Atypical manifestations in children with Guillain–Barré syndrome

Julia Brasileiro de Faria Cavalcante, Pedro Nogarotto Cembraneli, Renata Brasileiro de Faria Cavalcante, Volmer Fernandes Valente Junior, José Edison da Silva Cavalcante

ABSTRACT

Introduction: Guillain–Barré syndrome (GBS) is an acute single-phase inflammatory demyelinating polyneuropathy that occurs after an infection, characterized by a clinical pattern of acral paresthesias, ascending generalized weakness, and areflexia. Its worldwide incidence ranges from 0.5 to 1.5/100,000 children/year, predominantly males. In children, the predominant symptoms are vague paresthesias, significant, poorly localized pain, weakness manifesting as disturbance of gait, and cranial nerve abnormalities, with facial nerves most commonly affected. Case Report: A 13-month-old female patient, crying for five days, presented with low fever, progressive, asymmetric loss of strength in lower limbs, regular general condition, tachypnea, tachycardia, hypotonia of right upper limb and left lower limb, positive Babinski sign to the right, Achilles and patellar tendon areflexia, discreet neck stiffness, hypoesthesia, and pain from the lower limbs to the xiphoid process, leading to the diagnosis of GBS. The cerebrospinal fluid did not indicate any alterations and the electroneuromyography showed reduced motor unit action potentials and normal motor conduction velocity, revealing acute motor axonal neuropathy. The patient developed respiratory arrest, requiring intensive care therapy, and orotracheal intubation. Immunoglobulin therapy was initiated and the patient gradually recovered the movements and reflexes.

Conclusion: It is very important to point out that when GBS is suspected, even if it is atypical, the patient should be admitted to the pediatric intensive care unit. This allows intensive nursing care and continuous monitoring to reduce the frequency and severity of complications.

Keywords: Asymmetry, Guillain–Barré syndrome, Paresthesia

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INTRODUCTION

Guillain–Barré syndrome (GBS) is classified as an eponym that encompasses acute immune-mediated polyneuropathies. It is considered to be an acute monophasic paralyzing disease that usually occurs after an infection and the most common cause of flaccid paralysis in the world [1–3]. Its worldwide incidence ranges from 0.89 to 1.89/100,000 people/year (average 1.1) and, more specifically, 0.5 to 1.5/100,000 children/
year, predominantly affecting males. Although all age bands may be affected, the peak incidence ranges from 20 to 40 years, with an increase of approximately 20% every ten years after the first decade of life [1, 4–6].

The clinical presentation of GBS begins with paresthesias in the hands and feet, followed by progressive symmetrical muscle weakness, which begins in the lower limbs and may last hours or even months [1, 4, 5]. In children, proximal weakness is less common, whereas pain and difficulty in gait and greater involvement of cranial pairs predominate [7–9]. In approximately 70% of the cases, patients had a previous infection about 1–3 weeks before. Generally, this infectious condition was of gastrointestinal or respiratory origin and the most common etiological agents are: Campylobacter jejuni, cytomegalovirus, and Epstein–Barr virus. The first agent is frequently associated with the most severe type of this syndrome, the acute motor axonal neuropathy (AMAN) [10].

Guillain–Barré syndrome has four presentations, here listed from the most to the least common: acute demyelinating inflammatory polyneuropathy (AIDP), AMAN, Miller–Fischer syndrome, and acute motor and sensory axonal neuropathy. Acute demyelinating inflammatory polyneuropathy corresponds to 85–95% of cases, while AMAN represents 10–20% of them [1].

The diagnosis is primarily clinical. However, complementary exams such as cerebrospinal fluid (CSF) analysis and electroneuromyography (ENMG) are necessary to confirm the diagnostic hypothesis and rule out other causes of flaccid paraparesis [1, 3, 11]. After the diagnosis is confirmed, the treatment with immunoglobulin or plasmapheresis is initiated together with motor physical therapy [1, 12].

In general, the prognosis for children is better compared to that for adults, since approximately 85% of the pediatric patients have an excellent recovery [13]. Nonetheless, a small number of the children affected may be incapacitated or even progress to sepsis, pulmonary embolism, and death [1, 7].

Thus, we report a case of a 13-month-old female patient diagnosed with GBS, but with atypical clinical presentation and exam results.

**CASE REPORT**

A 13-month-old female patient was born by Caesarean section at 38 gestational weeks and 4 days, 3080 g, 47 cm, uneventful pregnancy and delivery, prenatal tests performed correctly. The baby was exclusively breastfed and walked at one year of age. She was referred to our service due to a history of low fever, accompanied by flu symptoms and crying for five days. She presented with progressive asymmetric loss of strength in lower limbs and cough. Given that she was followed up by a neurologist because of a diagnosis of macrocephaly since the age of six months, a magnetic resonance imaging (MRI) of the skull was carried out but showed no alterations.

The child evolved to a regular general state, with high respiratory rate (80 breaths per minute), characterizing tachypnea, associated with tachycardia (185 beats per minute), with ascending hypotonia of right upper limb and left lower limb. In addition, she cried constantly and presented with coldness to touch in the left lower limb.

The patient was examined by a neurosurgery team, who observed that she had axial and bilateral lower limb hypotonia, positive Babinski sign to the right, Achilles and patellar tendon areflexia, discreet neck stiffness, and hypoesthesia and pain from the lower limbs to the xiphoid process. The diagnosis of GBS was proposed based on two diagnostic criteria, namely progressive weakness in more than one limb and hyporeflexia/areflexia.

The examination of CSF revealed no protein increase, negative cultures, normal glucose level, and increased cellularity. The patient underwent ENMG to confirm the diagnostic hypothesis. This exam detected reduced motor unit action potentials and normal motor conduction velocity, indicating acute motor axonal neuropathy.

The patient developed respiratory arrest, requiring intensive care therapy, and orotracheal intubation. She was intubated for 10 days and simultaneously underwent immunoglobulin therapy. She had improvements in the respiratory condition and showed gradual recovery of movements and reflexes. After being discharged from the intensive care unit (ICU), the patient remained hospitalized under the care of a neurologist and a pediatrician.

**DISCUSSION**

Guillain–Barré syndrome was first described in 1916 by the French neurologists Guillain, Barré, and Strohl, who reported the cases of two soldiers who developed acute paralysis with muscle weakness, areflexia, and albuminocytologic dissociation in the CSF [14]. Since polio eradication, GBS has become the most frequent cause of acute and subacute flaccid paralysis in the world [15–17].

Approximately 70% of GBS cases appear about 1–3 weeks after an infection, either respiratory, gastrointestinal, or any other type that induces an aberrant autoimmune response. Given that it is benign, most often this infection might be minimized or forgotten by the patient [16–19]. The most widely reported agent is C. jejuni, but other infections associated with this condition are those caused by cytomegalovirus, Epstein–Barr virus, Measles morbillivirus, influenza virus, Mycoplasma pneumoniae, as well as enterovirus D68 and Zika virus [20–28].

One of the hallmarks of GBS is progressive, bilateral, ascending weakness that usually begins in the lower distal extremities but may begin more proximally in the lower and upper limbs, giving the false impression of a pyramidal lesion [29–32]. Weakness peaks can take place within 2–4 weeks after the onset of symptoms and a small number

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of patients have paraparesis [32]. In addition, patients may initially have sensory signs, ataxia, and characteristic autonomic dysfunction. Approximately one-third of the patients have muscle or nerve root pain even before they develop weakness [33]. Most patients present with reduced tendon reflexes in the affected limbs that were initially normal [34]. This syndrome may progress for up to six weeks after its onset. About 20–30% of the patients develop complications and may require mechanical ventilation during the course of the illness [29].

Regarding the pathogenesis of this disease, for many years its severity was related to the extent of axonal lesion due to demyelination. However, it is currently known that several phenotypes, such as acute inflammatory demyelinating polyneuropathy, in which the injury related to the immune system attacks the myelin sheath, in addition to acute axonal motor neuropathy, when the axonal membranes are the main target [16]. Guillain–Barré syndrome generally affects healthy people and is not associated with an autoimmune disease or another systemic disorder. The assumption that GBS is primarily a T cell-mediated disease has been challenged by the discovery of anti-glycolipid Abs in GBS variants and chronic dysimmune neuropathies [35].

It can be difficult to diagnose GBS in young children because their complaints are frequently atypical and their neurological examination is more challenging [36]. Table 1 summarizes GBS diagnostic criteria based on clinical exams, although additional examinations may be required [13]. In general, the exclusion diagnosis is based on two main tests, CSF evaluation and ENMG. In the first, the combination of high CSF protein level and CSF cell count within normal limits (known as albuminocytological dissociation) points to a GBS diagnosis. In the second, demyelinating or axonal neuronal lesions indicate GBS [1, 11]. Although not specific, post-gadolinium enhancement of the anterior and the posterior nerve roots of cauda equina can be seen on MRI in up to 95% of the patients presenting with GBS [37, 38].

The neurological examination helps the diagnosis, since symmetrical weakness of the lower limbs with decreased or absent osteotendinous reflexes and neuropathic pain are frequently found in patients with GBS. Hughes functional grading scale for GBS (Table 2) is used to assess patients’ motor impairment [39].

In general, GBS is a life-threatening disease, with a mortality rate of 3–7% [40, 41]. Higher prevalence of death is due to ventilatory insufficiency, complications, or autonomic dysfunction [42]. Patients show improvement mainly within one year from GBS onset [43]. Worst outcomes are usually associated with older age (>40 years), diarrhea, or C. jejuni infection in the four weeks preceding the disease [16].

Treatment requires a multidisciplinary approach consisting of general medical care in addition to immunological treatment (Table 3). Respiratory, cardiac, and hemodynamic functions should be monitored, and complications should be prevented or treated [16]. For

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<th>Table 1: Diagnostic criteria of Guillain–Barré syndrome [13].</th>
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<td><strong>Clinical features</strong></td>
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<td>Progressive weakness over a period of up to six weeks in the legs and arms (sometimes only in the arms)</td>
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<td>Hypo or flexlexia (sometimes normal or even hyperreflexia)</td>
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<td>Relative symmetry</td>
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<td>Mild sensory symptoms or signs</td>
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<td>Ache</td>
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<td>Autonomic dysfunction</td>
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<td>Complications, such as respiratory failure, requiring ventilation, aspiration pneumonia, sepsis, cardiac arrhythmia, hyper or hypotension, and urinary retention</td>
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<th>Table 2: Hughes functional grading scale for Guillain–Barré syndrome [39].</th>
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<th>Table 3: Therapeutic approach to Guillain–Barré syndrome [16].</th>
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<td><strong>General health care</strong></td>
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<td>Respiratory, cardiac, and hemodynamic monitoring</td>
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<td>Deep venous thrombosis prophylaxis</td>
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<td>Management of possible bladder and bowel dysfunctions</td>
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<td>Early physical therapy and rehabilitation</td>
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<td>Psychosocial support</td>
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<td>Treatment of pain using non-steroidal opioids or anti-inflammatory drugs</td>
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<td><strong>Immune treatment with documented efficacy</strong></td>
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<td>Intravenous immunoglobulin therapy</td>
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<td>Plasmapheresis</td>
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<td><strong>New controls under evaluation</strong></td>
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<td>Interferon-beta</td>
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pain control, the use of non-steroidal opioids or anti-inflammatory drugs is recommended [44]. Although no specific drug has been endorsed for the treatment of GBS, various drugs have been used to target the components of the immune response. Immunomodulatory treatments with immunoglobulin or plasmapheresis have been shown to be effective in accelerating recovery from GBS in addition to improving outcomes [1, 45].

CONCLUSION

It is very important to emphasize that if a diagnosis of GBS is suspected, even in atypical presentations, the child should be admitted to a pediatric ICU, under the care of a neurologist and a pediatrician, as the child of the present case report. The patients should remain there, inasmuch as they require continuous monitoring of hemodynamic and ventilatory parameters to provide life support, reduce the frequency and severity of complications, and detect autonomic changes early.

REFERENCES

in children, South Wales, United Kingdom, October 2015 to January 2016. Euro Surveill 2016;21(4).

Author Contributions

Julia Brasileiro de Faria Cavalante – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.

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