

## Neck stiffness in Guillaine-Barre syndrome subsequent to cytomegalovirus infection

### *Sitomegalovirüs enfeksiyonunu takiben gelişen Guillaine-Barre sendromunda ense sertliği*

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#### ABSTRACT

Guillain-Barre syndrome is an acute inflammatory demyelinating polyradiculoneuropathy that can be seen at any age. The classic symptoms such as flaccid paralysis and areflexia are not always predominant in children. In this study, we presented a 3-year-old girl with Guillain-Barre syndrome associated with cytomegalovirus infection who referred with showed atypical symptoms including neck stiffness.

**Key words:** Guillain-Barre syndrome, Cytomegalovirus, neck stiffness, pain

#### INTRODUCTION

Guillain-Barre syndrome (GBS) is the most common cause of acute flaccid paralysis in healthy infants and children.<sup>1</sup> The precipitating cause is not always obvious in GBS. Approximately two-thirds of patients have a history of an antecedent respiratory tract or gastrointestinal infection.<sup>1,2</sup> Patients usually present with symmetrical ascending muscle weakness along with areflexia. The diagnosis of GBS is relatively easy in patients with typical clinical and neurophysiologic findings. Rarely children may present with a clinical picture of meningeal irritation.<sup>3,4</sup>

In this manuscript, we reported a patient diagnosed with GBS associated with cytomegalovirus (CMV) infection who had an atypical presentation with signs of meningeal irritation and pain.

#### ÖZET

Guillain-Barre sendromu her yaşta görülebilen akut inflamatuvar demiyelinizan bir poliradikülopatidir. Çocuklarda flask paralizi ve arefleksi gibi klasik semptomlar her zaman belirgin olmayabilir. Bu çalışmada, ense sertliği benzeri atipik bulgular gösteren 3 yaşındaki bir kız hastada sitomegalovirusa bağlı Guillain-Barre sendromu sunuldu.

**Anahtar kelimeler:** Guillain-Barre sendromu, Sitomegalovirus enfeksiyonu, ense sertliği, ağrı

#### CASE

A 3-year-old girl who was otherwise healthy until ten days ago, had complaints of fever, vomiting and symptoms of upper respiratory infection which resolved with amoxicillin therapy. The patient referred to our clinic with complaints of fever, irritability, vomiting and leg pain since two days. Medical, developmental and family histories were obtained and deemed unremarkable.

General physical examination revealed an irritable and groaning child with normal vital signs except for an elevated body temperature (38°C). Normal mental status, diminished patellar reflexes, prominent neck stiffness and positive Kernig's and Brudzinski's signs were determined in neurological examination. Cranial nerve examination proved normal. There was no bladder or bowel involvement. Muscle strength testing was limited by pain but was

deemed as probably normal, and the patient was capable of walking alone. Gross sensory examination also proved normal.

Initial laboratory studies showed that white blood cell count was  $19.400/\text{mm}^3$  (70% lymphocytes and 30% neutrophils), hemoglobin 12.8 g/dl, and platelet count  $136.000/\text{mm}^3$ . Serum electrolyte and creatine kinase levels plus liver function tests were found normal. Initial cerebrospinal fluid examination showed 8 white blood cells/ $\text{mm}^3$  (all lymphocytes), glucose 63 mg/dl, protein 132 mg/dl (concomitant blood glucose level was 75 mg/dl). No white blood cells were determined and protein level was found elevated in the subsequent cerebrospinal fluid examination. Magnetic resonance imaging of the spine and brain proved normal.

Initial pre-diagnoses were bacterial or viral meningitis, partially treated meningitis and viral myositis. Intravenous ceftriaxone was administered against bacterial meningitis. Muscle weakness deteriorated significantly on the second day of hospitalization and the patient lost her ability to walk by the third day. Deep tendon reflexes disappeared completely in the lower extremities and muscle weakness started to advance to the upper extremities. Neck stiffness remained persistent. Lumbar puncture was repeated and albumino-cytological dissociation was determined (protein 252 mg/dl).

Nerve conduction and electromyography studies revealed inflammatory demyelinating polyradiculoneuropathy suggesting GBS. Mycoplasma, influenza, parainfluenza, enterovirus, human immunodeficiency virus (HIV), herpes simplex virus (HSV), Epstein Barr virus (EBV) serologies and venereal disease research laboratory (VDRL) tests were found negative. Cerebrospinal fluid culture, urine culture and stool cultures for salmonella, shigella and campylobacter were also found negative. No IgG antibodies were determined against GM1 and GM1b in enzyme-linked immunosorbent assay. CMV infection was determined with serology and was confirmed with polymerase chain reaction performed with blood samples.

A diagnosis of GBS was established and plasmapheresis therapy was initiated on the fourth day of hospitalization. The weakness in lower extremities was resolved and the pain in the back and legs was reduced at day 9, after five sessions of plasmapheresis. The clinical picture of meningismus

was normalized at 14 days. All complaints of the patient were resolved in the follow-up examination performed at one month.

## DISCUSSION

GBS is an acute or subacute inflammatory demyelinating polyradiculoneuropathy that can be seen at any age. GBS is readily diagnosed in who usually present with herald paresthesias, followed by ascending or generalized weakness and hyporeflexia, often following an infectious disease.<sup>2,3</sup> However, classic symptoms are not always predominant in children. Instead, pain is often the most prominent symptom in children. The most common pain syndrome noted in 83% of patients involves the back and lower limb.<sup>5</sup> Pain, observed in pediatric patients with GBS causes a significant irritability and it might be difficult to establish a diagnosis due to the presence of symptoms atypical of GBS including neck stiffness.

Controlled epidemiological studies have suggested that GBS is associated with campylobacter jejuni and viral infections including cytomegalovirus and Epstein Barr virus<sup>6</sup>. Winer et al.<sup>7</sup>, have reported preceding respiratory symptoms and gastrointestinal symptoms in 38% and 17% of patients with GBS, respectively. Serological evidence of C.jejuni and cytomegalovirus infections have been determined in 14% and 11% of patients, respectively. Neck stiffness has often been reported in GBS cases associated with C. jejuni infection.<sup>8,9</sup> Although CMV is the second most common cause of infection-related GBS, no association has been reported with pseudomeningoencephalitis. According to our research, this is the first case in the literature that indicates an association between neck stiffness and CMV infection.

Early diagnosis is of great importance in GBS to initiate intravenous immunoglobulin or plasmapheresis as soon as possible. Our patient had presented with neck stiffness, irritability, and pain prior to any weakness or fatigue, all of which suggested meningitis in the first place. The establishment of Guillain-Barre diagnosis was thus delayed in this case. The diagnosis was considered with the emergence of significant muscle weakness ascending to the upper extremities, and plasmapheresis therapy was started. Weakness in the lower and upper extremities was decreased on day 9, whereas neck

stiffness and pain, although started earlier, took 14 days to resolve with plasmapheresis therapy. This later resolution of neck stiffness and accompanying pain could also suggest a possible spinal pathology, however radicular pain due to nerve root inflammation is a more anticipated pathology in GBS. Possible mechanisms of meningeal or nerve root irritation in GBS include the release of effectors or by-products into the subarachnoid space as a result of the immune-mediated nerve root demyelination, and irritation of nervi nervorum.<sup>3,10</sup>

Consequently, in this report we suggest that neck stiffness and pain should be considered as part of the clinical spectrum in pediatric GBS to avoid delay in diagnosis and onset of appropriate treatment.

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