

## SHORT REPORT

## Acute small fibre sensory neuropathy: another variant of Guillain-Barré syndrome?

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Six patients who presented with acute sensory neuropathy were studied. All patients underwent detailed clinical assessment along with electrophysiological tests and relevant laboratory investigations. All patients had acute onset numbness, reaching the peak deficit within 4 weeks. Four of them had associated burning dysaesthesia. An antecedent illness was reported in four; diarrhoea in three, and urinary tract infection in one. The neurological examination disclosed normal muscle strength, symmetric glove and stocking type sensory loss for pain and temperature, normal proprioception, and vibration senses with normal or brisk tendon reflexes. Analysis of CSF demonstrated albuminocytological dissociation in all. Routine motor and sensory nerve conduction studies were normal. Sympathetic skin responses were also normal except for the lower limbs in one patient. Stool cultures for *Campylobacter jejuni* were negative. The outcome was favourable. Burning dysaesthesia disappeared within 4 months. Numbness and objective sensory loss tended to persist longer.

The clinical features and normal routine nerve conduction studies, which assess large diameter nerve fibre function, indicate small sensory fibre dysfunction in the group. Their presentation and CSF findings would fit into the diagnosis of sensory Guillain-Barré syndrome. The current study suggests that acute small fibre sensory neuropathy (ASFSN) is another clinical entity which could perhaps be included in the heterogeneous range of Guillain-Barré syndrome.

Guillain-Barré syndrome has typically been defined to be an illness characterised by progressive and symmetric motor weakness of more than one limb with areflexia.<sup>1</sup> However, several variants of the syndrome with different clinical manifestations have been reported.<sup>2,3</sup> The possibility of a pure sensory variant of Guillain-Barré syndrome has been raised by several authors.<sup>4–6</sup> The existence of sensory Guillain-Barré syndrome has now been established beyond doubt and it is shown to be a demyelinating neuropathy electrophysiologically.<sup>7</sup> The current report is of six patients who would fit into the diagnosis of pure sensory variant of Guillain-Barré syndrome with clinical and electrophysiological features suggestive of small fibre sensory neuropathy.

## PATIENTS AND METHODS

During a period of 15 months we encountered six patients with acute onset peripheral sensory neuropathy at Ratnapura General Hospital. Detailed clinical histories were obtained from all. Details were obtained regarding exposure to toxins and chemicals, long term drug therapy, alcohol intake, history of diabetes mellitus, and family history of neuropathy. The initial neurological examination was followed by monthly assessments at the clinic by the same clinician (US).

Analysis of CSF was performed in all patients within the first 4 weeks of disease. Basic haematological and biochemical screening tests including erythrocyte sedimentation rate, fasting blood sugar, blood urea, liver profile, rheumatology profile, full blood count, and blood picture were also carried out in all patients. Antiganglioside and anti-sulfatide antibodies were not tested for. Stool culture for *Campylobacter jejuni* was performed in three patients who had experienced preceding diarrhoea. Urine was cultured from one who had an antecedent urinary tract infection. Chest radiographs and ECG were performed in all patients.

All six patients underwent an electrophysiological assessment within the first 4 weeks of their illness. The investigation comprised motor nerve conduction studies along with F wave studies (median, ulnar, and peroneal nerves), sensory nerve conduction studies (median, ulnar and sural nerves), sympathetic skin responses (hands and feet), and needle EMG. Detailed autonomic function tests were not performed except for postural blood pressure recording and routine ECG.

The first five patients did not receive any form of immunomodulatory therapy. Patient 6 was treated with a course of oral prednisolone starting on the 12th day of illness (60 mg daily for 1 week and tailed off over 2 weeks). Amitriptyline (10 mg three times a day) was given to patients 3, 4, 5, and 6 as symptomatic treatment for burning dysaesthesia.

## RESULTS

## Clinical features

There were four men and two women with ages ranging from 27 to 67 years (table 1). All of them presented with acute onset numbness of the upper and lower limbs. One patient complained of numbness over the face as well. Four had associated burning dysaesthesia in the limbs. Severe pain in the limbs at the onset of illness was reported by one. Four patients experienced their first symptom in the legs and two in the hands. All six had symptoms involving both upper and lower limbs. None complained of muscle weakness. A preceding illness was reported by four patients, diarrhoea in three, and urinary tract infection, which was treated with norfloxacin, in one. There was no evidence of diabetes mellitus, alcohol intake, exposure to chemicals and toxins, or long term medication to account for peripheral neuropathy in any of the patients. No one had a history or a family history of neuropathy.

On neurological evaluation cranial nerves and muscle power were normal in all. Tendon reflexes were either normal or brisk. All six had symmetric “glove and stocking” type sensory loss for pinprick and temperature with intact vibration and proprioception. None of them had ataxia or other signs of

**Abbreviations:** ASFSN, acute small fibre sensory neuropathy; SSR, sympathetic skin response

**Table 1** Clinical features and investigations

| Patient | Age (y), sex | Symptoms                              | Site of onset | Signs in limbs |          |          | Preceding illness             | CSF        |                    |                   | SSR latency (s) |      |        |
|---------|--------------|---------------------------------------|---------------|----------------|----------|----------|-------------------------------|------------|--------------------|-------------------|-----------------|------|--------|
|         |              |                                       |               | P and T        | PC and V | reflexes |                               | PR (mg/dl) | Po/mm <sup>3</sup> | l/mm <sup>3</sup> | Time of LP      | Hand | Foot   |
| 1       | 30, M        | Numbness                              | Feet          | A              | N        | N        | A                             | 102        | 3                  | 5                 | 10 days         | 1.5  | 1.8    |
| 2       | 28, M        | Numbness                              | Feet          | A              | N        | N        | Diarrhoea (1.5 months before) | 53         | 1                  | 1                 | 3 weeks         | 2.7  | 2.8    |
| 3       | 27, F        | Numbness and burning sensation        | Hands         | A              | N        | N        | UTI (1 week before)           | 55         | 1                  | 1                 | 2 weeks         | 1.6  | 2.6    |
| 4       | 33, M        | Numbness and burning sensation        | Feet          | A              | N        | B        | Diarrhoea (3 weeks before)    | 63         | 0                  | 0                 | 1 week          | 1.9  | Absent |
| 5       | 67, M        | Numbness and burning sensation        | Feet          | A              | N        | B        | A                             | 95         | 6                  | 2                 | 4 weeks         | 3.4  | 1.9    |
| 6       | 44, F        | Numbness, pain, and burning sensation | Hands         | A              | N        | N        | Diarrhoea (3 days before)     | 92         | 4                  | 1                 | 10 days         | 2.9  | 2.1    |

P, pain; T, temperature; PC, proprioception; V, vibration; A, absent; N, normal; B, brisk; UTI, urinary tract infection; PR, protein; Po, polymorphs; L, lymphocytes; LP, lumbar puncture; SSR, sympathetic skin response

cerebellar dysfunction. Other system examinations were essentially normal in all patients. Postural hypotension or heart rate irregularities were not found in any patient.

### Investigations

All six patients had albuminocytological dissociation in CSF (table 1). Both stool and urine cultures were negative. The haematological and biochemical tests along with chest radiographs and ECG were all normal. The sensory and motor nerve conduction studies including F wave studies were essentially normal in all patients. None of them showed any evidence of demyelination or axonal degeneration. The sympathetic skin responses were recorded from hands and feet of five patients. In one patient it was elicited in the hands but absent in the feet. Needle EMG studies were all normal.

### Disease course and outcome

After an acute onset, numbness and burning sensation increased gradually to reach the peak deficit within 4 weeks (range 2 days to 4 weeks) (table 2). Thereafter those symptoms would remain static (plateau phase) for a period ranging from 7 to 14 days, followed by gradual recovery.

In patients 1 and 2, complete resolution of symptoms occurred within 2 weeks. Those who presented with numbness and burning dysaesthesia, experienced relief from the second symptom first, usually within 4 months (range 1 to 4 months). Objective sensory loss for pain and temperature persisted longer than subjective feeling of numbness.

Complete recovery was reported in two patients. The outcome of the rest also seems to be satisfactory. At the last follow up visit, they only had mild numbness with peripheral sensory loss, which did not cause appreciable disability.

### DISCUSSION

Guillain-Barré syndrome is heterogeneous, consisting of several clinicopathological entities. Their clinical, pathological, and electrophysiological characteristics have been reviewed elsewhere.<sup>8</sup> Acute sensory neuropathy as a type of Guillain-Barré syndrome has been described. It is now identified as sensory Guillain-Barré syndrome. Oh *et al* reported eight patients with sensory Guillain-Barré syndrome, who fulfilled the following diagnostic criteria; acute onset symmetric sensory loss, progression up to 4 weeks, diminished or absent reflexes, normal muscle power, electrophysiological evidence of demyelination in at least two nerves, monophasic course, no alternative cause for neuropathy, no family history of neuropathy, and increased CSF protein (in some).<sup>7</sup>

The group of six patients studied by us meet seven of the nine criteria described above. They differ from the series reported by Oh *et al* in their electrophysiological features and having normal or brisk reflexes. Even though the overall picture is compatible with sensory Guillain-Barré syndrome, those two features suggest that the involved nerve fibre type could possibly be different in our patients.

Nerve fibres can be classified depending on the diameter. According to the scheme proposed by Lloyd, unmyelinated nerve fibres with the smallest diameter are classified as group IV.<sup>9</sup> Postganglionic autonomic fibres and sensory fibres carrying pain and temperature belong to this category. Vibration and proprioception are carried along large myelinated fibres. Therefore, in peripheral neuropathies with selective involvement of small diameter fibres, identified as small fibre neuropathy, there should be peripheral sensory loss for pain and temperature with intact tendon reflexes. Small diameter nerve fibres have been shown to be affected in neuropathies in association with several conditions including diabetes mellitus,<sup>10</sup> malignancies,<sup>11</sup> vasculitis,<sup>12</sup> and amyloidosis.<sup>13</sup> Small fibre neuropathy is characterised by impaired pain and temperature sensation, burning painful dysaesthesia, and autonomic dysfunction with relative sparing of tendon reflexes, proprioception, and muscle power.

**Table 2** Disease course and outcome

| Patient | Time to peak deficit | Duration of plateau phase | Duration of symptoms |                            | Signs in extremities at last follow up visit |          |          | Duration of follow up |
|---------|----------------------|---------------------------|----------------------|----------------------------|--|----------|----------|-----------------------|
|         |                      |                           | Burning dysaesthesia | Numbness                   | P and T                                      | PC and V | Reflexes |                       |
| 1       | 1 week               | 10 days                   | –                    | 6 weeks                    | N  | N        | N        | 6 months              |
| 2       | 1 week               | 2 weeks                   | –                    | 2 months                   | N  | N        | N        | 5 months              |
| 3       | 4 weeks              | 1 week                    | 4 months             | Face 4 months UL 10 months | A  | N        | N        | 13 months             |
| 4       | 2 days               | 2 weeks                   | 1 month              | Present at last follow up  | A  | N        | B        | 5 months              |
| 5       | 15 days              | 2 weeks                   | 2 months             | Present at last follow up  | A  | N        | B        | 5 months              |
| 6       | 2 days               | 1 week                    | 1 month              | Present at last follow up  | A  | N        | N        | 3 months              |

UL, upper limbs.

All six patients described here demonstrate clinical features compatible with small fibre sensory neuropathy. Routine motor and sensory nerve conduction studies assessed large myelinated fibres. Normal findings in this study exclude demyelinating and axonal neuropathies involving large diameter nerve fibres. Sympathetic skin response (SSR) is an electrophysiological technique to measure peripheral sympathetic conduction through small unmyelinated fibres. The SSR is considered abnormal when it is absent, indicating peripheral sympathetic fibre dysfunction.<sup>14</sup> It was elicited in all except for the legs in one patient, which suggests that peripheral sympathetic fibres are generally unaffected. The overall clinical picture along with electrophysiological findings is in favour of selective involvement of small diameter sensory fibres with relative sparing of large myelinated fibres and small sympathetic fibres in the group.

In general, the outcome seems to be favourable. The burning dysaesthesia tends to disappear within 4 months. Numbness and peripheral sensory loss seem to last longer. However, the residual deficits are not serious enough to cause significant disability. Oh *et al* reported a good response to steroids in one of the patients in their series of patients with sensory Guillain-Barré syndrome.<sup>7</sup> However, in our study, one patient was treated with oral steroids and her outcome does not seem to be significantly different from the rest.

These six patients could perhaps be considered a subgroup of sensory Guillain-Barré syndrome, as they fulfill most of the diagnostic criteria described previously.<sup>7</sup> It seems reasonable to identify this clinical entity as acute small fibre sensory neuropathy (ASFSN), based on their clinical and electrophysiological features, even though quantitative sensory testing was not performed for confirmation of small fibre involvement.

In different clinicopathological types of Guillain-Barré syndrome, antibody mediated damage seems to occur at different sites such as myelin sheath,<sup>15</sup> axons,<sup>16</sup> and dorsal root ganglia.<sup>17</sup> Small fibre involvement in Guillain-Barré syndrome has been shown in a postmortem study, although not in isolation.<sup>18</sup> There is evidence that in peripheral neuropathies, functionally different small fibre systems are affected independently, and selective involvement of different small fibre types is frequent.<sup>19</sup> This study hints that in Guillain-Barré syndrome small sensory fibres are a possible target for selective damage by antibodies. Further research in this regard should be aimed at detailed electrophysiological tests to assess small fibre function such as quantitative thermal sensory testing, quantitative sudomotor axon reflex testing, and cardiovascular autonomic testing, immunological studies to identify the antibodies involved, and trials of immunomodulatory therapy to assess its efficacy and outcome.

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