

Guillain-Barre Syndrome in Patients with Seroconversion of IgG Antibodies to *Borrelia Burgdorferi* sensu lato

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ABSTRACT

*A case of polyneuroradiculitis (Guillain-Barre Syndrome) is presented, which was diagnosed in a 62 year-old man after progressive weakness in the legs and arms and double vision, preceded by severe pain in the back. Diagnosis was made on the basis of electromyoneurography, a specific finding of cerebrospinal fluid (albumino-citological dissociation), and the clinical course of the disease. Serological analysis of serum included *Borrelia Burgdorferi sensu lato* (BBSL). Positive findings (slowing of conduction velocity of sensor and motor neurones, and marked albumino-citological dissociation), together with the dynamics of these findings on the 33rd, 67th and 101st days and one year and a half after the first clinical signs of disease, indicated the possibility of BBSL infection. Because of the absence of clear clinical and serological signs of other infections it was assumed that BBSL might be the possible trigger for Guillain-Barre Syndrome. The fact that there were no obvious clinical signs of infection with BBSL, only serological, suggests that in the case of unclear aetiology of Guillain-Barre Syndrome BBSL should not be excluded.*

Key words: Guillain-Barre Syndrome, neuroborreliosis, *Borrelia Burgdorferi*

Introduction

Guillain-Barre Syndrome is an immunologically mediated disorder in which the immunological system attacks the roots of the spinal and cranial nerves, resulting in focal inflammation, damage to the myelin sheath, and even of the axons themselves. The true cause of this autoimmune disorder is unknown and the reason why Guillain-Barre Syndrome attacks only certain individuals is also not known.

Vaccination, pregnancy, malignant diseases, bone marrow transplantation are also connected with the occurrence of this syndrome^{1,2}. The main clinical characteristic of the syndrome is progressive symmetrical muscular weakness and paralysis of the extremities, which develops within 3–4 weeks. It is accompanied by pare-

sthesia in the hands and feet, back pain and weak or absent muscular reflexes.

Specific antiborrelia IgM antibodies can be determined in the serum of patients 3–6 weeks after infection, and IgG antibodies after 1–3 months³. Damaged cranial nerves are also not a rare occurrence and most frequently involve oculogyria with consequent double vision (diplopia), prozones and aniso corea^{4,5}.

The pathognomic signs of Guillain-Barre Syndrome, apart from the clinical status, are pathological changes (lesions) in the cerebrospinal liquor and electrodiagnostic abnormalities of the peripheral nerves.

The course of the disease is generally monophasic and the rate of relapse is around 30%. The most satisfactory

treatment effect is achieved with plasmapheresis and/or intravenous application of immunoglobulins with symptomatic therapy and careful monitoring. The mortality rate is around 5%. Satisfactory recovery with slight or minimal neurological defects in the peripheral nerves occurs in 70–80% of patients⁵.

Our case is interesting because of the absence of obvious clinical signs of unusual infection, which can be interpreted as possible triggers for the syndrome. Also the serological findings were inconclusive. Consequently, the possibility of infection with *Borellia burgdorferi* Sensu Lato was investigated.

Case report

The patient was male, aged 62 years, a geodesic technician. He was a non-smoker and denied alcohol consumption. As a child he had suffered from rubella and varicella. He had never had any serious illness apart from appendicitis, resulting in appendectomy, in 1989. Digestive tract bleeding had occurred on one occasion during the same year. Gastroscopy was found to be normal. In childhood he was vaccinated against various diseases, after which he did not receive any vaccine. He denied ever losing consciousness or having significantly disturbed consciousness. He had not previously consulted a physician for cervical or lumbosacral radiculopathy, and stated that in principle he “avoided the use” of any kind of medication. Over-sensitivity to medication had not been noticed. Family case history normal. He denied being bitten by a tick. Because of the nature of his work and hobby (hunting) he spends much of his time in the countryside. The area in which he spends most time is known as an endemic focal area for meningoencephalitic ticks and other diseases, such as Lyme disease, tularemia and human ehrlichiosis. He denied having travelled to risk areas for infectious diseases.

The disease started at the beginning of 2001 with unexpected, severe pain in the abdomen beneath the right rib arch. The patient spent a sleepless night.

During the following five days the pain spread throughout the abdomen, back and to both legs. During the day the pain was less intense, while at night it was exceptionally severe and analgesics failed to alleviate the pain. On the sixth day vision deteriorated in his right eye, with double vision. He was unable to read and eventually his sight was completely lost in the right eye.

On the eighth day his legs felt weak and he was unable to walk. Severe pain continued in the abdomen and legs and he was unable to sleep at night. During the day he slept for very short periods, waking with severe pain.

Sphincter control was normal.

For the following ten days the situation was unchanged. On the 24th day lumbar puncture was performed and Guillain-Barre Syndrome was diagnosed on the basis of the finding of cerebrospinal fluid, electromyoneurography, clinical status and disease course.

Because of the pain in his legs and insomnia, physical therapy was carried out. From the 35th day of the disease, four treatments by plasmapheresis were performed in intervals of three to four days.

The nape of the neck was free, Lasegue negative bilaterally. Double vision occurred in the ortho-position, right bulbus lateral deviation. When looking to the left the right bulbus was delayed, and when looking to the right the left bulbus was delayed. Movements of the bulbus higher and lower were restricted, dissociated. The identically round pupils showed normal reaction to light and accommodation. Consensual reaction normal, moderately impaired vision in the right eye (at a distance of one meter the patient was unable to count the fingers on the hand of the examiner). Affective and spontaneous facio-motorics symmetric, satisfactory, with no lateralisation or loss of facial sensation. Other innervation of the cranial nerves normal.

Basic physical strength of the arms symmetric, satisfactory. The patient had difficulty raising his legs and holding them in an antigravitational position, symmetrically. Dorsal and plantar flexion of the feet severely impaired, symmetrically. The quality of all sensations was decreased non-symmetrically towards the periphery on the legs. The patient had normal sphincter control. Independent reflexes in the legs absent and induced with difficulty in the arms, symmetrically. Abdominal reflexes normal. Plantar responses induced with great difficulty symmetrically. Remaining neurological status normal.

Intellectual and cognitive functions satisfactory. Psychiatric functions satisfactory.

Routine laboratory findings (repeated several times) were normal. All the serological findings for BBSL were considered positive. Tumour markers: PSA total, CA 19–9, CEA normal; electrocardiogram (ECG) normal. Digestive system: gastroscopy, ultrasound of the abdomen, irrigography, computerised tomography (CT) of the abdomen – normal findings. X-ray of the whole spine – suspected angioma of the L2 spine. X-ray of the pelvis normal.

Craniogram normal. CT of the brain normal. Nuclear magnetic resonance (NMR) of the brain and whole spine, electroencephalogram (EEG), Fundus oculi bilaterally – normal findings.

Lumbosacral puncture: Pandy positive, proteins 2.0 gr/L, leukocytes 2/3, lymphocytes 5/3, glucose in liquor (GUL) 3.5 mm/L, chlorides 124 mmol/L.

Electromyoneurography (EMNG): (six weeks after the start of the disease): severe loss of motoneurons in both feet, slight loss of motoneurons in both lower legs and both hands and a significant decrease of motor and sensor neurone velocity. This finding, in correlation with the clinical finding, indicated polyradicular neuropathy.

Results of the analysis of liquor and serum for *B. burgdorferi* sensu lato (BBSL):

- Modified Kelly-Pettenkofer’s medium (MKP) was used for cultivation of *B. burgdorferi* sensu lato⁶. One ml of CSF obtained by lumbar puncture was inoculated into

a tube with 6.5 mL of MKP and cultivated at 33 °C for nine weeks.

- IgM and IgG antibodies to BBSL in serum and CFS were determined by indirect immunofluorescent test (IFA) without absorption⁵. A local isolate of *Borrelia aafzeli* was used as an antigen⁶.
- Titres of $\geq 1:256$ in serum and $\geq 1:8$ in CSF were interpreted as positive.
- There was no isolation of BBSL from CFS. Intrathecal borreliar IgG antibodies were negative.

All the above findings were considered positive serological findings for BBSL (Table 1).

TABLE 1
RESULTS OF SEROLOGICAL TESTING

Day from the start of disease	Serum	
	IgM	IgG
33	negative	1:512
67	negative	1:512
101	negative	1:256
365 (one year)	negative	1:256
547 (one and a half years)	negative	1:258

Results of serological testing

After the third treatment by plasmapheresis vision improved in the right eye and double vision was less pronounced. The pain was less intense and the patient was able to sleep. By the end of treatment the patient could get up without help and walk a short distance with help, slowly and with difficulty.

After physical rehabilitation in a spa for a period of six weeks further improvement occurred. The patient had no pain and was able to walk with a walking stick. Four and a half months after commencement of the disease double vision completely disappeared.

One year after the commencement of disease and specific treatment the following were determined during a routine neurological check-up. Subjectively: slight paresthesia in both hands, the lower legs and feet, and increased fatigue. Objectively: voluntary leg reflexes induced with difficulty, basic motor function normal.

Moderately severe to severe loss of motoneurons in the lower legs and feet, slight loss in the forearms and hands.

Discussion

Guillain-Barre Syndrome was diagnosed in a male patient on the basis of the finding of cerebrospinal fluid, electromyoneurography, clinical status and course of the disease. Because of the lack of obvious clinical and serological signs of other infections it was assumed that BBSL might be the possible trigger for Guillain-Barre

Syndrome, and the fact that there were no clinical signs of infection with BBSL, only serological, suggests that when the aetiology is unclear the possibility of Guillain-Barre Syndrome should not be ruled out.

Today *Campylobacter* infection is considered the most frequent causal trigger of Guillain-Barre Syndrome in 25–40% of patients^{7–10}. Importance is also attached to infections with Epstein-Barr and cytomegalo viruses. If the occurrence of Guillain-Barre Syndrome is preceded by a viral infection it is possible for the virus to change the nature of the cells of the nervous system so that its own immunological system no longer recognises them and consequently treats them like a foreign body (unknown cell). Another possibility is the effect of the virus on the immunological system, so that it hardly recognises the cells attacking it¹¹.

Correlation has been observed with other causal agents of infectious diseases, including *Mycoplasma* of pneumonia, leptospira, AIDS virus, BBSL^{5,12}. In the second stage of neuroborreliosis, which includes Garin-Biadoux-Bannwart's Syndrome, lymphocytic meningitis, lymphocytic meningo-radicalitis, encephalitis, myelitis, BBSL infection can cause damage to the peripheral nervous system, such as radiculoneuritis, which can result in the appearance of Guillain-Barre Syndrome^{13,14}. Neurological symptoms occur most frequently several weeks or months after the beginning of infection, when the

main clinical sign of the early stage of Erythema migrans (EM) disease has disappeared, if ever clinically present. Evidence of neuroborreliosis is the isolation of BBSL from liquor¹⁵. The finding is positive in 10% of patients.

Specific anti-borrelia IgM antibodies can be determined in the serum of patients 3–6 weeks after infection, and IgG antibodies after 1–3 months³. With the development of the disease the percentage of seropositive findings increases. The majority of patients with neuroborreliosis are reported at the end of summer, although they are diagnosed during the whole year.

All known factors which could have triggered the disease in our patient were negative^{16–18}. Thus, the question arises of whether positive IgG antibodies to BBSL at the commencement of the disease and their fourfold decrease during one year is a sufficiently reliable indicator that it was in fact infection with this causal agent which preceded and triggered the occurrence of Guillain-Barre Syndrome in our patient. This hypothesis is further supported by epidemiological data, the occurrence of the disease in the winter months (incubation period), and absence of common symptoms of the disease, which usually occur in the early manifest stage of infection with BBSL.

Whether or not it was necessary to include specific antimicrobial therapy in the case of this patient, and whether it can be assumed that at least one part of Guillain-Barre Syndrome of unknown aetiology related to the part that induced BBSL, are questions which remain unanswered.

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GUILLAIN-BARRE SINDROM U BOLESNIKA SA SEROKONVERZIJOM IgG ANTITIJELA KASNO OSJETLJIVE BORRELIJE BURGENDORFERI

SAŽETAK

Prikazujemo slučaj poliradikuloneuritisa (Guillain-Barre Sindroma) koji je dijagnosticiran u 62-godišnjeg muškarca nakon progresivne slabosti nogu i ruku i dvoslike, praćene jakim boli. Dijagnoza se temeljila na elektromiografiji, specifične promjene cerebrospinalnog likvora (albumino-citološka disocijacija), i kliničke karakteristike bolesti. Sero-loške analize seruma uključujući Borellia Burgdorferi kasno osjetljivi oblike (BBSL). Pozitivni testovi (usporeenje provođenja senzornim i motornim neuronima, i jasna albumino-citološka disocijacija), zajedno sa dinamikom tih pokazatelja 33, 67, 101 dan i godinu i godinu i pol nakon prvih kliničkih znakova bolesti, upućivali su na moguću BBSL infekciju. Odsustvo drugih jasnih kliničkih i seroloških znakova drugih infekcija može upućivati na moguću BBSL uzrok Guillain-Barre Sindroma. Nije bilo klinički jasnih znakova infekcije sa BBSL, osim serologije, koji bi upućivali na moguću nejasnu etiologiju Guillain-Barre Sindroma sa BBSL koji bi je mogli isključiti.