SYSTEMIC LUPUS ERYTHEMATOSUS-LIKE SYNDROME AMONG EPILEPTIC PATIENTS

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ABSTRACT

It is quite known that 18% of systemic lupus erythematosus (SLE) develop seizures. The aim of this study was to detect the epileptic patients who developed drug-induced lupus (DIL) and to identify the criteria of such patients who are liable to develop SLE-like syndrome. Over 6 months, 163 epileptic patients were followed up by the Neurology Clinic of Al-Azhar University Hospitals.

Among them only seven patients were found to develop DIL. Those patients were all females ranging from the second to fourth decades of life. More than 85% of DIL cases had generalized seizures. The latter finding was statistically significant in developing DIL. The EEG pattern was normal in 57% of cases who had positive antinuclear antibodies (ANA), antiribonuclease antibodies (ADA), antihistone antibodies (AHA), anticardiolipin (ACL) and antiphospholipid (APL).

Most antiepileptic drugs e.g. phenytoin, carbamazepine and valproate had the potentiality to induce SLE that improved greatly on drug withdrawal and adding prednisolone 40 mg daily. This study concluded that female epileptic patients aged 20-40 years having generalized seizures of more 5 years duration are liable to develop DIL.

INTRODUCTION

It is quite known that 18% of patient suffering from systemic lupus erythematosus (SLE) develop different neurological deficits (Sibley et al.,
Among them 6% have some sort of seizure events. On the other hand, it was observed that some patients who are proved to have epilepsy develop SLE manifestations, which could be explained on disease pathogenesis or drug-induced bases. Anyhow, most central nervous system (CNS) events are self-limited, reversible and not associated with poor outcome unless accompanied by multisystem disease activity.

Approximately 10% of patients with SLE develop epileptic seizures (Aaril et al., 1993) Long-term treatments with antiepileptic drugs may precipitate SLE or epilepsy and both may occur as manifestations of genetically determined predisposition.

Some patients develop IgA deficiency during phenytoin treatment. This condition is reversible and IgA becomes normalized when phenytoin is withdrawn (drug-induced IgA deficiency). It is possible that the relationship between epilepsy and immune disturbance is related to common genetically determined susceptibility.

It was reported (Formiga et al., 1998) that some patients had antecedents of epilepsy that were not attributable to a cause other than SLE. Epileptic seizures are mainly generalized. A finding of antiphospholipid antibodies (Toubi et al., 1995) (APLA) is associated strongly with the inactive CNS/SLE patients. CNS disease in SLE is significantly associated with the presence of APLA. CNS manifestations can occur in about half of SLE patients without any other evidence of lupus activity. To determine whether the occurrence of seizures is correlated to the presence of serum APLA in SLE patients Herranz et al. (1994) reported that epilepsy, as a primary neuropsychiatric event is significantly associated with moderate to high titer anticardiolipin (ACL) in SLE patients. Their results suggested that APLA could have a role in the etiopathogenesis of SLE. APLA was also associated with venous and arterial thrombosis (Golstein et al., 1993) in SLE patients. APLA syndrome can be associated with neuro-ophthalmological manifestations of SLE, regardless of whether or not the mechanism of neurological involvement is thrombotic. SLE patients with APLA may be at risk for future neurological manifestations.

Twenty-one cases with epilepsy, that was not attributed to any causes other than SLE, were identified (Liou et al., 1996) after being followed up for 5 years. Epilepsy as a primary neuropsychiatric event among lupus patients is associated with a high titer of ACL antiphospholipid.
syndrome (Sachse et al., 1995). An elevated amount of ACL IgG was significantly associated with spontaneous abortion, thrombocytopenia, livido reticularis and positive direct Coomb’s test but not with CNS diseases such as epilepsy and psychosis.

SLE –like symptoms developed associated with positive antinuclear antibody (ANA) two weeks after administration of carbamazepine (CBZ) (Kanno et al., 1992). Similarly drug-induced SLE was described by Boon et al. (1992) on giving CBZ prescribed for epilepsy. The symptoms disappeared when CBZ was replaced by oxcarbazepine. With a simple decision scheme on serological findings, differentiation between idiopathic SLE and drug induced SLE is possible.

After one year of treatment with valprote (Gilgli et al., 1996), patients develop arthralgia muscular weakness, fatigue and fever associated with high titer of ANA giving he pattern of drug-induced SLE. This criterion was supported by detection of anti-histone antibodies. When valprote dosage was tapered and discontinued, resolution of clinical and immunological as well as hematological signs of SLE took place.

**METHODS**

This study was based on descriptive criteria of patients who developed symptoms and signs of SLE. We collected the data of all epileptic patients who were being followed up in the Out-patients of the Neurology Department of the General Hospital over a period of 6 months. We then examined all epileptic patients for any sign of SLE. Those patients who had clinical and laboratory evidences of SLE were selected for demographic, clinical and biochemical evaluation using antinuclear antibodies (ANA) anti-histone antibodies (AHA) anti Deyoxyribose antibodies (ADA) anti cardiolipin antibodies (ACL) antiphospholipid (APL) and erythrocyte sedimentation rate (ESR). Both groups epileptic and antiepileptic induced lupus (AEIL) groups were compared regarding age gender type of epilepsy, EEG changes, duration of epilepsy and drug used.

**RESULTS**

Over six months duration, 163 epileptic patients were followed up at the Neurology Outpatient Clinic for regular visits. Out of those patients, seven developed symptoms and signs of drug-induced SLE. All seven cases
demonstrated laboratory evidences of being positive to ANA, AHA, ADA, ACL, APL and high ESR.

Both groups were compared, tabulated and statistically correlated to each other to identify the risk factors of developing drug-induced SLE. The DIL group was all females (table 1). While epileptic patients ranged from the age of the first to the sixth decades, the DIL group was restricted to the second to the fifth decades (table 2).

Table (1): Gender.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPI group</td>
<td>104</td>
<td>52</td>
</tr>
<tr>
<td>DIL group</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>104</td>
<td>59</td>
</tr>
</tbody>
</table>

p<0.001.

Table (2): Age distribution by decades.

<table>
<thead>
<tr>
<th>Age</th>
<th>First</th>
<th>Second</th>
<th>Third</th>
<th>Forth</th>
<th>Fifth</th>
<th>Sixth</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPI group</td>
<td>13</td>
<td>27</td>
<td>52</td>
<td>39</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>DIL group</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>28</td>
<td>55</td>
<td>41</td>
<td>15</td>
<td>11</td>
</tr>
</tbody>
</table>

p<0.5.

The type of seizures was mainly partial in the epileptic group (62%) whereas it was generalized in (86%) of the DIL group (table 3). The duration of epilepsy ranged from less than 5 years in 72% of cases and it was only 25% in the DIL group in the same duration of epilepsy (table 4). Normal EEG findings were detected in 17% of epileptic patients and in 57% of the DIL group (table 5). Most antiepileptic drugs used were phenytoin, carbamazepine and valprote, and so are indulged in the pathogenesis of DIL with no statistical difference (table 6).

Table (3): Type of epilepsy.

<table>
<thead>
<tr>
<th>Type</th>
<th>Partial</th>
<th>Generalized</th>
<th>Unclassified</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPI group</td>
<td>97</td>
<td>51</td>
<td>8</td>
</tr>
<tr>
<td>DIL group</td>
<td>1</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>98</td>
<td>57</td>
<td>8</td>
</tr>
</tbody>
</table>

p<0.01
DISCUSSION

Some patients who were treated for seven years with phenytoin developed malar rash and laboratory evidence of leucopenia and high titer of anti ds-DNA antibodies giving the pattern of SLE. Symptoms and signs of drug induced SLE disappeared immediately on receiving 40 mg of prednisolone daily. On the other hand, seizures are known to be one the first manifestations of SLE. Such cases could be diagnosed as SLE and thought of that the epileptic seizure that developed seven years ago had been the first manifestations of SLE. In a prospective study of neurological manifestations in all patients with SLE, two patients experienced seizures whereas cerebral psychosis was a relatively rare presentation in such patients with SLE.

In patients who present with a neurological problem, efforts should be made to ascertain the underling cause, especially if this may be an infection. Almost 86% of our drug induced SLE had generalized convulsions. Our finding was in favor of Formiga et al. (1996) who found a similar figure since generalized seizures were experienced by 87% of their cases. All our DIL cases showed positive ANA, AHA, ADA, ACL and
APL. No association was found between positive APL and epilepsy indicated with SLE. On the other side, Liou et al. (1966) indicated that epilepsy, as a primary neuropsychiatric event among lupus patients is associated with a high titer of ACL antibodies. The later finding was confirmed by Toubi et al. (1995) who reported that epilepsy in systemic lupus erythematosus was significantly associated with the presence of APL antibodies.

Anticardiolipin antibodies (ACL), one of a group of antiphospholipid antibodies, which may occur in association with SLE and are less commonly, detected in other diseases.

Anticardiolipin antibodies could be found in epileptic patients without SLE while our findings revealed restriction of ACL antibodies to epileptic patients who developed DIL.

All antiepileptic drugs without significant difference could induce an SLE pattern. Gigli et al. (1996) as well observed this finding. Anyhow, gradual withdrawal of antiepileptic drugs induced clinical remission. Normal EEG pattern was seen in 57% of our DIL patients. To the contrary, Glanz et al. (1998) identified 80% of cases having left hemispherical abnormalities of 478 cases they studied. Our temporal lobe abnormalities were shown in 43% of 7 cases we studied our result was not statistically significant due to small studied sample.

MRI findings were detected more in patients with clinically focal CNS lupus than in patients with seizures or patients without clinically localized finding. Cerebral MRI proved to be the method of choice for the non-clinical diagnosis of neuropsychiatric SLE. Unfortunately our study missed this tool in diagnosing such cases.

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**SLE-Like Syndrome in Epileptics**

Dahab & Abul-Ela

**شبيه الذنبة الحمراء لدى مرضى الصرع**

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من المعروف أن 18% من مرضى الذنبة الحمراء قد يصابون بنتيجة صرعية. كان الهدف من وراء إجراء هذا البحث هو الكشف عن مرضى الصرع الذين يصابون بشبيه الذنبة الحمراء ودراسة حالاتهم. فعلى مدار 6 أشهر تم متابعة 163 مريض بالصرع من خلال عيادة الأعصاب. أصيب منهم فقط 7 مريض ذنبة الحمراء وكانوا كلهم إناث تتراوح أعمارهم بين العقدتين الثانية والرابعة.

فكان أكثر من 85% من الحالات تعاني نوبات صرعية عامة مما له دلالة إحصائية هامة.

كانت فترة الاصابة بالصرع التي تزيد على 5 سنوات ذات مؤشر إحصائي هام في ظهور شبيه الذنبة الحمراء. وكان تخطيط كهربائية الدماغ (رسم العين) طبيعيا في 57% من الحالات. كما أوضحت الاختبارات المعملية إصابة كل مريض شبيه الذنبة الحمراء بالأجسام المضادة للحمض النووي، والريبوسوكينوز، والنيسترون والكارديويلين والفسفولين.

انتهت النتائج إلى أن المقايير مضادات الصرع كاليتارتيتوين والكارابازين والكاتبوبين والفاترومات لها القدرة على توفير الاستعداد للاصابة بمرض الصرع شبيه الذنبة الحمراء التي غالبا ما تستجيب للشفاء بالوقت المفتوح عن تعاطي مضادات الصرع. وrack 40 مجم يوميا من الكوريتيلين عن طريق الفم، ووصفت الدراسة في النهاية أن الإناث المصابات بالصرع التي تتراوح أعمارهن بين عشرين وأربعين عاما ويعانون من نوبات صرعية عامة لمدة تزيد لديهم الاستعداد للإصابة بشبه الذنبة الحمراء.