

GUILLAIN-BARRE SYNDROME AND *CAMPYLOBACTER* INFECTION

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Abstract. *Campylobacter* infection of the gastrointestinal tract has been observed as an antecedent illness in some patients with Guillain-Barre syndrome (GBS); these patients have been reported to have poor prognosis. We investigated 29 patients with GBS, admitted to our hospital from January 1996 to December 1999 for recent *Campylobacter* enteritis by culture of their stool specimens. *Campylobacter upsaliensis* and *C. jejuni* were isolated from stools of one patient each with acute motor axonal neuropathy (AMAN) and acute inflammatory demyelinating polyradiculoneuropathy (AIDP) respectively. The patient with *C. upsaliensis* infection was a 7 year-old male child who developed features of AMAN, 7 days after onset of diarrhea. He recovered gradually within 24 days with residual deficit in the form of foot drop. This deficit has persisted for last three and half years. The other patient with *C. jejuni* infection was a 9 year-old boy, who developed AIDP after 9 days of acute diarrhea. This patient recovered completely within 28 days of illness without any deficit. None of the patients had relapse of GBS. The present findings indicate the need of planned systematic studies to explore the role of *C. upsaliensis* and other campylobacters as agents of antecedent diarrhea in patients of GBS with different clinical presentations and prognosis.

INTRODUCTION

Guillain-Barre syndrome (GBS) is an autoimmune disorder of the peripheral nervous system characterized by weakness, usually symmetrical evolving over a period of several days or more (Adams and Victor, 1993). The trigger for this immune attack is unknown but usually follows an infectious illness (Winer *et al.*, 1988). In recent studies, *Campylobacter jejuni* infection has emerged as single most important antecedent event associated with GBS. Upto 40% of patients with GBS have culture or serological evidence of antecedent *C. jejuni* infection (Mishu *et al.*, 1993; Rees *et al.*, 1995). Recently *C. upsaliensis* infection has been reported as trigger for GBS (Ho *et al.*, 1997; Lastovica *et al.*, 1997). Presently many variants

of GBS have emerged which include acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor-sensory axonal neuropathy (AMSAN) and Fisher's syndrome (FS) (Griffin *et al.*, 1996). All these forms of GBS have been associated with preceding *C. jejuni* infection (Allos, 1998; Ho *et al.*, 1995; Yuki *et al.*, 1994). *C. jejuni* and possibly other *Campylobacter* infections are thought to be much more common in developing countries (Taylor, 1992) but their association with GBS, to a large extent remains unexplored in these countries. So far, no published reports on this subject are available from India. Therefore, we planned to culture the stool specimens for *Campylobacter* species from some of the GBS patients admitted to our hospital.

MATERIAL AND METHODS

Patient population

Single stool specimen from 29 patients (aged between 3 to 76 years; mean 27 ± SD

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20) with GBS admitted to our hospital from January 1996 to December 1999 were cultured for *Campylobacter* species. Different patterns of GBS were diagnosed by electrophysiological and other clinical studies. Routine nerve conduction studies were performed by standard techniques. Intercostal nerve conduction studies were done by the surface recording over the rectus abdominis muscle (Pradhan and Troly, 1989). Electromyography was performed by concentric needle electrode.

Isolation and identification of *Campylobacter* species

Fecal specimens were plated on selective medium, Campy-BAP (Difco) with antibiotic supplements (Blaser *et al*, 1989). In addition to primary plating on selective medium, stool samples were also cultured on non-selective blood agar medium using filtration method (0.45 µm cellulose acetate filter) (Piersimoni *et al*, 1995). The plates were incubated at 42°C in candle jar with a MacConkey plate seeded with *Escherichia coli* for better microaerophilic condition as described earlier (Prasad *et al*, 1991). The characteristic colonies were identified by Gram staining, biochemical and antibiotic sensitivity tests (On, 1996; Prasad, 1999).

RESULTS

Of 29 patients, 7 (24.1%) had history of diarrhea within 6 weeks preceding illness. *Campylobacter* was recovered from stool of 2 patients; overall isolation from patients with GBS was 6.9% but isolation from patients with history of diarrhea was 28.6%. One strain was recovered only on non-selective medium using filtration technique and this strain was identified as *C. upsaliensis*. The other strain was isolated on both selective and non-selective media and was identified as *C. jejuni*.

Patient 1, a 7-year male child had a history of acute diarrhea for a period of 4 days. Eight days after the onset of diarrhea, he developed sudden weakness in all four limbs, which was more marked distally with no sensory symp-

toms or signs. AMAN type of GBS was diagnosed on clinical and electrophysiological grounds. His motor nerve conduction study showed marked reduction in the amplitude of compound motor action potentials with mildly reduced conduction velocity in upper as well as lower limbs. Sensory conduction study was essentially normal except for the borderline low sensory nerve action potentials from both sural nerves. Phrenic and intercostal nerve conduction studies were essentially normal. Electromyography done 3 weeks after the illness revealed acute denervation at rest and reduced recruitment on efforts, which was more marked in the distal muscles. No pathogen other than *C. upsaliensis* was isolated from his stool. The patient recovered gradually within 24 days with residual weakness in the form of foot drop. The patient is on follow up for more than three and half years with persistent foot drop but no symptom of relapse.

Patient 2, a 9-year boy had the history of varicella-zoster virus (VZV) infection and watery diarrhea 20 and 9 days prior to neurological illness respectively. He developed progressive weakness from proximal to distal muscles in the lower limbs followed by upper limbs. AIDP was diagnosed on clinical and electrophysiological basis. Nerve conduction study revealed decreased conduction velocity in motor as well as in sensory nerves with only mild reduction of amplitudes. Conduction block was demonstrable in both the median nerves. Phrenic and intercostal nerves showed only mild slowing. No denervation potential was observed on electromyography. *C. jejuni* was isolated as sole pathogen from stool. The patient recovered within 4 weeks with no residual deficit.

DISCUSSION

Among 29 patients with GBS in our study, 2 (6.9%) had evidence of *Campylobacter* enteritis by stool culture preceding illness. Recovery of campylobacters from stool has been reported to vary from 8-30% of GBS patients (Rees *et al*, 1995; Kurki *et al*, 1993). Ropper (1988)

isolated *Campylobacter* from 4 (44.4%) of 9 patients with diarrhea preceding GBS as compared to 2 (28.6%) of our 7 patients with antecedent diarrhea. Though majority of our GBS patients were young adults (median age 27 years), both the patients with antecedent *Campylobacter* infection were children. This may be due to high prevalence of *Campylobacter* infection in children in developing countries including India. There are reports that majority of pediatric patients with *Campylobacter* associated GBS require mechanical ventilatory support and recover with severe neurologic deficits (Ho *et al*, 1997; Cole and Mathew, 1987). The relatively benign course of our two patients with *Campylobacter* infections is also evident from the borderline normal or only slightly deranged phrenic and intercostal nerve conductions; severe abnormality of these nerves are known to precipitate ventilatory failure (Pradhan, 1990). However, both of our patients recovered without ventilatory support and one patient with AMAN and preceding *C. upsaliensis* enteritis has a foot drop. So far, two cases of GBS related to *C. upsaliensis* have been reported in literature; one 64 year old US woman with AMAN improved quickly following plasmapheresis (Ho *et al*, 1997) and the other, a South African child had less severe form of illness as compared with *C. jejuni* biotype 2 associated GBS (Lastovica *et al*, 1997). No nerve conduction study was performed on the African patient; thus the pattern of GBS is not known. In a recent study, majority of GBS and FS patients who had anti-*C. upsaliensis* antibodies also had anti-*C. jejuni* antibodies and anti-*C. upsaliensis* antibodies were absorbed by *C. jejuni* surface proteins (Koga *et al*, 1999). Therefore, detection of anti-*C. jejuni* antibodies as done in most of the recent studies may not always be able to distinguish enteritis caused by different *Campylobacter* species. Role of *C. upsaliensis* and other *Campylobacter* infections as trigger for GBS need further evaluation.

Patient 2 in the present study had AIDP pattern with antecedent *C. jejuni* and VZV infections. This patient recovered completely within 28 days with no neurological deficit.

VZV is also known as trigger of GBS (Hughes and Rees, 1997). Two precipitating antecedent factors, *C. jejuni* and VZV infections are probably being reported first time in a GBS patient.

From the present study, it is clear that *Campylobacter* associated GBS exists in this region and perhaps is more common among children. Also, the disease is probably not always that severe as reported from the developed countries. It is known that in developing countries the exposure to *Campylobacter* infection occurs in early life with often reinfection. Whether pre-existing antibodies have some role to determine the course and severity of disease is not known. Systematic studies are needed worldwide, especially in developing countries to find out the role of whole spectrum of campylobacters in GBS and their effects on clinical course of the disease.

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