (range 9-64). Death occurred in twenty one patients (20.2%). Forty four patients (47.3%) had glomeluronephritis (GN) and twenty four (25.8%) had end-stage renal disease (ESRD) on hemodialysis. Forty two (45.2%) patients had positive anti-phospholipid antibodies (APLA) and twenty four (25.8%) had negative APLA with twenty seven (29%) patients with unavailable levels.
**Seizures types:**
Twenty eight (23.3%) patients had focal seizure, five (4.2%) had generalized seizure, seventeen (14.2%) had pseudoseizure and seventy (58.3%) had an unknown type of seizure.
The onset of SLE was before the onset of seizure in twenty seven (46.6%) patients and in twenty three (39.7%) patients the onset of seizure preceded the diagnosis of SLE.

**APLA and Type of Seizures:**
Forty two out of ninety three patients had positive APLA (45.2%) regardless the type of seizure. Thirteen of twenty four patients with focal SZ (88.4 %) had positive APLA compared to two of three patients with generalized SZ (80 %)  (P = 0.65).

**Relationship between onset of seizure, before or after SLE and type of seizure whether focal or generalized:**
Eleven out of nineteen (77%) with focal seizure had the onset of seizure after the diagnosis with SLE compared to none of three patients (0%) with generalized seizure (P= 0.006).

**Type of seizure and relation with other characteristics:**
We found no significant relation between the type of seizure and each of race, sex, glomeluronephritis, end-stage renal disease and +APLA.

**Conclusion:**

Pseudoseizures do occur in patients with SLE, with a frequency of 14.2% as seen in our sample. This is the first report about SLE patients suffering from pseudoseizures. We hope there will be further research into the possible reasons and risk factors for developing those kinds of seizures so we can offer better and more appropriate treatments.

The association of positive APLA in our patients with SLE and any type of seizure was (45.2%); which is a lot higher than SLE patients not suffering from seizures (historic control), however we did not find an association between positive APLA and focal seizure.
This might be due to the limitations of our study, so a significant association might still exist in reality but we failed to show its significance.

Several limitations and bias are present in our study, mainly the retrospective design with its major disadvantages and the amount of missing and unknown values. There was no selection bias in our opinion since the studied group was required to be very specific by our definitions so this would not have affected the prevalence or the results.

Finally we found that seizures occurring after the diagnosis of SLE are more likely to be of focal type. This support the previous reports about SLE causing local brain scars or damage that can be the trigger for focal seizures. More research in this area is needed along with imaging techniques like MRI (Magnetic Resonance Imaging) and Transcranial Doppler to find more about the lesions or abnormalities more common in this population.

References:


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<td><strong>Total</strong></td>
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<td><strong>Sex</strong></td>
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<tr>
<td>Male</td>
<td>13 (10.9%)</td>
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<td><strong>Race</strong></td>
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<td>Caucasian</td>
<td>63 (58.9%)</td>
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<td><strong>Age</strong></td>
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<tr>
<td>At diagnosis of seizure</td>
<td>Mean 28+/-11.5 (3-64)</td>
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<tr>
<td>At diagnosis of SLE</td>
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<tr>
<td><strong>GN</strong></td>
<td>Present</td>
<td>44 (47.3%)</td>
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<td>24 (25.8%)</td>
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<td>Generalized</td>
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<td></td>
<td>Pseudoseizure</td>
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<td>Unknown type</td>
<td>70 (58.3%)</td>
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<td></td>
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<td>23 (19.2%)</td>
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<td><strong>APLA</strong></td>
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<td></td>
<td>Negative</td>
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Table 1: General Description of our sample