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ORIGINAL ARTICLE

A case report on rapid clinical recovery and satisfactory outcome of a toddler with probable Guillain-Barré Syndrome.

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Abstract

Introduction: Guillain-Barré Syndrome (GBS) is the most frequent cause of acute and sub-acute flaccid paralysis after polio eradication. Although rare, it is recognized as the leading cause of flaccid paralysis among the admissions to pediatric intensive care for acute neuromuscular diseases.

Objective: To report the case of a 14-month-old male patient with a probable diagnosis of GBS with acute, myelinated motor sensitive neuropathy, with probable secondary axonal involvement, with rapid clinical recovery.

Case Report: A male patient admitted in a reference hospital in the Federal District, Brazil, residing in the Integrated Development Region of the Federal District and Surroundings. The child was 14 months old and 8.6 kg, with an updated vaccination status and neuropsychomotor development appropriate for his age, with a condition of paresis in the lower limbs, without cognitive changes. After 14 hours of admission, due to the worsening of his clinical situation and the albumino-cytological dissociation identified by the analysis of cerebrospinal fluid, it was started immunotherapy with intravenous human immunoglobulin, 0.7g/kg/day for three days. Twenty four hours after start of treatment, the child showed a clinical improvement of his general condition. The patient was discharged after five days of hospitalization. After 76 days of discharge, there was a significant improvement in neuropsychomotor development, despite a slight delay in its development.

Conclusion: Due to the rarity of Guillain-Barré Syndrome among young children, it is important that health professionals remain sensitive to capture and treat unusual cases in a timely manner. We also recommend that the identified cases be monitored carefully, in order to check if the Guillain-Barré Syndrome, and its variants, can explain developmental disorders a posteriori.

Keywords: Guillain-Barre Syndrome, Child Health, Child Development.

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Authors summary

Why was this study done?
Guillain-Barré Syndrome (GBS) is considered a rare syndrome. Its involvement in children is even less frequent, especially under the age of 18 months. Although its diagnosis is a challenge, such a syndrome must be included among the differential diagnoses for neurological disorders in children, as its treatment is more effective and with less risk of sequelae when performed in a timely manner. This report presents a case of a 14-month-old child with a probable diagnosis of GBS, to alert the medical-pediatric community.

What did the researchers do and find?
Treatment with immunoglobulin was initiated two days after the establishment of lower limb paresis with an evident clinical improvement within 24 hours after start of treatment. The hypothesis of GBS is supported by clinical signs, analysis of cerebrospinal fluid and electroneuromyography. The developmental milestones were investigated with a validated instrument in current use, detecting partial interruption of the motor and orofacial functions, with subsequent return, but with a slight delay in walking and language. Currently, the child has a satisfactory clinical evolution.

What do these findings mean?
Diagnosis and appropriate intervention performed in a timely manner are inalienable rights of users of the National Health System (SUS-Sistema Único de Saúde). However, the rarity of GBS, particularly in young children, highlights the vulnerability of this population. It is up to health professionals to help with their experience in awareness and continuous updating to contribute with other professionals involved in the care of patients with GBS. In this case, so far, the syndrome has not irreversibly compromised the child's development, but it is important that his growth and development is carefully monitored.

INTRODUCTION

Guillain-Barré Syndrome (GBS) is the most frequent cause of acute and sub acute flaccid paralysis after polio eradication and is considered a rare neurological disease of autoimmune origin with a low incidence among children[1-3]. It is the main cause of flaccid paralysis among children in pediatric intensive care units for acute neuromuscular diseases, according to study carried out in a children's hospital in Boston[4].

Other causes of flaccid paralysis in childhood are acute myelitis, acute disseminated encephalomyelitis, chronic demyelinating inflammatory polyradiculoneuritis), myasthenia gravis, congenital myasthenia gravis, infantile botulism, hypokalemic periodic paralysis, rhabdomyolysis, dermatomyositis and myopathy[4,5].

The incidence of GBS in the world is unspecified, but it is known that for every 10 years of increasing age, there is a 20% increase in the risk of developing GBS[6]. Between 1990 and 1996, the annual incidence coefficient in Brazil, in children under 15 years old, was 0.39 to 0.63 cases/100,000 inhabitants[7]. In a health unit in the city of São Paulo, between 1995 and 2002, the incidence coefficient for this age group was 0.11/100,000 inhabitants, with the highest proportion of cases observed among children aged 0 to 4 years[2]. National data reported to World Health Organization (WHO), between 2000 and 2008, showed an average incidence coefficient of 0.4 cases/100,000 inhabitants under 15 years of age8. However, it is possible that these magnitudes are influenced by the prevalence of infections with neurotropic behavior[9], such as the Zika and Chikungunya arboviruses[10].

There are few cases reported in the literature in children under the age of eighteen months. We aim to report the case of a male patient, aged 14 months with a probable diagnosis of Guillain-Barré Syndrome compatible with motor sensitive, acute, myelinated neuropathy, with probable secondary axonal involvement, with rapid clinical recovery.

CASE REPORT

Male patient, resident in the Integrated Development Region of the Federal District and Surroundings , aged 14 months and 8.6 kg - with growth and weight within the normal curve11, diagnosed with sickle cell through blood test , updated vaccination status at September 11, 2019 (latest vaccines: triple viral, Pneumococcal conjugate and Meningococcal C conjugate), age-appropriate neuropsychomotor development, without previous hospitalizations, blood transfusions, surgeries or drug allergies. The patient was admitted on 21 October 2019 in the emergency room of Hospital Materno Infantil de Brasília (HMIB) with paresis in lower limbs, without cognitive changes.

The mother reported, that the child had a history of intestinal infection with watery and darkened diarrhea accompanied by low fever that started on September 30, 2019 and lasted for three days. The condition was evaluated by a pediatrician in the city of origin and treated with symptomatic drugs. On the night of October 13, the child presented pain in the pelvic region, hoarseness, runny nose and fever, diagnosed as laryngitis by the same pediatrician, on October 14, and medicated with Dexamethasone Disodium Phosphate, Ibuprofen and Saline Spray.

The pelvic pain condition gradually worsened, with episodes of lower limb myasthenia on October 17, when he returned to the pediatrician who prescribed Dipyrone, Amoxicillin associated with Clavulanate and nebulization with saline and Ipratropium Bromide. On October 18, the child had episodes of paresis of the lower limbs and difficulty for walking, a pediatrician examined him and detected impairment of balance and orthostatism, raising a diagnostic hypothesis of encephalitis or cerebellitis. The child was referred to the hospital.

Once the child was at HMIB, the medical evaluation showed that the child was in good general condition. No signs of cerebellitis or other neurological changes were detected and the child was released to his home with instructions and the same medications.

On the afternoon of October 19, the child developed persistent lower limb paresis, hip and lower limb pain relieved by prone position and worsened in other positions, without trunk control, stiff neck with preserved

cervical support, crying, gait and static limited. Preserved bowel and bladder sphincter control. On October 21, in his origin city, the pediatrician re-evaluated the child and detected signs of meningeal irritation with motor deficit in the lower limbs, with no capacity to support the body, pointing to the diagnosis hypotheses of encephalitis and meningitis. Again, the pediatrician referred the child to the HMIB.

In an anamnesis, the mother reported that his child had persistence of fever and myalgia of the lower limbs, despite the administration of pain relievers and antipyretics, with myalgia being characterized as "pain from the waist down" that led the child to adopt a relief position, evolving to difficulty followed by disability to wander.

Upon hospital admission, the child was in regular general condition, flushed, hydrated, acyanotic, anicteric, eupneic, afebrile, active and reactive, without rash or haematoma, pain when he is touched or sustained with relief in prone position, presenting discomfort to hip palpation, crying when placed in the fetal position, symmetrical hypotonia of the lower limbs, negative bilateral plantar skin reflex (Babinski sign) and inability to stand. Osteotendinous reflexes, plantar skin reflex in flexion and sensitivity and visual field examination were not recorded.

The diagnosis for admission to the pediatric unit was hypothesis of neuropathy. The treatment started with intravenous antibiotic therapy (Cefotaxime). After 14 hours of admission, on October 22, due to the worsening of the clinical condition and the albuminocytological dissociation identified by the analysis of cerebrospinal fluid (CSF), it was decided to start immunotherapy and prescribed intravenous human immunoglobulin (0.7g/kg/day per day for three days). The antibiotic therapy was suspended and the patient was referred to the pediatric ICU with a diagnostic hypothesis of Guillain-Barré Syndrome. Twenty four hours after the start of immunoglobulin treatment, the child showed an improvement in his general condition.

Differential diagnosis

The State Department of Health performed the laboratory exams, CSF analysis and electroneuromyography. The results of multiple blood tests carried out on October 18 and October 22, 2019 are shown in Table 1. As for the red series, a slight change in Mean Cell Hemoglobin (MCH), Mean Cell Hemoglobin Concentration (MCHC) and Mean Platelet Volume (MPV) below the predicted reference levels, while platelets showed high levels and a progressive increase. In the white series, slight changes were observed in comparison to the reference levels. The minerals, Magnesium, Calcium and Phosphorus showed levels slightly above the reference value, while creatinine was below. The enzymes CPK-MB, alkaline phosphatase and LDH indicated a marked change above the reference level, but the first one tended to decrease, comparing the two blood tests.

Table 1: Comparison of Blood tests during hospitalization

Tests (unit of measure)	October 18	October 22
Red cells (X106/uL)	4.69	5.07
MCV (fl)	78.9	78.7
Hemoglobin (g/dL)	11.9	13
MCH(pg)	25.4	25.6
Hematocrit (%)	37.0	33.9
MCHC (g/dL)	32.2	32.6
RDW (%)	12.2	12.2
ESR	-	26
Leukocytes (X103/uL)	10.2	15.1
Segmented leukocytes (%)	40	41
Segmented	4.1	6.2
Neutrophils (%)	40	41
Neutrophils	4.1	6.2
Bastonetes (%)	0	0
Eosinophils (%)	0	1
Eosinophils	0	0.2
Basophils (%)	0	0
Monocytes (%)	11	6
Monocytes	1.1	0.9
Lymphocytes (%)	49	49
Lymphocytes	5	7.4
Atypical lymphocytes (%)	-	3

Continuation - Table 1: Comparison of Blood tests during hospitalization

Tests (unit of measure)	October 18	October 22
Platelets (X103/uL)	553	702
MPV (fl)	6	5.8
Total proteins (g/dL)	7.1	-
Albumin (g/dL)	4.6	4.6
Globulin (g/dL)	-	2.5
Relation A/G	-	1.8
Glucose (mg/dL)	118	120
Urea (mg/dL)	-	16.1
Creatinine (mg/dL)		0.25
Chloride (mEq/L)	-	102
Magnesium (mg/dL)	-	2.7
Potassium (mEq/L)	-	4.66
Calcium (mg/dL)	-	12
Phosphor (mmol/L)	-	5.7
Sodium (mEq/L)	-	136.6
Glutamyl Transferase Range (U/L)	-	22.1
OGT (U/L)	25	23
GPT (U/L)	15	12
Alkaline phosphatase (U/L)	-	553
CPK-MB(U/L)	48.2	26.8
Creatinophosphokinase (UI/L)	46	42
LDH (U/L)	483	495

The CSF analysis performed at the time of hospital admission showed pleocytosis (nucleated cells 12mm³), glucose 75mg/dl (glycemia 120mg/dl), total protein 247 mg/dl, bacterioscopy and culture for negative pyogenic, polymerase chain reaction (PCR) for Neisseria, Pneumococcus and negative Meningococcus (Table 2).

Table 2: Analysis of cerebrospinal fluid. October 21, 2019

Color (before and after centrifugation)	Colorless
Appearance (before and after centrifugation)	Clear
Protein	247 mg/dL
Chlorides	118 mEq/L
Glucose	75 mg/dL
Red cells	0 /mm3
Nucleated cells	12 /mm3
Bacterioscopy	Gram-staining microorganisms were not seen in the examined sample
Culture for Bacteria	There was no bacterial growth
Molecular tests for bacterial meningitis (qPCR) for Neisseria meningitidis, Streptococcus pneumoniae and Haemophilus influenzae	Negative for surveyed agents

Investigation was carried out for polio, acute diffuse encephalomyelitis, reaction arthritis and myositis, these diagnoses being ruled out. The diagnostic hypothesis of GBS was based on the Brighton criteria (6): clinical, albumin-cytological dissociation in cerebrospinal fluid (examination performed on October 21, 2019) delayed electroneuromyography (performed on November 26, 2019) compatible with acute, myelinated motor sensory neuropathy, with probable secondary axonal involvement.

Still, regarding electroneuromyography of upper and lower limbs, the study of sensory and motor conduction detected reduced conduction speed and amplitude in the median and ulnar nerves bilaterally.

As for arbovirus infection, serological research

was carried out on October, 22/2019 for Dengue and Zika (IgM antibodies by MAC-ELISA) both non-reactive.

Follow-up and outcome

On the first day of admission to the ICU, the patient remained afebrile and with improvement in his clinical condition, the neurological tests indicated that the neurological response of cranial pairs was preserved, with adequate cervical control, the ability to sit with support, without trunk control; Babinski's sign frustrated and increased muscle strength of lower limbs, but without the ability to move them against gravity. On this date, a blood sample was collected for serological diagnosis (IgM antibody search by MAC-ELISA) of Zika and Dengue, both non-reactive.

On the second day of admission to the ICU, the last day of immunoglobulin infusion, the child had a satisfactory evolution of his clinical condition, contact, continues with an adequate response of the cranial pairs with improvement in neurological responses, managing to overcome the severity of the limbs, greater movement of upper limbs and still with loss of strength in lower limbs and difficulty in controlling the trunk, despite being able to remain seated without support at times.

On the third day of admission to the pediatric ICU, the child remained afebrile, had no more pain complaints, with low movement of the lower limbs, but with low ability to remain seated alone, supporting himself with his hands. He was discharged from the pediatric ICU and admitted to the pediatric ward of the same hospital.

On October 27, 2019, after five days, considering the improvement of the child's clinical condition, who had good trunk support, the ability to sit quickly and increased movement and strength of the lower limbs, without pain complaints, he was discharged from hospital.

The child maintained the cognitive, respiratory capacity and normal physiological eliminations, as well as the hemodynamic stability throughout the hospital follow-up period.

After 36 days of hospital discharge, the child underwent physiotherapy consultation at a referral unit for motor rehabilitation. Good motor function was detected, with no need for rehabilitation sessions.

On December 12, the blood tests with IgM and RT-qPCR antibody tests, for Zika, Dengue and Chikungunya, and IgG antibody testing for Chikungunya, were all non-reactive.

Forty days after the physical therapy consultation, the child underwent an examination of his neuropsychomotor development11, comparing his development prior to the onset of symptoms related to GBS, during and after the remission of the clinical condition (Figure 1). So far, the child shows a significant improvement in his neuropsychomotor development after symptoms remission, despite a slight delay in his development.

Figure 1: Milestones of neuropsychomotor development, based on a child development monitoring instrument.

Function	Framework of Development	Age in months reached	Lost or reduced function?	Date of loss/ reduction of function	Date of resumption of function
Auditive	Reacts to sound	1	No	.	.
	Finds the sound	4	No	.	.
Cognitive and Language	Social smile when stimulated	3	No	.	.
	Active response to social contact	4	No	.	.
	Emits sounds	6	No	.	.
	Play hide and seek	6	No	.	.
	Duplicates syllables	7	No	.	.
	Imitates gestures	7	No	.	.
	Produces "jargon"	8	No	.	.
	Shows what he/she wants	9	No	.	.
	Puts blocks in the mug	9	No	.	.
	Says a word	12	No	.	.
	Says three words	Missing	.	.	.
	Opens hands	3	No	.	.
Manual	Holds objects	4	No	.	.
	Active object search	6	No	.	.
	Puts objects in her/his mouth	4	No	.	.

Continuation - Figure 1: Milestones of neuropsychomotor development, based on a child development monitoring instrument.

Function	Framework of Development	Age in months reached	Lost or reduced function?	Date of loss/ reduction of function	Date of resumption of function
	Transfer objects from one hand to the other	6	Reduced	October 18	October 25
	Makes tweezers	6	Loss	October 18	November 20
	Uses spoon or fork	14	Loss	October 18	November 20
	Posture: belly up, legs and arms flexed, head lateralized	2	Loss	October 19	October 22
Motor	Lift her/his head	2	Reduced, just managed to lateralize	October 19	October 23
	Actively move members	2	Lost to lower limbs	October 19	October 22
	Face down, lifts head, leaning on forearms	5	No	.	.
	Actively changes position (roll)	5	Loss	October 19	November 15
	Sits without support	6	Loss	October 19	October 26
	Walk with support	13	Loss	October 19	November 30
	Walk without support	Missing	.	.	.
	Walk back	Missing	.	.	.
Orofacial Motricity	Breastfeeding	Breastfeeding interrupted at five months of age			
	Can chew and swallow	5	Reduced, with frequent gagging	October 16	November 09
	Observe a face	2	No	.	.
Visual	Build a 2-cube tower	7	Loss	October 19	November 09
	Build a 3-cube tower	7	Loss	October 19	November 09

DISCUSSION

This paper reports a probable case of GBS in a 14-month-old child, a rare clinical condition, possibly associated with a post-vaccination reaction or diarrheal syndrome. Its clinical presentation was compatible with a classic case of GBS, with progressive and ascending bilateral paralysis[12]. Although the case required ICU admission, the child's age in synergy with the opportunity for diagnosis and the provision of specific treatment may have influenced his quick recovery.

Laboratory changes related to the red series, showed mild anemia, possibly related to the trait of sickle cell disease identified at birth. In addition, high platelet counts, with low mean platelet volume, also indicate abnormalities. Perhaps another hematological pathology that contributes to these findings should be investigated.

The slight changes observed in the white series, with the absence of leukopenia or leukocytosis, point to a possible lack of viral or bacterial infection. Corroborating the results of the diagnostic tests for arboviruses - all non-reactive.

Low creatinine, without changes in urea, may reflect the nutritional status of the child, who has not been eating properly since the onset of laryngitis symptoms. In this sense, the slight increase in minerals may be a reflection of the intake of multivitamins, in this case recommended by Brazilian pediatric societies, in dosages compatible with SUS protocols.

The high values of LDH and glucose may be related to not fasting prior to the blood test. However, even with regard to enzymatic changes, alkaline phosphatase is related to possible liver changes, which raises the need for

further investigation of the condition.

The evident and rapid improvement of the neurological condition should be highlighted. This finding is uncommon among adults[13]. Perhaps, the child's age is a positive point[14], it is known that the identification of a diagnostic hypothesis with rapid transferring to a referral hospital, and drug therapy with immunoglobulin initiated in a timely manner also influenced positively in the evolution and outcome of the case[13].

As for neuropsychomotor development, considering the development milestones used in the investigation[11] in line with the electroneuromyographic findings, there is a small delay in motor functions. Despite the accentuation of symptoms in the lower limbs, changes were also observed in the upper limbs.

The patient had some developmental milestones of manual ability at an earlier age than expected. However, these functions were compromised during the course of the GBS, especially the ability to perform the pinch movement, taking up to 32 days for its full recovery. Nascimento and colleagues, in a recent systematic review, found no studies that analyzed manual function in children up to 18 months of age diagnosed with developmental dysfunction[15], demonstrating the importance of monitoring this type case study in order to analyze the evolution of this function.

Another finding regarding child development concerns his ability to swallow. Although not completely affected, episodes of choking raise the alert for impaired orofacial motricity possibly related to the involvement of cranial nerve pairs[12]. In this sense, the possible neuronal impairment in line with the traumas arising from the clinical condition, such as pain and staying in an unknown environment, may have contributed to the delay observed in language development.

Among the limitations of this report, we highlight the lack of identification of the etiological agent that triggered the neurological condition. However, it is important to remember that diarrheal and respiratory conditions are frequent in children of this age group and, therefore, samples are rarely collected to identify the responsible agent[14]. Also, the lack of additional laboratory tests on consecutive days, after hospital admission, compromises the biochemical analysis of the condition. A magnetic resonance imaging was not performed to analyze areas of demyelination or inflammation, a limitation common to other studies[16,17]. Given the fast favorable evolution of the case, as well as the limited resources of SUS, especially with regard to the magnetic resonance exam in a child of this age who probably would require sedation, these procedures may have been discarded. However, tests of high complexity and indispensable for the highest level of diagnostic certainty of GBS (CSF analysis and electroneuromyography), were performed in a timely manner.

Given the rarity of GBS cases among children of this age group, it is important that health professionals remain sensitive to the reports of their guardians and parents in order to capture and treat cases in a timely manner. We also recommend that the identified cases be monitored carefully, at least until they complete their neuropsychomotor developmental milestones up to three years of age, to verify if GBS, and its variants, can explain developmental disorders a posteriori.

Ethical aspects

This study is part of a project approved by the Research Ethics Committee with human beings at the University of Brasília (CAAE: 61551116.3.3001.5558) and the Federal District Health Department (CAAE: 61551116.3.0000.5553). The legal representatives of the child were explained in relation to the objectives and all procedures involved in this case report and signed a free and informed consent form, authorizing the use of their responses, medical records, test results and their publication in an unidentified manner.

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Resumo

Introdução: A Síndrome de Guillain-Barré (SGB) é a causa mais frequente de paralisia flácida aguda e subaguda desde a erradicação da poliomielite. Embora rara, é reconhecida como a principal causa de paralisia flácida entre pessoas internadas em terapia intensiva pediátrica por doenças neuromusculares agudas.

Objetivo: Relatar um caso de paciente do sexo masculino, com 14 meses de idade, com diagnóstico provável de Síndrome de Guillain-Barré com neuropatia sensitivo motora, aguda, mielínica, com provável comprometimento axonal secundário, com rápida evolução e melhora.

Descrição do caso: Foi admitido em hospital público materno-infantil de referência para o Distrito Federal um paciente masculino, residente na Região Integrada de Desenvolvimento do Distrito Federal e Entorno. A criança tinha 14 meses de idade e 8,6kg, situação vacinal atualizada e desenvolvimento neurospicomotor adequado para a idade, com quadro de paresia em membros inferiores, sem alterações cognitivas. Após 14 horas da admissão, diante do agravamento do quadro clínico e da dissociação albomino-citológica identificada pela análise de líquido cefalo-raquidiano foi iniciada imunoterapia (imunoglobulina humana endovenosa, 0,7g/kg/dia por três dias). Após 24 horas do início do tratamento, a criança apresentou melhora em seu estado geral. O paciente teve alta hospitalar após cinco dias de internação. Após 76 dias da alta, foi constatada melhora significativa no desenvolvimento neuropsicomotor, apesar de leve atraso em seu desenvolvimento até o momento.

Conclusão: Diante da raridade de casos em crianças, é importante que os profissionais de saúde se mantenham sensíveis a captar e tratar os casos de maneira oportuna. Recomendamos ainda que os casos identificados sejam acompanhados cuidadosamente, afim de verificar se a SGB, e suas variantes, podem explicar transtornos de desenvolvimento à posteriori.

Palavras-chave: Síndrome de Guillain-Barré, saúde da criança, desenvolvimento infantil.