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Short report

Acute autonomic neuropathy following primary herpes simplex infection

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SUMMARY A 13-year-old girl presented with postural hypotension, severe abdominal pain and diarrhoea, parotid pain and a transient encephalopathy. There was evidence of an acute autonomic neuropathy and some electrophysiological evidence of a transient peripheral somatic neuropathy. The likely cause was primary herpes simplex infection.

There have been reports of eleven previous patients with acute autonomic neuropathy with ages ranging from 6 to 49 years since the original description in 1969.[1–10] Diabetes melitus and infectious mononucleosis[8] were the likely cause in two patients. Although in three previous patients the CSF protein was raised, and in one there was an electron microscopic abnormality of a peripheral nerve,[10] electrophysiological evidence of peripheral neuropathy has not been previously documented.

Case history

This previously normal girl presented in April 1980 aged 13 years with a four day history of painful mouth ulcers, anorexia and lassitude, and a two day history of drowsiness, headaches and photophobia. For one day she had had severe abdominal pain and vomiting.

1 Encephalopathy
The initial drowsiness, headache and photophobia with moderate neck stiffness lasted for only five days. A CSF protein was initially 650 mg/l with 4 white cells per cubic millimetre, and at six weeks was normal. EEG performed on day fifteen was abnormal with focal sharp and slow wave activity bilaterally, and six weeks later there was some improvement. A CT brain scan was normal.

2 Peripheral neuropathy
Despite early complaints of parasthesiae and weakness of the left hand, there were no objective signs. Electrophysiological studies showed borderline values but, when considered with the later test results were regarded as showing evidence of a mild generalised affection of large myelinated sensory and motor fibres.

	April 1980	*Sept. 1982*	*Normal*
L Sural SAP	11 μv	20 μv	>10
R Radial SAP	18 μv	30 μv	>20
R Median MNAP	20 μv	25 μv	>20
L Abductor Hallucis MAP	2·6 mv	7 mv	>2

The CSF, IgG was 84 mg/l (normal range: 5–45) with a normal albumin level.

3 Postural hypotension
Severe postural hypotension limiting sitting and preventing standing was present for the first six weeks. This recovered over a total of six months. Initial blood pressure readings were 100/70 mm Hg lying and unrecordable standing. Ephedrine was tried briefly without effect. Two years later she had transient symptoms on two occasions with heavy colds.

4 Gastrointestinal problems and amenorrhoea
She developed abdominal pain, vomiting, and profuse watery diarrhoea from day six, requiring intravenous replacement. During the first month her weight fell from 48 kg (at the 90th centile) to 37 kg (<25th centile) and recovered slowly thereafter. Her menses ceased for eighteen months and resumed at a weight of 50 kg, but were not regular thereafter. The colicky pains were very severe and recorded faecal weights varied from 200 to 800 g daily. During the initial phase, adequate intravenous hydration with 150 mM saline, sufficient to produce satisfactory urinary sodium outputs (>20 mmol/day), failed to correct the postural hypotension proving that this was not simply the result of salt depletion. A number of drugs were used and codeine phosphate was most effective in reducing the stool frequency.

There were never any striking physical signs, apart from variable dehydration and abdominal tenderness. Rectal and sigmoidoscopic examinations were normal to the

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recto-sigmoid junction. The following show no abnormality: radiography of abdomen, full blood count, Vickers profile, barium meal and follow through, faecal cultures and clostridium difficile toxin, salmonella serology, faecal fat excretion, urine/faecal screen for laxatives, GI hormone profile (including VIP, gastrin), thyroid function tests and scintilography; urinary porphyrins, glucose tolerance test, serum amylase (during attacks of pain), fasting serum cholesterol and triglycerides, serum magnesium levels. Calcitonin levels were persistently raised: (N = 0·08). Oct 1980—0·43 μg/l; Nov 1980—1·63 μg/l; Jan 1981—1·13 μg/l; Aug 1981—2·32 μg/l. There was no clinical or genetic evidence of thyroid disease. The ESR was initially raised at 43 mm in the first hour and fell to 13 mm in the first hour within three weeks.

5 Parotid pain

From the time that she recommenced eating after the onset of this condition, she complained of pain behind the angles of the jaw on smelling or tasting food, particularly acidic flavours. This was worse on the right side and accompanied by profuse sweating on the right side of the face. Parotid duct dilatation on two occasions produced only transient improvement. A salivary scan, sialogram and investigation of the temporo-mandibular joint were normal. There was no response to carbamazepine or dilatation of the duct. This problem persists two and a half years after the onset of the condition but is waning in severity.

6 Autonomic denervation

In addition to postural hypotension, the ratio of the RR interval on standing between the 15th and 30th beats was 0·995 (N = 1·25 ± 0·05) but all other vascular reflexes were normal. 2·5% methacoline produced myosis. Schirmer's test showed only 5 mm of lacrimation bilaterally. Body temperature was raised 1°C producing sweating confined to a part of the trunk. Intradermal histamine on the abdomen produced a wheal and flare, and on the forearm produced a small flare and there was no response on the shin. Over six months later the methacoline response and sweating deficiency persisted but postural hypotension and tear production had recovered.

7 Primary herpes simplex infection

The extensive stomal ulceration recovered after ten days. Antibodies to herpes simplex were:

	7 April 1980	*17 April 1980*	*21 May 1980*
Serum	<10	80	40
CSF			<2

8 She developed very severe facial oedema in response to sunlight on one occasion two years after the original illness.

Discussion

Twelve patients including the present one have been reported with acute autonomic neuropathy.

Postural hypotension has occurred in nine and recovered completely. Ileus or constipation is the most frequent gastrointestinal problem which has occurred in eight, usually with complete recovery but, in one patient, this has required long-term parasympathomimetic drugs. The bladder problems have usually been those of an atonic bladder (in seven) requiring catheterisation in the acute phase with frequency of micturition in only two. Hypohidrosis was present in nine, almost always accompanied by a dry mouth and reduced tear production. An internal ophthalmoplegia was also reported in nine. Impotence occurred in all three adult males on whom full information was available. Parotid pain has only been present in one previous patient.[5]

The vomiting, abdominal pain and watery diarrhoea are ascribed to autonomic dysfunction with slow resolution over a 2 year period. Bowel disturbance is well recognised in patients with autonomic neuropathy. In diabetics both severe constipation and diarrhoea can occur.[11] In a review of 297 cases of chronic autonomic neuropathy from various causes in adults, 41% experienced constipation and only 5% diarrhoea.[12] In Shy and Drager's original report,[13] both cases had constipation with episodes of rectal incontinence. The two patients with an acute onset of autonomic neuropathy previously described both had severe abdominal pain and constipation, although one had profuse transient diarrhoea at the onset. The present case is unusual in that she had copious and persistent diarrhoea with much abdominal pain, but no constipation at any stage. Unfortunately no patho-physiological explanation for the diarrhoea was obtained in this case.

Diarrhoea can occur in patients with medullary carcinoma of the thyroid (MCT) with a raised level of calcitonin. There was no evidence of thyroid disease and calcitonin levels may be normally rather higher in children. Three patients have had evidence of encephalopathy, two mild as in the present patient, and one more severe with status epilepticus followed by temporal lobe epilepsy and recent memory defect.

The natural history of acute autonomic neuropathy has been complete recovery in three of the twelve patients, partial recovery in eight, and major symptoms have persisted in only one.

The features of interest in the present patient are the severity of the gastrointestinal problems, the presence of parotid pain and evidence of a mild encephalopathy. The original features are the demonstration of primary herpes simplex infection, and electrophysiological evidence of a mild demyelinating neuropathy.

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