Cerebellar ataxia in systemic lupus erythematosus: three case reports

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SUMMARY Three patients presented with cerebellar ataxia among 350 cases of systemic lupus erythematosus (SLE) seen over the last 14 years. Cerebellar signs were unilateral in one and bilateral in the other two patients. Other neurological findings were present in all three patients. One initially presented with only cerebellar ataxia; other features of SLE appeared a few years later. Lupus anticoagulant test was positive in one patient. Corticosteroids given in the early stages appeared to benefit these patients by ameliorating cerebellar dysfunction.

Key words: neuropathy, radiculopathy, deafness, diplopia, lupus anticoagulant, central nervous system.

Case reports

Case 1

A 14 year old girl developed symmetrical non-deforming polyarthritis and fever in December 1983. In August 1985 she also developed alopecia, anorexia, and bleeding from the rectum. There were no other significant findings on general examination. Investigations showed normal blood counts, normal urine analysis, and positive antinuclear antibody in high titres (379 IU/ml). Bleeding and coagulation profile showed prolonged activated partial thromboplastin time (APTT), Russell’s viper venom time (RVTT), and kaolin clotting time (KCT) (Table 1).1 2 A diagnosis of SLE was considered likely. She improved with chloroquine phosphate (250 mg daily) and non-steroidal anti-inflammatory drugs (NSAIDs) over the next three months.

In November 1985 she complained of unsteadiness of gait and difficulty in walking, with exacerbation of fever, polyarthritis, oral ulcers, and alopecia. All drugs (chloroquine and NSAIDs) were withdrawn. After two weeks she deteriorated with marked ataxia (truncal and limbs), nystagmus, and diplopia. Complete blood counts, blood urea, sugar, serum transaminases, alkaline phosphatase, electrocardiogram, chest and skull radiographs were normal. Urine analysis showed proteinuria (0.46 g/24 h). Antinuclear antibody test was positive (500 IU/ml),

Table 1 Coagulation profile of patient 1

<table>
<thead>
<tr>
<th></th>
<th>Patient</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count/l</td>
<td>240×10⁹</td>
<td>150-450×10⁹</td>
</tr>
<tr>
<td>Bleeding time (min)</td>
<td>3–5</td>
<td>2–4.5</td>
</tr>
<tr>
<td>Prothrombin time (s)</td>
<td>13</td>
<td>10–14</td>
</tr>
<tr>
<td>Prothrombin consumption index (%)</td>
<td>43</td>
<td>0–30</td>
</tr>
<tr>
<td>Activated partial thromboplastin time (APTT) (s)</td>
<td>47</td>
<td>35–45</td>
</tr>
<tr>
<td>Russell’s viper venom time (RVTT) (s)</td>
<td>21</td>
<td>11–15</td>
</tr>
<tr>
<td>RVVT with inosinith (s)</td>
<td>12</td>
<td>8–13</td>
</tr>
<tr>
<td>Kaolin clotting time (KCT) (s)</td>
<td>176</td>
<td>58–120</td>
</tr>
<tr>
<td>Mixing pattern with KCT</td>
<td>Type 1*</td>
<td></td>
</tr>
</tbody>
</table>

*Prolonged KCT with the patient’s plasma could not be corrected by addition of normal plasma.
C3 and C4 values were low (460 and 120 mg/l; normal 700–1200 and 200–500 respectively), and C reactive protein was normal. Computed tomography scan of the head was normal. Cerebrospinal fluid examination showed sugar 600 mg/l, protein 300 mg/l, no cells, and IgG 90 mg/l (normal 20–24). The electroencephalogram (EEG) showed dysfunction of the posterior right hemisphere, suggesting the origin of epilepsy from the same area with generalisation. She was treated with prednisolone 30 mg daily with improvement over the next month.

In March 1986, while receiving prednisolone 2-5 mg daily and chloroquine, she noticed the sudden onset of tinnitus and partial deafness, which gradually improved over four days. About three weeks later this recurred, then subsided gradually in a week. When examined a week later there were no signs except mild ataxia. Auditory brain stem and visual evoked responses were normal.

She remained well with prednisolone 5–10 mg daily, though serological activity (low C3, C4 concentrations, and high antinuclear antibody and anti-dsDNA titres) persisted. In January 1987 she developed an episode of intractable vomiting, abnormal behaviour, and dizziness, which improved after about two weeks without any specific treatment. At present she is asymptomatic.

No other associations of the lupus anticoagulant—for example, venous or arterial thrombosis, thrombocytopenia, pulmonary hypertension, positive Coombs’ test, etc—were seen in the follow up.

CASE 2
A 34 year old unmarried woman was admitted in 1971 at the age of 18 years with a diagnosis of idiopathic cerebellar degeneration. Detailed clinical evaluation and investigations, including pneumoencephalogram and cerebrospinal fluid examination, did not show any abnormality. Her erythrocyte sedimentation rate was 32 mm/1st h. A few months later she developed tingling and numbness in both legs, which was diagnosed as peripheral neuropathy. In 1973 she had a left sided pleural effusion and fever, for which she was given antituberculous treatment and corticosteroids; she subsequently improved. In 1978 she developed pneumonia of the right middle zone, associated with polyarthritis, oral ulcers, and fever. In 1979 she had a photosensitive facial rash. In 1981 she developed a pleural effusion on the right with fever, which responded to aspirin and corticosteroids.

In 1983 evaluation showed features of bilateral cerebellar ataxia, mild peripheral neuropathy in the legs, photosensitive erythematous skin rash, alopecia, anaemia, proteinuria, and pneumonitis of the right lower zone. The antinuclear antibody titre was positive (speckled pattern 1/500). Other investigations included a positive LE cell test, non-reactive Venereal Disease Research Laboratory test, negative Coombs’ test and rheumatoid factor, normal C3 and C reactive protein concentrations. She responded well to prednisolone 40 mg and chloroquine phosphate 250 mg daily. She remained well with prednisolone 7.5–10 mg daily until April 1984, when she developed hypertension and recurrence of fever.

When last seen in October 1987 she continued to have cerebellar signs (mild ataxia and nystagmus), mild occasional fever, alopecia, Raynaud’s phenomenon, anaemia, and depression. Investigations showed a positive antinuclear antibody test (100 IU/ml), antibody to nRNP, normal C3 and low C4 concentrations, negative lupus anticoagulant, and mild proteinuria.

CASE 3
A 20 year old girl presented in August 1987 with fever and non-deforming polyarthritis (two years), malar rash, alopecia and Raynaud’s phenomenon (six months), headache and severe pain in the left lower leg with paraesthesiae (15 days), tingling and numbness in the right foot, tremors in the left arm, unsteadiness of gait, and clumsiness in picking up objects with the left hand (four days). Her grandmother had definite rheumatoid arthritis. Examination showed cerebellar signs on the left side, more in the arm, and diminution of touch (15% in S1 and L5 areas), pain (90% in S1 area), joint position (lost in big toe), and vibration sensation (lateral malleolus) on the right side.

Investigations showed a positive antinuclear antibody test (300 IU/ml, speckled pattern), positive anti-dsDNA (1/40 by passive hemagglutination), C3 320 mg/l, C4 160 mg/l; normal urine analysis, blood counts, liver and renal functions; negative lupus anticoagulant and raised cerebrospinal fluid protein (560 mg/l) and globulin. EEG, auditory brain stem and visual evoked responses were normal. Nerve conduction studies showed slowing of motor nerve conduction velocity in the right leg (posterior tibial, common peroneal), markedly prolonged F wave latency in the right leg, no response in the left leg, absent H reflex on both sides, compatible with bilateral multiple root involvement. Computed tomography scans of brain and lumbosacral spine were normal.

She was treated with prednisolone 30 mg daily and carbamazepine 600 mg in divided doses. Her cerebellar symptoms gradually subsided, but she continued to have root pains till her last visit (November 1987).
Discussion

Although neuropsychiatric manifestations are very common (up to 75%) in SLE, cerebellar dysfunction has rarely been described.3–8

The sudden onset of nystagmus, ataxia, and other cerebellar signs in our patients suggested cerebellar involvement. The clinical and laboratory findings suggested that SLE was the most likely cause of this. Moreover, EEG abnormality and an episode of tinnitus and deafness in case 1, peripheral neuropathy in case 2 and radiculopathy in case 3 suggest a more generalised involvement of the nervous system.

A variety of mechanisms have been suggested as possible pathogenetic factors in central nervous system involvement in SLE.9,10 Lupus anticoagulant and anticardiolipin antibody have been found to be associated with various neurological manifestations.10–13 The mechanism of central nervous system involvement by this factor is not well understood. Gurani et al and Lafer et al have explored the possibility of cross reaction of antiphospholipid antibodies with epitopes on central nervous system phospholipids like sphenoglycan.9,14,15 In case 1 APTT, RVVT, and KCT were prolonged, and type 1 KCT mixing pattern suggested the presence of lupus inhibitor.1 The presence of lupus anticoagulant in one of these patients suggests that this factor might have been operating through one of the previously proposed mechanisms.15,16 Further investigations are required to elucidate the role of these antibodies in various central nervous system disorders.

Corticosteroids given at presentation seemed to ameliorate the cerebellar signs in cases 3 and 1, while the residual cerebellar dysfunction seen in case 2 might have been due to starting treatment late.

Clearly, patients presenting with cerebellar dysfunction of no obvious cause, and especially those with features of systemic immunoinflammation, should be investigated for SLE.

References

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