Status dystonicus: the syndrome and its management


1The Royal Free Hospital, 2The National Hospital for Neurology and Neurosurgery, and 3The Hospital for Sick Children, Great Ormond Street, London, UK

Summary

Patients with dystonic syndromes sometimes develop increasingly frequent and relentless episodes of devastating generalized dystonia which we call status dystonicus. Twelve cases of status dystonicus, of various underlying aetiologies, are presented. Possible precipitating factors were identified in only five cases: intercurrent infection (one); discontinuation of lithium (one) and tetrabenazine (one); and the introduction of clonazepam (two). Nine patients required mechanical ventilation and three others were sedated with intravenous chlormethiazole. Drug therapy used included benzhexol, tetrabenazine, pimozide, baclofen, chlorpromazine, haloperidol, carbamazepine and acetazolamide. Two patients underwent thalamotomies, one of whom improved. Two patients died, five returned to their pre-status dystonicus condition, two eventually made a full recovery and three were worse. Patients with status dystonicus should be managed on an intensive care unit as they may develop bulbar and respiratory complications which may require ventilation. Metabolic problems encountered can include rhabdomyolysis with acute renal failure. Drug therapy with benzhexol, tetrabenazine and pimozide or haloperidol may be beneficial in some cases.

Keywords: status dystonicus; syndrome; management

Introduction

Patients with primary and secondary dystonic syndromes occasionally develop severe episodes of generalized dystonia and rigidity (status dystonicus) which may be refractory to standard drug therapy. The most severe cases may develop bulbar and ventilatory complications. As a consequence of the intense muscle activity, metabolic complications such as rhabdomyolysis, leading to acute renal failure, may ensue.

There are few references to this potentially life threatening complication in the literature (Jankovic and Penn, 1982; Marsden et al., 1984; Narayan et al., 1991; Vaamonde et al., 1994) and its management is difficult.

We therefore report 12 patients, with a broad spectrum of dystonic syndromes, who developed severe dystonia culminating in status dystonicus necessitating management on an intensive care unit.

Methods

The case records, over a 10-year period, of the Batten–Harris medical intensive care unit at the National Hospital for Neurology and Neurosurgery were reviewed for cases of severe dystonia. Some cases were obtained from the records of consultants specializing in movement disorders (N.Q. and C.D.M.). One case was treated at The Hospital for Sick Children, Great Ormond Street, London (see Table 1).

Patients were defined as having status dystonicus when they developed increasingly frequent and severe episodes of generalized dystonia which had necessitated urgent hospital admission. All developed one or more of the following life threatening complications: bulbar weakness compromising upper airway patency with the risk of pulmonary aspiration; progressive impairment of respiratory function leading to the development of respiratory failure; exhaustion and pain; and metabolic derangements.

All patients were investigated for secondary causes of dystonia. Investigations included some or all of the following: routine haematology and biochemistry; wet blood film for acanthocytes; uric acid; copper and caeruloplasmin; syphilis serology; autoantibodies; CSF examination; plasma and CSF lactate and pyruvate; plasma and urinary amino acids; white cell enzymes; urinary amino acids, oligosaccharides, mucopolysaccharides and organic acids; muscle biopsy for
Table 1  Clinical details of patients

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years) at onset of dystonia</th>
<th>Age (years) at status dystonicus</th>
<th>Diagnosis</th>
<th>Ventilation (days)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>13</td>
<td>Primary torsion dystonia</td>
<td>Yes (31)</td>
<td>Improved with higher doses of benzhexol. Sedated with clorermethiazole. Improved with benzhexol, pimozide, tetrabenazine. Died.</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>11</td>
<td>Primary torsion dystonia</td>
<td>No –</td>
<td>No benefit from bilateral thalamotomy. Died. Rhabdomyolysis, renal failure. Improved with haloperidol and acetozolamide.</td>
</tr>
<tr>
<td>3</td>
<td>6/12</td>
<td>11</td>
<td>Athetoid cerebral palsy</td>
<td>Yes (77)</td>
<td>Died.</td>
</tr>
<tr>
<td>4</td>
<td>8/12</td>
<td>14</td>
<td>Athetoid cerebral palsy, premature neonatal meningitis</td>
<td>Yes (300)</td>
<td>No benefit from bilateral thalamotomy. Died.</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>5</td>
<td>Athetoid cerebral palsy with myoclonus</td>
<td>Yes (20)</td>
<td>Required tracheostomy for 1 month. Sedated with clorermethiazole for 3 days. Improved with pimozide, tetrabenazine and benzhexol. Full recovery.</td>
</tr>
<tr>
<td>6</td>
<td>21</td>
<td>34</td>
<td>Post-traumatic dystonia</td>
<td>Yes (1)</td>
<td>Improved with pimozide, tetrabenazine and benzhexol.</td>
</tr>
<tr>
<td>7</td>
<td>30</td>
<td>31</td>
<td>Post-traumatic dystonia</td>
<td>No –</td>
<td>Sedated with clorermethiazole for 48 h. Thalamotomy 2 years later: recovery.</td>
</tr>
<tr>
<td>8</td>
<td>23</td>
<td>35</td>
<td>Post-traumatic dystonia</td>
<td>Yes (1)</td>
<td>Improved with pimozide, tetrabenazine and benzhexol.</td>
</tr>
<tr>
<td>9</td>
<td>22</td>
<td>38</td>
<td>Post-encephalitic dystonia</td>
<td>No –</td>
<td>Sedated with clorermethiazole for 48 h. Thalamotomy 2 years later: recovery.</td>
</tr>
<tr>
<td>10</td>
<td>18/12</td>
<td>20</td>
<td>Infantile striatal necrosis</td>
<td>Yes (7)</td>
<td>Improved with tetrabenazine.</td>
</tr>
<tr>
<td>11</td>
<td>28</td>
<td>34</td>
<td>Neuroacanthocytosis</td>
<td>Yes (24)</td>
<td>Improved with tetrabenazine, clorazepam, sulpiride, haloperidol.</td>
</tr>
<tr>
<td>12</td>
<td>21</td>
<td>21</td>
<td>Relapsing/remitting dystonia, aetiology unknown</td>
<td>Yes (11)</td>
<td>Ventilated on two further occasions. Eventual full recovery.</td>
</tr>
</tbody>
</table>

Evidence of a mitochondrial cytopathy; slit lamp examination; cranial CT and/or MRI; evoked responses; nerve conduction tests and electromyography; electroencephalography. All patients had previously had an unsuccessful trial of levodopa therapy.

**Case 1. Primary torsion dystonia with myoclonus**

This 12-year-old boy developed dystonia of his left leg at the age of 5 years. Gradually the abnormal movements spread to involve all four limbs. Two years prior to admission he had developed myoclonic jerking, particularly of his left shoulder. Most recently his speech was noted to be slurred.

A few days prior to the development of his status dystonicus, clonazepam (1 mg t.i.d.) had been started for the myoclonic jerks. However, the dystonia and myoclonus worsened necessitating sedation with intravenous chlorermethiazole. Reduction of the drug showed him to have severe generalized dystonia and myoclonus which also affected the diaphragm resulting in hypoxaemia. He was therefore transferred to the intensive treatment unit and was paralysed with an infusion of atracurium and ventilated. He was sedated with an infusion of thiopentone and morphine.

Initial medical treatment for the dystonia consisted of tetrabenazine (25 mg t.i.d.) and pimozide (4 mg) without benefit. Other drugs tried included sodium valproate, primidone and propanolol, none of which had a significant effect. With the introduction of higher doses of benzhexol the movement disorder improved.

Once weaned off the artificial ventilation (after a period of 1 month), his condition gradually returned to his pre-admission state and he was mobile with the help of a zimmer frame.

The pimozide was gradually reduced and he was maintained on tetrabenazine 25 mg t.i.d. and benzhexol 6 mg t.i.d.

**Case 2. Primary torsion dystonia**

At the age of 8 years, this boy, who was born of a normal pregnancy and delivery and who had reached his motor milestones normally, was noted to have an abnormal gait. There were associated jerky movements of the left leg. There was no family history of dystonia.

Examination revealed a variable equino varus deformity of the left foot, bilateral clonus and brisk reflexes. His condition deteriorated with the development of choreic movements of both hands and writer’s cramp. He required an electric wheelchair for mobility. Treatment with steroids and L-dopa were without benefit and he was diagnosed as having idiopathic torsion dystonia.

Three years later, he was admitted with a 2-month history of increasing and painful spasms of his limbs, trunk and neck which had become continuous. He was unable to speak...
or eat, and required a nasogastric tube for feeding. He was sedated with an intravenous infusion of chlorpromazine, at variable doses, for 22 days. During this period pimozide and tetrabenazine were added to his drug regimen of benzhexol, diazepam and baclofen. Paralysis and ventilation were not necessary. His crisis gradually resolved and he was discharged on tetrabenazine 50 mg, pimozide 5 mg b.i.d., benzhexol 22.5 mg/day and clonazepam 5 mg b.i.d.

On review 6 months later, he had not experienced any further dystonic crises, he had greater control of his limbs but his swallowing and speech were still impaired. He was still wheelchair bound.

**Case 3. Athetoid cerebral palsy**

An 11-year-old boy was born of a normal pregnancy and delivery. He had never walked and required an electric wheelchair for mobility. He was intellectually impaired. Mild athetosis had been noted a few years previously. In the 2 weeks prior to admission this had deteriorated dramatically, with no obvious precipitating factors, such as change in his drug therapy or intercurrent infection. There was severe hyperextension of all four limbs with internal rotation of the arms with repetitive flapping movements of the legs at the rate of 2 Hz. There was also a torticollis to the right, tachypnoea and severe hyperventilation.

Initial management over a 2-week period was by sedation with infusions of clonazepam and chlorpromazine but each time these were weaned the dystonic spasms returned. He was subsequently transferred to the intensive treatment unit for sedation, paralysis, tracheal intubation and ventilation because of exhaustion and severe discomfort. A tracheostomy was performed. Sedation was maintained during the period of ventilation with a thiopentone infusion.

Specific antidystonia treatment consisted of gradually increasing doses of tetrabenazine (25 mg t.i.d.), benzhexol (50 mg t.i.d.), baclofen (20 mg t.i.d.) and pimozide (20 mg b.i.d.). The last drug resulted in acute myocardial dysfunction with cardiomegaly and pulmonary oedema which necessitated discontinuation of the drug and the introduction of temporary inotropic support. The effect of these drugs was assessed every 2–3 days by reducing the thiopentone anaesthesia. However, it was apparent that the underlying dystonic spasms were refractory to drug therapy. The patient developed a *Clostridium difficile* infection and died 3 months after admission.

At post-mortem, macroscopically, the only abnormal finding in the brain was generalized cerebral atrophy. Microscopically, there was evidence of mild hypoxic damage to the thalamus, consistent with neonatal hypoxia.

**Case 4. Athetoid cerebral palsy due to premature birth (32 weeks) and neonatal meningitis**

This boy was born by forceps delivery at 32 weeks gestation. During the first post-natal week he developed a gram-negative meningitis. At the age of 2 years he was noted to have a rigid quadriaparesis with athetoid movements of his arms. In addition, he had a torticollis to the right, poor tongue movements and was unable to close his lower jaw. By the age of 13 years, he had deteriorated further, being unable to sit without support, and had developed painful muscle spasms of his arms and trunk which initially responded to benzhexol.

He deteriorated further with increasingly severe episodes of opisthotonus with marked retrocollis. The addition of tetrabenazine and increasing the dose of benzhexol to 20 mg t.i.d. were of no benefit but the retrocollis improved with local injection of botulinum toxin. Oral baclofen and pimozide were of no benefit. The dystonic posturing worsened, compromising bulbar function, and he developed bouts of laryngeal stridor and with obstructive apnoea. Following tracheal intubation, he was sedated with propofol and morphine infusions and paralysed using an infusion of atracurium. Five days later, reduction of sedation and paralysis resulted in a recurrence of his severe spasms requiring further paralysis and ventilation. Subsequently a tracheostomy was performed. Drug therapy tried over a period of 3 months, without any improvement of the underlying dystonic and rigid spasms, included: benzhexol (60 mg/day), tetrabenazine (50 mg/day), oral baclofen (60 mg/day), intrathecal baclofen and haloperidol (33 mg/day). Pimozide (14 mg/day) resulted in a junctional bradycardia and was therefore stopped.

During his 11 months on the intensive treatment unit, he was sedated with titrated doses of midazolam, at times requiring 45 mg/h. During episodes of intercurrent infection, the dystonic spasms became more prominent and he required further paralysis to allow effective ventilation.

Six months after admission he underwent a left stereotactic thalamotomy of the ventrolateral nucleus. The axial and right-sided spasms improved temporarily but his dysphagia worsened. Eleven weeks later a right thalamotomy was performed without any improvement.

He died of a gram-negative septicemia 11 months after admission. A post-mortem was not performed.

**Case 5. Athetoid cerebral palsy with myoclonus**

This 5-year-old boy was born of a normal pregnancy and delivery but had delayed motor milestones. At 12 months he developed athetoid movements of his limbs. At 15 months he started having generalized seizures treated with sodium valproate. He was mobile with a frame and required bilateral lower limb orthoses.

A few weeks prior to admission he was noted to have stimulus-sensitive and action myoclonus for which clonazepam was prescribed. Two days later his involuntary movements became much worse and he developed rhabdomyolysis (creatinine kinase 43 000 IU), a metabolic acidosis (pH 7.23, pCO2 1.63 kPa, pO2 kPa 13.2; base excess 18.5) and renal failure with a urea of 15.9 mmol/l. His severe abnormal movements and metabolic derangement required paralysis, tracheal intubation and ventilation. The metabolic
acidosis was corrected with bicarbonate infusions and a period of hyperventilation. The renal failure was treated with fluid replacement and dopamine.

The underlying movement disorder was treated with tetrabenazine (12.5 mg t.i.d), benzhexol (2 mg t.i.d), acetozolamide (62.5 mg b.i.d) and haloperidol (4 mg b.i.d). The athetoid movements seemed to improve with the introduction of the acetozolamide and increasing the dose of haloperidol. His trachea was extubated 2 weeks after admission. The benzhexol was gradually tailed off without any deterioration.

On review 3 months later, the myoclonus was still present and he was noted to be more ataxic and hypotonic. He was now unable to stand without support.

**Case 6. Post-traumatic dystonia**

At the age of 21 years, following a motor cycle injury to his right leg which required a period of immobilization with plaster of Paris, this patient developed pain and a equinovarus deformity of his right foot. There was no family history of dystonia. Two years later he developed increased tone and a tremor affecting the right leg. Shortly afterwards, he was noted to have increased tone in all four limbs, a flexion deformity of the left arm and right hand and episodes of generalized dystonia which responded to intravenous diazepam. He subsequently developed torticollis accompanied by dysphonia and dysphagia.

Thirteen years later, he was admitted with a left palmar cellulitis resulting from his finger nails digging into his hand. On admission his treatment included benzhexol up to 65 mg/day, Sinemet and tetrabenazine. Following admission, however, his condition deteriorated with increasing generalized dystonic spasms, during which ventilation and swallowing were compromised. He was therefore intubated and ventilated for a period of 3 weeks during which a tracheostomy was performed. Sedation was achieved with a midazolam infusion. The palmar infection resolved with antibiotic therapy. Following treatment with increasing doses of pimozide his severe dystonia gradually subsided and he returned to his previous state with flexion deformities of his left arm and hand. He continued to experience intermittent daily spasms, particularly on standing, rendering him wheelchair bound.

**Case 7. Post-traumatic dystonia**

At the age of 28, this ballet dancer developed a painful, swollen right knee. A year later, the leg was noted to be mottled and blue with hyperpathia. A diagnosis of reflex sympathetic dystrophy was made and treatment with guanethidine blocks was temporarily helpful. On review 2 years later, there was tonic inversion of the right foot with spasms of the right leg. These movements were strong enough to crack a plaster of Paris cast which had been applied whilst the patient was anaesthetized. EMG recordings revealed contraction of the affected muscles. There was no family history of dystonia.

A year later, her condition had progressed with the development of retrocollis and dystonia of the left arm. Treatment with benzhexol and Sinemet were of no benefit. Subsequently, while in hospital, whole body spasms necessitated sedation with intravenous boluses of midazolam and clonazepam followed by an infusion of chlormethiazole which required cardiac and respiratory monitoring on the intensive treatment unit. Mechanical ventilation was not required. During this period, pimozide and tetrabenazine were prescribed for the generalized dystonic spasms, in addition to benzhexol.

Following this episode her condition gradually improved and 5 years after her original presentation she had made a complete recovery and was off all drug therapy.

**Case 8. Post-traumatic dystonia**

At the age of 11 years, this woman had an accident twisting her left knee. Subsequently, she underwent a meniscectomy and a femoral nerve crush in order to release the quadriceps spasm she had developed on that side. Twelve years later she developed writer’s cramp of the right hand followed by the development of stiffness and cramps in her feet. Her condition deteriorated further with torticollis to the right as well as blepharospasm of the right eye.

At the time of admission, she was experiencing frequent and painful spasms which consisted of flexion of both arms, dystonic posturing and tremor of the right foot and leg. These required the administration of intravenous midazolam. Trials of tetrabenazine, pimozide, clonazepam, Madopar, carbamazepine and lithium were unsuccessful.

On stopping the lithium, the spasms worsened requiring larger and more frequent doses of midazolam. In view of her increasing exhaustion and severe discomfort, she was electively paralysed with atracurium and ventilated. She was sedated with infusions of midazolam, propofol and morphine for a period of 10 days. By day 8, she was self-ventilating on midazolam.

She was gradually weaned off the midazolam, and during this period started on a combination of pimozide (gradually increasing to 12 mg/day), tetrabenazine 25 mg t.i.d. and benztrpine. The latter was subsequently stopped because of urinary retention. She was discharged on tetrabenazine, pimozide and intermittent oral clonazepam to be taken in the event of recurring spasms.

**Case 9. Post-encephalitic hemidystonia**

At the age of 17 years, whilst on holiday in Italy, this woman became unwell with headache and diplopia. A viral encephalitis was suspected but not proven, the CSF examination being normal. Following this, she experienced increasing bradykinesia and 1 year later had an acute psychotic illness treated with depot fluphenazine decanoate
which rendered her markedly parkinsonian. These features improved when the drug was stopped. However, her motor disorder continued to worsen with increasing difficulty using her legs and the development of a jerky tremor of the upper limbs. Investigations revealed no underlying cause. During a period of EEG monitored sleep, attacks of spasms occurred during arousal but she did not wake until after the attack, suggesting an organic aetiology.

Her condition progressively deteriorated with the development of generalized dystonia, the right limbs affected more than the left. There was marked dystonic posturing of the right arm, hand and leg superimposed on which were jerky spasms and a tremor. She was dysarthric.

Previous drug therapy included tetrabenazine, pimozide, benzhexol, Sinemet, baclofen and carbamazepine.

At the age of 38 years, she was admitted with increasing frequency of her generalized spasms, which lasted between 20 min and 8 h. During these attacks, the right arm was flexed and internally rotated behind her back which was opisthotonic, the neck was retrocollic, the legs were both flexed and she was dysarthric.

In view of her exhaustion and severe pain during the attacks, she was admitted to the intensive care unit and sedated with a chlormethiazole infusion for 24 h, following which her spasms settled to their previous state. Between attacks, the right arm had a dystonic posture and she walked with a hemiplegic gait.

Two years later, a stereotactic left thalamotomy was carried out which, on review 6 months later, resulted in a virtually normal right side, a reduction in the severity of her spasms, and it also improved left sided dystonic spasms.

**Case 10. Infantile striatal necrosis**

This boy was born at term following a pregnancy that was complicated by maternal hypertension and a breech presentation that was uncomplicated. He walked at 12 months but at the age of 18 months was unwell for 1 week following which he developed spasms affecting his arms and legs and lost some of his motor skills.

By the age of 8 years, he had developed generalized jerky dystonic movements associated with a pseudobulbar palsy. A CT scan revealed heavy calcification in the basal ganglia and the dentate nucleus. The routine investigations for dystonia, including muscle biopsy, were unhelpful, and a diagnosis of possible infantile striatal necrosis was made.

He was admitted at the age of 20 years because of increasing generalized dystonic spasms affecting his limbs, trunk and bulbar muscles. Trials of baclofen, benzhexol, Sinemet, bromocriptine and carbamazepine were unsuccessful. Following admission the worsening dystonic spasms resulted in alveolar hypoventilation and exhaustion. He was, therefore, paralysed with an infusion of atracurium, intubated and ventilated. Sedation was provided by an infusion of propofol. No obvious infective or drug precipitants were identified.

Treatment with pimozide resulted in a junctional bradycardia and was therefore stopped. The addition of tetrabenazine in gradually increasing doses resulted in an improvement with respect to the involuntary movements and his trachea was extubated after 6 days of ventilation.

Although still left with his generalized dystonic movements these were much improved.

**Case 11. Neuroacanthocytosis**

At the age of 22 years, this woman developed generalized seizures. Four years later she had become increasingly forgetful, had changed in personality and had also developed generalized chorea, tics and vocalizations. A wet blood film showed 12–15% acanthocytes. The involuntary movements improved with sulpiride. At the age of 28 years, her condition had deteriorated in that, as well as having dysphagia, she was unable to retain food in her mouth because of involuntary movements of the tongue. Although there was an improvement with the addition of tetrabenazine 25 mg b.i.d., she required a gastrostomy tube for feeding. She was now wheelchair bound. Her seizures were controlled with sodium valproate 500 mg t.i.d., vigabatrin 1 g b.i.d. and pheno-barbitone 60 mg o.d.

Six years later, having stopped the tetrabenazine of her own accord, she developed increasing problems swallowing and breathing. Soon after admission, she developed an aspiration pneumonia followed by a respiratory arrest.

Following paralysis with atracurium, she was intubated and ventilated. Sedation was obtained with an infusion of propofol. After resolution of her pneumonia, after 6 days, an attempt was made to extubate her trachea. She immediately developed severe dystonic stridor, paroxysmal chest movements and generalized choreic movements of her arms and legs. She was, therefore, re-sedated and reintubated. Tetrabenazine was restarted and clonazepam 5 mg b.i.d. was also added to her treatment regimen. Two further attempts at extubation again resulted in laryngeal stridor and retention of secretions. A tracheostomy was therefore performed. Her medication was increased to tetrabenazine 50 mg q.i.d., and haloperidol 10 mg b.i.d. in addition to the sulpiride 400 mg t.i.d. The clonazepam was reduced to 4 mg b.i.d. She was weaned off artificial ventilation 24 days after admission, at which time her involuntary movements had lessened considerably.

**Case 12. Relapsing/remitting symptomatic dystonia, aetiology unknown**

At the age of 21 years, this woman presented with a 6-month history of progressive stiffness of the left arm, dysphagia and unsteadiness of gait.

Examination revealed no evidence of cognitive impairment. The saccadic eye movements were hypometric and pursuit movements broken up. She was dysarthric with slow tongue movements and an expressionless face. A torticollis with left
till was noted. There was limb and body akinesia, a postural tremor and extrapyramidal rigidity as well as dystonic posturing of the feet. The tendon reflexes were pathologically brisk.

A few months later urgent admission was precipitated by the development of respiratory distress with severe dyspnœa and stridor. Examination showed her to be hunched forward with the head flexed to the chest which impaired her swallowing and breathing, marked rigidity in all limbs, dystonic feet postures and brisk reflexes. The vital capacity was reduced to 1.3 l.

In view of the impaired swallowing and upper airway obstruction she was paralysed, intubated and ventilated. She was sedated and paralysed during the period of mechanical ventilation with methohexitone and suxamethonium. Subsequently a tracheostomy was performed.

She required ventilation for a period of 11 days during which the underlying akinetic-rigid-dystonic syndrome was treated with a combination of Madopar, bromocriptine and benzhexol with gradual benefit. However, in view of the persisting swallowing problems the tracheostomy was left in situ for 8 months. Her condition relapsed 6 months later with increasing dyspnœa but ventilation was not required. A further relapse 4 years later again required tracheal intubation following which she required a tracheostomy for 4 months.

However, her condition gradually improved and 10 years after her original presentation, she had made a complete recovery.

Patients

The 12 patients described in this series had a mean age of 22.3 years (range 6–39 years) at the time of their status dystonicus, with five patients being under the age of 15 years. Five were female and seven male.

The underlying diagnoses were variable. Most were of unknown aetiology and the labels used were therefore partly descriptive: primary torsion dystonia (two cases), athetoid cerebral palsy (three), post-traumatic dystonia (three), post-encephalitic dystonia (one), infantile striatal necrosis (one), neuroacanthocytosis (one) and unknown symptomatic dystonia (one). Of the three cases of probable trauma-induced dystonia, one had suffered an injury to the right knee at the age of 20 years and presented with status dystonicus at the age of 34 years; another twisted her knee at the age of 11 years and presented with status dystonicus at the age of 35 years; the third patient in this group, a ballet dancer, injured her knee at the age of 29 and presented with status dystonicus 2 years later.

The patient with infantile striatal necrosis suffered a monophasic illness following which he had gradually developed increasing generalized dystonia. The CT scan revealed dense calcification of the basal ganglia and the dentate nucleus. The case of neuroacanthocytosis was diagnosed when she presented with chorea and a wet blood film showed 12–15% acanthocytes.

Precipitating factors leading to status dystonicus

In two cases, one with primary torsion dystonia with myoclonus and the other with cerebral palsy and myoclonus, the introduction of clonazepam coincided with the development of status dystonicus. In one patient, with dystonia secondary to trauma, the deterioration seemed to be related to a reduction of lithium treatment. The crisis of the patient with neuroacanthocytosis started after she had abruptly stopped her tetrabenazine of her own accord.

Infection seemed to be the precipitant in one patient, who had developed a palmar cellulitis as a result of his finger nails digging into his palm. The patient with athetoid cerebral palsy, due to birth trauma and neonatal meningitis, who remained on the intensive treatment unit for a period of 11 months was noted to have an exacerbation of his severe dystonic spasms with each episode of septicæmia, pneumonia or urinary tract infection.

Management on the intensive care unit

Nine of the 12 patients underwent tracheal intubation and mechanical ventilation. The indications included bulbar compromise (five), respiratory compromise (six), exhaustion/severe discomfort (nine) and metabolic derangement (one). A tracheostomy was performed in five patients. The mean duration of ventilation was 53 days (range 1–300 days). One patient, as a result of the severe dystonic spasms, developed rhabdomyolysis with a creatine kinase level of 43 000 IU precipitating renal failure with a urea of 15.9 mmol/l and an acidosis with a pH of 7.23. The acidosis was managed by hyperventilation and infusions of sodium bicarbonate.

Patients who were not ventilated were admitted to the intensive care unit because the levels of sedation required to control their dystonia necessitated close monitoring of their cardiovascular and respiratory indices. One patient with a predominantly right hemiplegic dystonia was sedated with an infusion of chlorothiazide on three occasions for periods of between 24 and 48 h. The other patient with trauma-induced dystonia was monitored similarly on the intensive treatment unit whilst being sedated with an infusion of chlorothiazide for 3 days. One patient with primary torsion dystonia required sedation with infusions of chlorothiazide for a period of 21 days.

Drug treatment

The following drugs were used in varying combinations: benzhexol, tetrabenazine, pimozide, baclofen, chlorpromazine, sodium valproate, carbamazepine and acetazolamide.

Pimozide resulted in severe heart failure in one patient; ECG changes showed prolongation of the QT interval and depressed ST segments. He required temporary inotropic support to restore cardiac function. Another patient developed a profound bradycardia with widespread ST segment changes.
on the ECG. Pimozide was also stopped in one other case because of a junctional bradycardia.

Tetrabenazine caused a profound psychotic depression in one individual.

Oral baclofen was tried in three patients without benefit. In one case an intrathecal infusion of baclofen was also unhelpful.

An improvement in the status dystonicus seemed to be related to the starting of benzhexol in one case; in another, treatment with tetrabenazine coincided with the onset of improvement of the status dystonicus. The introduction of acetozolamide and increasing the dose of haloperidol seemed to coincide with improvement in one individual. In one patient, whose deterioration was triggered by a palmar cellulitis, improvement coincided both with increasing doses of pimozide and treatment with intravenous antibiotics.

Finally, three cases, two with trauma-induced dystonia and one with primary torsion dystonia, seemed to improve with a combination of tetrabenazine, pimozide and anticholinergic (benzhexol or benztropine) medication.

Surgical treatment

The patient with cerebral palsy, who remained on the intensive treatment unit for a period of 11 months, underwent a left stereotactic thalamotomy to the ventrolateral nucleus [target \(V_{am}\) (nucleus ventro-intermedius) extending into \(V_{op}\) (nucleus ventralis-ovalis posterior)]; his axial and right leg spasms improved for a short period, but his swallowing was worse. Three months later, he underwent a right stereotactic thalamotomy without benefit.

The patient with a predominantly right dystonia/hemiplegia improved with a stereotactic left thalamotomy performed 2 years after her acute deterioration. Her right side returned to almost normal, and there was also an improvement in the severity of her spasms and the posture in the left arm.

Outcome

Two patients died. One had been on the intensive treatment unit for 11 months. All attempts at treatment including bilateral thalamotomy failed and he eventually succumbed to a gram-negative septicemia. The other also failed to respond to any medical therapy and was on the intensive treatment unit for 11 months. All attempts at treatment including baclofen were ineffective. However, he did respond to a continuous intrathecal infusion of baclofen to the extent that he was weaned off mechanical ventilation and discharged home with good control of his dystonia. Vaamonde et al. (1994) used the term ‘dystonic storm’ to describe his two cases. The first was a child with primary torsion dystonia who deteriorated over a period of 2 months following a febrile illness. His condition worsened despite treatment with benzhexol (15 mg/day), tetrabenazine (300 mg/day), pimozide (3 mg/day) and diazepam (10 mg/day). He was anaesthetized for 7 days because of severe discomfort and respiratory distress. Treatment with baclofen and haloperidol in addition to the four drugs above, which were prescribed in even higher doses, was of little benefit. With the introduction of carbamazepine (1200 mg/day), primidone (300 mg/day) and valproic acid (1500 mg/day) his dystonic storm seemed to abate. The second patient was a child with probable Hallervorden–Spatz disease, who presented with a rapid deterioration manifest as generalized dystonic spasms which to stand without support. A patient with primary torsion dystonia was left with severe difficulty swallowing and required long-term nasogastric feeding. The patient with neuroacanthocytosis required a long-term tracheostomy.

Five individuals returned to their pre-crisis state; one other patient with post-encephalitic hemiplegia and dystonia was significantly better after a thalamotomy performed 2 years later.

Discussion

The syndrome of status dystonicus

The clinical syndrome of status dystonicus is rare; the 12 cases described here were seen at the National Hospital for Neurology and Neurosurgery and Great Ormond Street Hospital for Children over a 10-year period.

Jankovic and Penn (1982) reported an 8-year-old boy with autosomal dominant primary torsion dystonia who deteriorated over 6 months and required paralysis and ventilation. His crisis seemed to respond to Sinemet (levodopa with carbidopa) but not carbamazepine. Marsden et al. (1984) described two children, with primary generalized dystonia, who presented with life threatening dystonia, as ‘desperate dystonics’. One, a 12-year-old boy, was paralysed and ventilated for a period of 2 weeks during which the underlying dystonic spasms improved with benzhexol, pimozode and tetrabenazine. The other, a 15-year-old boy, was anarthric, dysphagic and experienced frequent painful dystonic spasms which failed to respond to the same triad of drugs. Pimozide provoked a superadded acute dystonic reaction in the latter case. Narayan et al. (1991) described an 18-year-old man with predominantly axial dystonia, due to cerebral injury at birth, who deteriorated markedly after spinal surgery with opisthotonos and dystonic spasms of the legs, abdominal and respiratory muscles. He was paralysed and ventilated. Treatment with anticholinergics, tetrabenazine and oral baclofen were ineffective. However, he did respond to a continuous intrathecal infusion of baclofen to the extent that he was weaned off mechanical ventilation and discharged home with good control of his dystonia.
depressed his respiration. Treatment with thiopentone anaesthesia over 9 days was combined with chlorpromazine, haloperidol, pimozide, diazepam and benzhexol with no benefit. His condition improved with the introduction of baclofen (75 mg/day).

In some cases underlying infection is an important precipitating cause that must be vigorously sought and treated. In this series, one patient, who remained on the intensive treatment unit for 11 months, suffered a worsening of his severe dystonia with each episode of chest or urinary tract infection and septicemia. A change in drug therapy is another potential cause of deterioration. In this present series, the addition of clonazepam seemed to be incriminated in two individuals. This is unexpected since clonazepam, a GABA (gamma-aminobutyric acid) agonist, has a major inhibitory effect on neurons and has been used, without ill effect, in some patients in this series. In both cases the myoclonic jerks preceded the status dystonicus by days or a few weeks. The prescription of clonazepam may, therefore, have been coincident with the myoclonic jerks heralding dramatic changes within the brain that resulted in status dystonicus. Stopping the clonazepam had no effect in either case. An alternative explanation would be that clonazepam, by inhibiting GABAergic transmission between the caudate nucleus and the substantia nigra (Bloom, 1996) upset the balance within the neural networks resulting in dystonia. The tailing off of lithium in one patient and the abrupt stopping of tetrabenazine in another seemed to precipitate their crises.

An interesting observation in patients with dystonic cerebral palsy has been the deterioration around the time of puberty (personal observation of C.D.M.) as occurred in two patients in this series. The underlying mechanisms are unclear but hormonal changes may be speculated to play a role.

The intense muscle activity of status dystonicus can result in rhabdomyolysis, as described in one patient here. Hyperpyrexia, rhabdomyolysis and renal failure developed in the patient described by Jankovic and Penn (1982). It is necessary to institute paralysis, ventilation and sedation in most cases of status dystonicus in order to avert the bulbar and respiratory complications. These arise from dystonia affecting the lingual, masseter and pterygoid muscles making it impossible to open or close the mouth or to protect the airway. Dystonic spasms of the upper airway and respiratory muscles result in alveolar hypoventilation and hypoxaemia. Occasionally, adductor spasms of the vocal folds may cause inspiratory stridor similar to patients with multiple system atrophy (Munschauer et al., 1990). This may require emergency tracheal intubation and/or tracheostomy.

Paralysis, ventilation and sedation may also be indicated to relieve the severe exhaustion and excruciating pain that results from the incessant dystonic spasms seen in all the cases in this series. After a period of 4–6 days, the infusion of the paralysing and sedative agents need to be tailed off to assess the underlying dystonic spasms. It may be possible to continue with a sedating agent only.

The choice of sedative agent appears to be unimportant. Propofol has a pharmacokinetic profile that allows rapid awakening and assessment of the patient. Midazolam, in contrast, has a long half-life but has a less depressant effect on the cardiovascular system. In addition, midazolam has a spinal interneuron blocking action which may have a theoretical advantage in the treatment of these patients.

The anatomical and pathophysiological site for primary dystonia is unknown. It would seem reasonable to implicate the putamen since this is the commonest lesion site for symptomatic dystonias. Bhatia and Marsden (1994), in a review of the behavioural and motor consequences of focal

The management of status dystonicus

The pharmacological substrate of dystonia is ill defined and, to date, the treatment of dystonias has been empirical. A trial of levodopa is necessary in all early-onset cases to exclude dopa-responsive dystonia. Anticholinergic medication with drugs such as benzhexol is suggested as the next line for the treatment of dystonias, particularly in children (Fahn, 1983; Marsden et al., 1984). In more severe cases, tetrabenazine, which depletes all three monoamine neurotransmitters (dopamine, noradrenaline and serotonin), may be added. Postsynaptic dopamine blockade may be achieved with pimozide, haloperidol or a phenothiazine which augments the presynaptic effects of tetrabenazine.

The present series indicates that drug treatment with this triad of drugs—benzhexol, tetrabenazine and pimozide, as advocated by Marsden et al. (1984)—may be therapeutically helpful and should be tried. Such drugs, however, are not without significant side effects. Pimozide had to be stopped in three individuals because of cardiac toxicity which is well described (Magee, 1993). Perhaps haloperidol is a better choice. Tetrabenazine was stopped in one patient because of severe depression.

However, incomplete understanding of the pathopharmacological mechanisms underlying dystonia makes it difficult to explain the anecdotal reports suggesting that drugs such as baclofen, t-dopa and the anticonvulsant drugs may also be beneficial in some patients with dystonic storms (Vaamonde et al., 1994). It seems likely that clinical dystonic syndromes are the manifestation of a number of differing pathophysiological mechanisms each of which may respond to different classes of drugs. Similarly, it is unclear whether drug treatment, or simply ‘resting’ the dystonic muscles or the dystonic brain, plays the major role in recovery seen in most patients.
lesions of the basal ganglia, concluded that lesions of the lentiform nucleus were more likely to cause dystonia than those of the caudate. Within the lentiform nucleus, lesions of the putamen were more likely to result in dystonia than those of the globus pallidus.

The issue of peripheral trauma causing focal and generalized dystonia is, as yet, unresolved. Fletcher et al. (1991) studying the relationship between trauma and idiopathic torsion dystonia suggested that peripheral nerve injury may influence the basal ganglia and result in dystonia in idiopathic torsion dystonia gene carriers. Jankovic (1994), in a review of post-traumatic movement disorders, adopted the following criteria for the diagnosis of peripherally induced movement disorders: (i) injury must have been severe enough to cause local symptoms for at least 2 weeks or to require medical evaluation within 2 weeks after the peripheral injury; (ii) the onset of the movement disorder must have occurred within a few days or months (up to 1 year) after the injury; and (iii) the onset of the movement disorder must have been anatomically related to the site of injury. Two out of three cases in this series fulfilled these criteria. There is good evidence showing that biochemical changes occur within the basal ganglia after peripheral trauma (De Caballos et al., 1986). More recently, Kaji et al. (1995) demonstrated that stimulation of cutaneous or muscle afferents resulted in dystonic movements in patients with writer’s cramp. At present, therefore, although plausible mechanisms by which peripheral trauma may result in dystonia have been identified, the case is best summarized as not yet proven.

Surgical intervention may be indicated in drug resistant cases. Cooper (1976) reported an improvement in up to 70% of cases of dystonia following large thalamic stereotactic lesions. However, Andrew et al. (1983), using the same targets found an improvement in only 25% of those with generalized dystonia. Furthermore, there was a high incidence of dysarthria in those who had bilateral lesions. Patients with hemidystonia seemed to derive most benefit from thalamotomy (Andrew et al., 1983).

In the present series, one individual with athetoid cerebral palsy failed to respond to bilateral thalamotomies. The first thalamotomy was carried out 5 months after the onset of his status dystonicus. This length of time since the onset could have been a factor in his lack of response. Another possible reason for the lack of efficacy is that the lesion in the ventrolateral nucleus was not extensive enough. One patient with a predominantly right dystonia/hemiplegia responded well to stereotactic thalamotomy. However, she had recovered from her status dystonicus and the surgery was performed in view of the marked asymmetry of symptoms with persisting and troublesome right-sided spasms.

The increasing reports of the benefit of pallidal stimulation in the alleviation of parkinsonian symptoms and particularly of treating levodopa-induced dyskinesias, may in the future be extrapolated to the thalamic or pallidal nuclei for dystonia (Siegfried and Lippitz, 1994). This may represent a further avenue for treatment in this difficult situation.

In a number of the patients described in this series there was occasional concern that the involuntary movements had a non-organic basis. Certainly functional respiratory impairment may be severe and require paralysis and ventilation (Howard et al., 1993). In the present series the subsequent course of the illness made an organic cause likely in all cases, although complete recovery in two is unusual.

In summary, this series indicates that patients with status dystonicus should be managed in an intensive care setting because of the risk of bulbar, respiratory and metabolic complications. Paralysis and ventilation, which is often indicated because of bulbar or respiratory compromise as well as exhaustion, may itself be a useful therapeutic strategy. Drug therapy with benzhexol, tetrabenazine and pimozide or haloperidol should be tried since they may have a beneficial effect. If such treatment fails, baclofen, anticonvulsant drugs and levodopa should be used. Intrathecal baclofen may prove a further useful option. Local injections of botulinum toxin into selected muscles may also be of benefit. Finally, stereotactic surgery or stimulator implantation into thalamic or pallidal targets may be considered in the most resistant cases. The prognosis from this condition should be guarded and depends partly on the underlying aetiology. However, the majority of patients reverted back to their former status dystonicus and some recovered completely.

References
Jankovic J. Post-traumatic movement disorders: central and


Accepted September 17, 1997