Treatment of acute pandysautonomia with intravenous immunoglobulin

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Abstract
Acute pandysautonomia has been suggested to be an uncommon variant of Guillain-Barré syndrome. Acute pandysautonomia does not seem to have been treated with intravenous immunoglobulin or other therapies proved efficacious in Guillain-Barré syndrome. A patient is reported with severe acute pandysautonomia who responded dramatically to intravenous immunoglobulin. The findings are consistent with a dysimmune pathogenesis for this syndrome and suggest a possible treatment for future cases.

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Acute pandysautonomia was first described by Young et al in 1969. Since this time, 27 cases have been reported. The disorder presents with clinical features reminiscent of the autonomic failure of severe Guillain-Barré syndrome, including severe orthostasis, impairment of gastrointestinal motility and bladder function, impotence, impairment of pupillary reactivity and accommodation, and dryness of the eyes, nasopharynx, and skin. Recovery occurs slowly and is often incomplete. Commonly, patients are left with disabling residual symptoms.

Similarity between acute pandysautonomia and the autonomic failure of severe Guillain-Barré syndrome suggests that acute pandysautonomia may be an uncommon variant of Guillain-Barré syndrome. This hypothesis is strengthened by the existence of cases of acute pandysautonomia with varying degrees of sensory loss and dysaesthesia. Raised CSF protein in many cases of acute pandysautonomia is also consistent with this hypothesis.

Little is known regarding the treatment of acute pandysautonomia. Corticosteroids have been given with disappointing mixed results. More recently, one patient with acute pandysautonomia was treated symptomatically with 400 mg L-threo-3,4-dihydroxyphenylserine (L-DOPS) daily. This patient required daily symptomatic treatment for more than two years. To our knowledge, however, treatment of acute pandysautonomia with therapies proved efficacious in Guillain-Barré syndrome has not been reported. We hypothesised that acute pandysautonomia would respond to treatment with intravenous immunoglobulin (IVIg).

Case report
PRESENTATION
A previously healthy 26 year old woman was admitted to hospital at the University of Florida Health Science Center in November of 1994 with severe acute pandysautonomia. Four weeks earlier, she had developed a generalised rash while receiving trimethoprim/sulfamethoxazole for treatment of a urinary tract infection. She presented with a clinical syndrome characterised by orthostasis, syncope, abdominal pain, anorexia, nausea, vomiting, photophobia, dryness of her mouth, eyes, and skin, diarrhoea, and incontinence of stool. She also complained of burning dysaesthesiae in her feet. Evaluation at an outside hospital disclosed severe orthostatic hypotension without secondary tachycardia, due to absent responses to baroreceptors. One blood pressure recording was 130/70 mm Hg while supine and it dropped to 50/0 mm Hg while standing. Normal laboratory studies included renal and liver functions, complete blood count, erythrocyte sedimentation rate, antimicrobial antibodies, serological testing for syphilis, and porphyrins. There were no cells in the CSF; CSF protein was 78 mg/dl and glucose 75 mg/dl. Abdominal CT, a rectal biopsy, nerve conduction studies, and EMG were all normal. An upper gastrointestinal series disclosed pooling of barium in the stomach and much increased transit time. The patient was then transferred to our institution. She had no history of travel, botulism, exposure to toxins, medications, or infections other than that previously mentioned. Family history was negative, and there was no evidence of Adie’s, Riley-Day, or Shy-Drager syndromes.

EXAMINATION
Examination showed a photophobic young woman lying supine. On sitting upright, her blood pressure fell from 110/70 to 40/0 mm
Hg and she lost consciousness transiently. Although she lost peripheral pulses, her heart rate remained stable during hypotension (105 bpm supine, 110 bpm standing). Her mouth, pharynx, and skin were very dry. Higher cortical functions were intact. Her pupils were 5 mm bilaterally and unreactive to light or accommodation. Motor examination was normal. Sensory examination was notable for severe hyperaesthesia in the patient’s feet. Deep tendon reflexes were normal.

A “cold pressor test” was performed by submerging the patient’s hands into a large bucket of ice water for 60 seconds. This test was abnormal, with an absent rise in blood pressure. Nerve conduction studies and concentric needle EMG were normal. The sympathetic skin response was absent. A nuclear medicine gastric emptying study showed very reduced gastric emptying with no appreciable response to metoclopramide. ECG telemetry for eight days showed no sign of dysautonomic arrhythmia.

TREATMENT

Intravenous immunoglobulin (IV Ig) was given on days 1, 2, 3, 5, and 8 at a dose of 0.4 g/kg/day. Clinical improvement was obvious by day 3 in both subjective and objective measurements. Pupillary responses returned, now constricting from 5 mm to 3 mm bilaterally. This was accompanied by resolution of her photophobia. Her orthostasis improved and she regained heart rate responses to baroreceptors; she was now capable of developing tachycardia in the face of hypotension (supine blood pressure 125/82 mm Hg, heart rate 88 bpm; standing blood pressure 82/42 mm Hg, heart rate 126 bpm). She reported resolution of postural lightheadedness. Her mouth and pharynx became moist and sweat appeared on her skin. The incontinence resolved. On days 4, 6, and 7, in between IV Ig treatments, we noted transient worsening of dysaesthesiae. The dysaesthesiae had disappeared by the completion of IV Ig treatment. Nausea and anorexia resolved over the next few weeks. The patient was discharged after 16 days in hospital. On follow up over one year later, examination was notable only for milder, asymptomatic orthostatic hypotension (supine blood pressure 117/78 mm Hg, heart rate 85 bpm; standing blood pressure 104/62 mm Hg, heart rate 98 bpm). She was living independently with no complaints and no symptoms.

Discussion

This patient showed dramatic improvement of acute pandysautonomia temporally associated with administration of IV Ig. It is conceivable that symptomatic improvement in our patient was merely coincident with the IV Ig. Indeed, spontaneous resolution of acute pandysautonomia is not infrequent.1-7,9-12,14-16,18-20

However, our analysis of previously reported cases (table) showed that recovery from this condition is usually protracted and incomplete. Partial recovery in previously reported cases of acute pandysautonomia occurred after an average of 30 months and residual disability was not uncommon. By contrast, our patient improved rapidly after receiving IV Ig and recovered much more quickly than previously reported cases. Given the natural history of acute pandysautonomia, we suggest that improvement in our patient was not spontaneous, but was likely related to administration of IV Ig.

To our knowledge, this case represents the first time that acute pandysautonomia has been treated with therapy proved efficacious in Guillain-Barré syndrome.28-31 Plasma exchange is associated with various medical complications, including hypotension and cardiac arrhythmia.31,33 Intuitively, plasma exchange imposes an even greater risk of these complications in patients with severe dysautonomia. By contrast, administration of IV Ig in this setting probably poses considerably less risk. The extremely low incidence of acute pandysautonomia makes a clinical trial of treatment of this disorder unlikely. However, our findings suggest that acute pandysautonomia is in fact a variant of Guillain-Barré syndrome. We suggest that early treatment of IV Ig deserves consideration in cases of this syndrome.

We have no commercial or proprietary interest in the items discussed in this manuscript.

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