Unsuccessful treatment of subacute sclerosing panencephalitis treated with transfusion of peripheral blood lymphocytes from an identical twin

Subacute sclerosing panencephalitis (SSPE) is a rare and invariably fatal illness of childhood. Because of its association with various immunological abnormalities immunotherapy has been attempted in the past. We report our experience with a case of SSPE in one of two identical twins in whom treatment with transfusion of lymphocytes from the healthy twin failed.

The patient, a 19 year old girl, presented with a ten months history of involuntary movements, mental deterioration and personality change. The onset of her symptoms was insidious and there were no fever, rash, aches or other symptoms at any stage of her illness. Her initial symptoms were brief, sudden jerky movements of the limbs. A few weeks later she became forgetful, emotionally labile and incontinent of urine. The involuntary movements also increased in frequency and severity and spread to involve the face. Over the following few months her mental function progressively deteriorated and she became childish and also increasingly dependent on others for daily living activities.

She had uncomplicated measles in early childhood but was otherwise healthy. Her family history was non-contributory. The patient had an identical twin sister.

When seen at our hospital 10 months after her initial symptoms she had marked intellectual deterioration to the extent that a formal assessment of mental function was not possible. There were repetitive cries and utterances and stereotyped myoclonic jerks. Her tendon reflexes were symmetrically brisk in all limbs and both plantar responses were extensor. There were also multiple spider naevi. The rest of the physical examination was unremarkable.

Routine investigations were normal. EEG demonstrated repetitive stereotyped high voltage delta activity which occurred every 6–7s and was synchronous with the involuntary movements, findings which are typical of SSPE. A brain CT scan was normal. CSF protein was 0.26 g/l with normal cells and glucose. Oligoclonal bands were detected in the CSF. The CSF IgG percentage of total protein was 28.2% and IgG/albumin index was 2.48 (normal value is <10% and 0.22–0.66, respectively). Measles antibody titre was 1:2048 in CSF and 1:32 in serum. Peripheral blood lymphocytes (PBL) subsets were normal (table). The patient was transfused with 300 ml of PBL from her healthy ABO and HL A identical twin sister. This procedure was repeated three days later. Serial EEG’s following transfusion were similar to that at presentation. Repeated CSF examinations following transfusion were also similar to the pre-treatment values but PBL subsets measurements showed a significant reduction in total T lymphocytes and also in T helper cells (table). Despite treatment, the patient’s condition continued to deteriorate and she died five weeks later.

Life-long persistence of the measles virus

Table: Peripheral blood lymphocyte subsets before and after treatment

<table>
<thead>
<tr>
<th>PBL</th>
<th>Total T</th>
<th>T(H)</th>
<th>T(S)</th>
<th>B</th>
<th>NK</th>
<th>Protein</th>
<th>IgG</th>
<th>IgG/albumin</th>
</tr>
</thead>
<tbody>
<tr>
<td>71</td>
<td>64</td>
<td>48</td>
<td>39</td>
<td>23</td>
<td>54</td>
<td>11</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>74</td>
<td>43</td>
<td>29</td>
<td>36</td>
<td>16</td>
<td>16</td>
<td>10</td>
<td>8</td>
<td>0.26</td>
</tr>
<tr>
<td>54</td>
<td>31</td>
<td>24</td>
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<td>10</td>
<td>10</td>
<td>8</td>
<td>8</td>
<td>0.16</td>
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<tr>
<td>28</td>
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<td>20</td>
<td>16</td>
<td>16</td>
<td>16</td>
<td>9</td>
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in SSPE is well recognised but the reason for this is not clear. An attractive hypothesis is that a defect in immune mechanisms accounts for this phenomenon. In a detailed study of a large group of children with SSPE, Behan and Behan have demonstrated a subtle abnormality of PBL protein synthesis in these patients. This abnormality appears to be an intrinsic defect of lymphocytes which is not due to the presence of blocking factors or an abnormality of phyohaemagglutinin receptors and is probably caused by the persistent measles virus. A similar abnormality of lymphocytes was noted in patients with the measles virus. A similar abnormality of lymphocytes has led to a new understanding of the pathogenesis of SSPE has led to many unsuccessful attempts to stimulate or suppress the immune function. These included thymectomy, use of transfer factor, interferon and plasma exchange. Our experience with transfusion of lymphocytes in this case adds more evidence that the presently available immunotherapy is of no value in SSPE.

AMO BAKHEIT
PO BEHAN
Department of Neurology
University of Glasgow
Southern General Hospital
Glasgow G51 4TF, UK


Peripheral neuropathy as a complication of neuroleptic malignant syndrome

Neuroleptic malignant syndrome (NMS), an idiosyncratic reaction to treatment with neuroleptic drugs, is characterised by diffusely increased muscle tone, altered consciousness, hyperthermia and instability of the autonomic nervous system. 1 Only three cases of polyneuropathy in patients with NMS are known, one with unequivocal demyelinating 2 and two with no accurately classifiable neuropathy. 3 We report a patient with NMS complicated by peripheral neuropathy.

A 35 year old woman presented with severe rigidity and a temperature of 42.5°C after four weeks of treatment for hypomania with haloperidol and procyclidine and later, because of disabling Parkinsonian symptoms, sulpiride. On admission to the intensive care unit she was alert and cooperative but unable to move, phonate, swallow saliva or cough. Her mental state was affected by the rigor. On admission there was a marked Parkinsonian tremor, reflexes were brisk and symmetrical. Apart from a well demarcated decubital ulcer on the right heel examination revealed no obvious focus of infection (E coli was grown from urine culture and staphylococcus aureus from the heel swab; the white cell count was elevated to 13.5 × 10⁹, but blood cultures were negative). The creatinine kinase was elevated to 600 IU/l; other investigations including arterial blood gases, chest radiograph and routine biochemistry were unremarkable.

Although treatment with broad spectrum antibiotics, bromocriptine and dantrolene led to some improvement in muscle tone, her pyrexia only resolved when she was paralysed and ventilated and pneumonitis developed five days after admission. When paralysis was reversed 48 hours later pyrexia and rigidity recurred, but then the patient displayed active resistance and catatonic posturing instead of Parkinsonian rigidity. This responded well to a series of three electroconvulsive shocks and two weeks after admission she was well enough to be transferred to a medical ward.

Her mental state and muscle tone were now normal, she was able to speak a few words and she soon managed to swallow liquids. All her muscles ached, she was unable to lift her limbs from their resting position and her movement was painful. There was generalised wasting of all muscle groups and tendon reflexes were difficult to elicit. The power in her limbs slowly improved, but four weeks after admission she was still too weak to stand. After six weeks she complained of pain in her right foot. Examination showed footdrop with loss of the ankle jerk and sensation to pinprick in a stocking like distribution and a few days later similar symptoms occurred on the left side. Her weakness gradually resolved, but the paraesthesia in the right foot as well as the footdrop persisted. Fifteen weeks after admission she was independently mobile and discharged home.

Neuropathological studies were first performed 14 weeks after admission. Muscle compound potentials from the small foot muscles were absent or very reduced in amplitude (0.4 mV). Motor conduction velocity was normal where measurable (nerve fibre 45 m/s). Sensory nerve action potentials were normal or of reduced amplitude (3 mV). Sensory nerve conduction velocity was within normal limits (sural nerve 36 m/s). Fibrillations and positive sharp waves were present at rest and a reduced amount of motor unit action potentials were recorded on electromyography (EMG) in the peripheral muscles of both legs, but were more prominent on the right side. Repeat neuropathological studies three months later showed an improvement. However, there were still signs of denervation in both lower limbs and the right sural sensory nerve action potential was absent.

This is the first report of peripheral neuropathy of NMS, where the neuropathy was not complicated by other neuroleptic abnormalities. NMS is characterised by catatonia, delirium and muscle rigidity. Axonal neuropathy was first recognised as a complication of critical illness by Rivner et al 4 and Roelofs et al 5 in 1983 and was fully described by Bolton et al in 1984 6 who subsequently reported 19 cases. 7 Neuropathy was initially suspected because of failure to wean patients from ventilation and the diagnosis was then made by EMG or necropsy examination. Unifying features were onset about one month after admission to the intensive care unit, with areflexia, septicaemia, high pyrexia, multiorgan failure, treatment with multiple antibiotics and, in the nine survivors, complete resolution of the neuropathy within three to six months. No specific aetiological agent could be identified, and a circulating toxin as the cause of both multiple organ failure and neuropathy was proposed. Six patients with a very similar presentation were reported by Lopez Messa and Garcia in 1990 8 and a disorder of the oxidative metabolism secondary to infection was proposed. Williams et al 9 describe two further cases and speculated on the neuropathy could represent an atypical form of Guillain–Barré syndrome. In 1987 Lycklama et al 10 reported 13 patients with flaccid areflexic tetraparesis who showed no evidence of failure to wean from the ventilator. Although a high pyrexia was present in all their cases, septicaemia could not be proved by blood cultures. Ellis showed abundant spontaneous activity without significant slowing of conduction velocity and motor unit action potentials were increased in amplitude, but sensory potentials were not documented. Since the weakness recovered with resolution of the pyrexia it was attributed to muscle membrane dysfunction related to an inflammatory mediator such as cachectin.

The patient we report does not readily fit into either group. Although she was critically ill, pyrexial and septicaemic, she did not develop multiple organ failure, was only ventilated for three days and weaning was not a problem. Coincidental metabolic factors such as persistent pyrexia, septicaemia or an unidentified toxin cannot entirely be excluded. Further cases are needed to establish whether polyneuropathy is indeed a specific complication of NMS or just a non-specific manifestation of critical illness.

CHRISTINE ROFFE
Department of Medicine
VINOD PATEL
RICHARD JABBOTT
Leicester Royal Infirmary
Leicester LE1 5SW, UK

KRYSTINA CZAPLA
Department of Neurology
Stobhill General Hospital
Glasgow, UK

Correspondence to: Dr Roffe.