ACUTE POLYRADICULONEURITIS SYNDROME: CLINICAL OBSERVATIONS AND DIFFERENTIAL DIAGNOSIS

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SUMMARY – Guillain-Barré syndrome (GBS) and neuroborreliosis may clinically manifest with symptoms related to acute polyradiculoneuritis. The aim and purpose of this study was analysis of clinical picture in patients with acute polyradiculoneuritis and their differential diagnosis into patients with GBS or meningoradiculoneuritis within the framework of neuroborreliosis. In this retrospective study, medical records of patients with acute polyradiculoneuritis hospitalized at University Department of Neurology, Sestre milosrdnice University Hospital Center during a 4-year period were analyzed. The study included data on 27 patients. Definitive diagnosis of GBS was made in 23 patients and of neuroborreliosis in four (14.8%) patients. Acute inflammatory demyelinating polyneuropathy was recorded in 69% of GBS patients, Miller Fisher syndrome in four patients, and acute motor axonal neuropathy and/or acute motor and sensory axonal neuropathy in three patients. Clinically, patients with neuroborreliosis manifested flaccid tetraparesis, peripheral facial nerve paresis, bulbar paresis, ocular motility disorders, and sensory symptoms of radicular pain and paresthesias. Considering the relatively high prevalence of neuroborreliosis in north-west Croatia, it is important to exclude meningoradiculoneuritis caused by *Borrelia burgdorferi* on differential diagnosis of GBS in these patients.

Key words: *Neuroborreliosis; Guillain-Barré syndrome; Acute polyradiculoneuritis*

Introduction

Acute polyradiculoneuritis develops due to an inflammatory reaction that affects spinal and cranial nerve roots and peripheral nerves[1]. The clinical picture of acute polyradiculoneuritis in north-west Croatia usually appears within two entities: Guillain-Barré syndrome (GBS) and, more rarely, neuroborreliosis[2,3].

GBS is acute, rapidly progressive, autoimmune polyradiculoneuropathy that develops after respiratory or gastrointestinal bacterial or viral infection in two-thirds of patients. In its classic form, GBS is manifested with a symmetric, most commonly ascending motor weakness of extremities with areflexia and albuminocytologic dissociation in the cerebrospinal fluid[4]. According to the immune response intensity and the prevailing nerve damage, there are several clinical subtypes of GBS. In our region and in Western Europe, the most common GBS subtype is acute inflammatory demyelinating polyneuropathy (AIDP), recorded in 90% of GBS cases. Other forms of GBS are acute motor axonal neuropathy (AMAN), acute motor and sensory axonal neuropathy (AMSAN), Miller Fisher syndrome and very rare acute autonomic polyneuropathy. AMAN and AMSAN are characterized pathoanatomically and electrophysiologically by wallerian degeneration and axonal damage that affect motor and sensory peripheral nerves and their dorsal roots. Miller Fisher syndrome is a rare form of GBS that is clinically characterized by ophthalmople-

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gia, ataxia, areflexia and a mild, rapidly progressive ascending or descending, relatively symmetric muscular weakness that can be accompanied by paresthesias. Positive antibodies of the IgG class to GQ1b ganglioside are found in 90% of patients[4-7].

Acute polyradiculoneuritis within neuroborreliosis occurs after nervous system infection by the spirochete *Borrelia burgdorferi* (*B. burgdorferi*) that is transmitted by the *Ixodes ricinus* tick bite[8]. This tick is the most widespread tick species in Croatia, but its population is denser in the north of Croatia, so the largest number of patients suffering from Lyme borreliosis have been recorded in the City of Zagreb, Krapina-Zagorje County, Zagreb County and Koprivnica-Križevci County, whereas in Dalmatia it occurs very rarely[3]. Meningoradiculoneuritis caused by *B. burgdorferi* infection (Bannwarth's syndrome) is characterized by radicular pain and paresthesias, weakened/missing myotatic reflexes, various levels of motor weakness that is usually asymmetric, frequent involvement of cranial nerves and, especially, facial musculature weakness that is bilateral in 25% of cases. In cerebrospinal fluid, there is pleocytosis (often mild lymphocytosis) and proteinorachia with normal glucose content, and definitive diagnosis is made by detecting antibodies in serum and cerebrospinal fluid[8,9].

This study analyzed the characteristics of the clinical picture of patients with acute polyradiculoneuritis, as well as their differential diagnosis into patients with GBS or meningoradiculoneuritis within the framework of neuroborreliosis. The severity and level of disability in GBS patients were determined, as well as the course and outcome of the disease.

Subjects and Methods

The study was conducted at University Department of Neurology, Sestre milosrdnice University Hospital Center, for the period from January 1, 2007 to December 31, 2010. The Department provides neurological care for the catchment population of around 200,000 citizens residing in the City of Zagreb and Zagreb County.

Patient data were retrospectively collected and analyzed by searching the Hospital medical documentation database and medical history data. All patients hospitalized during the aforementioned period with the clinical picture of acute polyradiculoneuritis were sorted out.

Detailed medical history data on the onset and course of disease, neurologic status, cerebrospinal fluid analysis results and *B. burgdorferi* analysis of serum and cerebrospinal fluid were sorted out for all patients. All patients underwent electromyoneurography and magnetic resonance (MR) of the brain and cervical cord.

Disability of GBS patients was determined by use of GBS disability scale at admission and at discharge from the hospital[4,10].

The diagnosis of GBS was based on clinical criteria, occurrence of albuminocytologic dissociation in cerebrospinal fluid and characteristic electrodiagnostic features[5].

Definitive diagnosis of neuroborreliosis was based on positive laboratory result of intrathecal synthesis of specific antibodies in cerebrospinal fluid[8].

Results

The study included 27 patients hospitalized at the Department between January 2007 and December 2010 with clinical picture of acute polyradiculoneuritis. After complete diagnostic work-up, definitive diagnosis of GBS was made in 23 patients and of neuroborreliosis in four patients. The mean patient age was 56.8 (range 19-82) years. There were 14 men, mean age 59.2 (range 25-82) years and 13 women, mean age 54.2 (range 19-72) years. Demographic and clinical characteristics of patients with the clinical picture of acute polyradiculoneuritis are shown in Table 1.

Of 23 GBS patients, AIDP as the most common clinical variation of the syndrome was found in the majority of patients (n=16; 69%), Miller Fisher syndrome in four patients, and AMAN and/or AMSAN in three patients.

Table 1. Demographic and clinical characteristics of patients with clinical picture of acute polyradiculoneuritis

Feature	n	%
Guillain-Barré syndrome	23	85.19
Neuroborreliosis	4	14.81
Gender (men)	14	51.85
Age (yrs)	56.8 (19-82)	

Data on previous infection were obtained from patient history in 16 (69%) GBS patients, whereas provoking agent could not be identified in seven patients. The most frequent preceding infections were respiratory infections in ten (62.5%) patients, followed by gastrointestinal infections in 5 patients and urinary infection in one GBS patient.

All patients were hospitalized within one week of symptom onset. The initial GBS symptoms were motor extremities weakness in 70% and sensory symptoms (paresthesias, hypoesthesias, pain and dysesthesias) in 65% of patients. Bulbar paresis occurred in five and bilateral peripheral facial nerve paresis in two patients. Symptoms of autonomic nervous system involvement were present in 50% of patients; the most common symptoms were urinary retention and constipation. Respiratory insufficiency developed in two patients requiring mechanical ventilation for 5 and 10 days, respectively. As mechanical ventilation was used for a short period of time, there was no need for tracheostomy.

Lumbar puncture was performed in all patients within 14 days of symptom onset. Albuminocytologic dissociation was demonstrated in 80% of GBS patients. On electrophysiological diagnosis, demyelinating polyneuropathy prevailed; it was determined in 19 patients, axonal polyneuropathy in three patients, and polyneuropathic neurographic changes in one patient.

According to GBS disability scale at admission, 11 patients were able to move independently or with assistance, while 12 patients were not able to move, two of whom were mechanically ventilated due to respiratory insufficiency. There was no intrahospital death. At discharge, all patients showed improvement on GBS disability scale by at least one level. Two patients remained immobile and confined to wheelchair. Clinical characteristics of GBS patients are shown in Table 2.

Immunomodulation therapy with parenteral immunoglobulin, 0.4 g/kg body weight for 5 days was introduced in all patients within 24 hours of admission and within ten days of symptom onset, according to the respective guidelines for GBS treatment[4,7,11].

In two of four patients with neuroborreliosis, there were positive history data on a preceding tick bite. In the clinical picture of two patients, there was tetraparesis with weakened reflexes, all patients had unilateral or bilateral facial nerve paresis of various severity, while in two patients other cranial nerves were also affected and clinically manifested with bulbar paresis and ocular motility disorders. Regarding stimulating sensory symptoms, radicular pain and paresthesias occurred in two patients. Patients with positive serologic and cerebrospinal fluid results for neuroborreliosis were administered parenteral ceftriaxone therapy for 21 days.

Table 2. Clinical characteristics of patients with Guillain-Barré syndrome (GBS)

Feature	n	(%)
Clinical variation GBS:		
AIDP	16	(69)
MFS	4	(18)
AMAN, AMSAN	3	(13)
Preceding infection:	16	(69)
Respiratory	10	
Gastrointestinal	5	
Urinary	1	
Unknown	7	(31)
Clinical symptoms:		
Motor weakness	16	(70)
Sensory symptoms	15	(65)
Bulbar paresis	5	(22)
Autonomous dysfunction	12	(50)
Facial paresis	2	
Albuminocytologic dissociation	18	(80)
Electrophysiological findings:		
Demyelination	19	(83)
Axonopathy	3	(13)
GBS disability scale:	Admission	Discharge
0	0	1
1	0	3
2	4	6
3	7	11
4	10	2
5	2	0
6	0	0

GBS = Guillain-Barré syndrome; AIDP = acute inflammatory demyelinating polyneuropathy; MFS = Miller Fisher syndrome; AMAN = acute motor axonal neuropathy; AMSAN = acute motor and sensory axonal neuropathy

Discussion

According to literature data, the annual incidence of GBS varies from 1.2 to 2.3 *per* 100,000 population, which corresponds to the GBS incidence in the present population[11]. On average, 290 new patients suffering from Lyme borreliosis are registered in Croatia every year, yielding an incidence of 6.55 *per* 100,000 population. However, until now there was no systematic data collection regarding nervous system involvement, so the proportion and incidence of neuroborreliosis remain unknown[3]. As Lyme borreliosis mostly occurs in north-west Croatia, and very rarely in Dalmatia, neuroborreliosis is also expected to occur more frequently in inland Croatia[3]. Studies have shown that 10%-15% of patients with untreated Lyme borreliosis develop neurologic symptoms; extrapolated to Croatia, it would yield approximately 30 new patients *per* year[12,13]. It should be noted that the present study included only those patients with neuroborreliosis who clinically manifested acute polyradiculoneuritis syndrome.

In Europe and North America, AIDP is the most common GBS form, and similar results were also obtained in this study[3,14]. However, our study included a larger number of axonal GBS forms that, according to previous studies, occur in 5%-10% of patients in North America and Europe[3,14]. This study also recorded a greater number of patients with Miller Fisher syndrome, the prevalence of which is reported to be higher in Japan than in Europe[3,14].

In this study, clinical symptoms were preceded by an infection a month before the onset of symptoms in two-thirds of GBS patients, which is consistent with the results of previous studies[15]. In the study performed by Koga *et al*., respiratory infections of upper airways were most common, followed by diarrhea[16]; similar results were also obtained in our study. However, in our study, data on previous infection or any other possible autoimmune trigger were not available in seven patients. One of the possible explanations could be the fact that the patients included in this study did not undergo routine serologic examination during diagnostic procedure, which would confirm or exclude a recent infection with one of the currently known infectious autoimmune triggers such as *Campylobacter jejuni*, cytomegalovirus, Epstein-Barr virus, *Mycoplasma pneumoniae* and *Haemophilus influenzae*.

Previous studies have shown that GBS mortality is 2%-12% and the risk significantly increases with age[3]. In this study, no death was recorded. One of the reasons is that only two younger patients developed respiratory insufficiency, which required mechanical ventilation.

According to our knowledge and literature search, no similar study on the occurrence, prevalence and differential diagnosis of acute polyradiculoneuritis syndrome has been published in Croatia. In this study, acute polyradiculoneuritis syndrome was caused by *B. burgdorferi* infection in 14.8% of patients. Because of different therapeutic approaches, this entity should be paid due attention on GBS differential diagnosis, especially in patients from north-west Croatia.

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Sažetak

SINDROM AKUTNOG POLIRADIKULONEURITISA: KLINIČKA ZAPAŽANJA I DIFERENCIJALNA DIJAGNOZA

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Guillain-Barréov sindrom (GBS) i neuroborelioza mogu se klinički manifestirati simptomima iz okvira akutnog poliradikuloneuritisa. Cilj i svrha istraživanja bila je analiza kliničke slike bolesnika s akutnim poliradikuloneuritisom kao i njihova diferencijalna dijagnoza u bolesnike s GBS-om ili meningoradikuloneuritisom u okviru neuroborelioze. Provedeno je retrospektivno istraživanje pretraživanjem i analizom baze medicinske dokumentacije bolesnika s akutnim poliradikuloneuritisom hospitaliziranih na Klinici za neurologiju KBC "Sestre milosrdnice" u razdoblju od četiri godine. U istraživanje je bilo uključeno 27 bolesnika, definitivna dijagnoza GBS-a postavljena je u 23 bolesnika, dok je dijagnoza neuroborelioze postavljena u 4 (14,8%) bolesnika; 69% bolesnika s GBS-om imalo je akutnu upalnu demijelinizirajuću polineuropatiju, u 4 bolesnika ustanovljen je Miller-Fisherov sindrom, dok je u 3 bolesnika ustanovljena akutna motorna i/ili senzomotorna aksonalna polineuropatija. Bolesnici s neuroboreliozom klinički su manifestirali flakcidnu teteraparezu, perifernu parezu ličnog živca, bulbarnu parezu, poremećaje bulbomotorike, a od osjetnih simptoma radikularne bolove i parestezije. S obzirom na relativno visoku učestalost neuroborelioze u bolesnika s područja sjeverozapadne Hrvatske, u diferencijalnoj dijagnozi GBS-a važno je isključiti meningoradikuloneuritis uzrokovan bakterijom *Borrelia burgdorferi*.

Ključne riječi: *Neuroborelioza; Guillain-Barréov sindrom; Akutni poliradikuloneuritis*