

Recurrent apparent life-threatening event as the first manifestation of congenital myasthenia

Evento com aparente risco de morte recorrente como manifestação inicial de síndrome miastênica congênita

Evento con aparente riesgo de muerte recorrente como manifestación inicial de síndrome miasténico congénito

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ABSTRACT

Objective: To alert pediatricians about the importance of a careful investigation on recurrent apparent life-threatening events. Reports of the association of these events with congenital myasthenic syndromes were not found.

Case description: A seven-month-old infant with recurrent apparent life-threatening events was admitted for investigation. During hospital stay, she presented cyanosis and respiratory failure, requiring mechanical ventilation for three days. After clinical improvement, hypotheses of gastroesophageal reflux and pulmonary aspiration were ruled out. The presence of eyelid ptosis, general hypotonia and weak crying led to the suspicion of congenital myasthenia, which was confirmed. Treatment with oral pyridostigmine led to neurological and nutritional normalization, without any other apparent life-threatening event during the next three years.

Comments: The careful etiological investigation of apparent life-threatening events may lead to rare diagnosis that requires specific treatments, such as congenital myasthenia.

Key-words: infantile apparent life-threatening event; myasthenia gravis; muscle hypotonia; apnea; infant.

RESUMO

Objetivo: Alertar os pediatras sobre a necessidade de investigar criteriosamente a etiologia de eventos com aparente risco de morte recorrente. Não foram encontrados relatos associando tais eventos à miastenia congênita.

Descrição do caso: Lactente de sete meses apresentando história de eventos com aparente risco de morte recorrente foi internado para investigação. Durante a internação, apresentou cianose e dispnéia progressiva, com necessidade de ventilação mecânica por três dias. Após a melhora clínica, e tendo sido descartadas as hipóteses de doença do refluxo gastroesofágico e aspiração pulmonar como desencadeantes, notou-se ptose palpebral bilateral, hipotonia apendicular e choro fraco, que conduziram à suspeita clínica de miastenia congênita. Após confirmação do diagnóstico, foi mantido tratamento ambulatorial com piridostigmina, com recuperação nutricional e neurológica, sem novos eventos com aparente risco de morte nos três anos seguintes.

Comentários: A investigação minuciosa das causas de eventos com aparente risco de morte pode levar a diagnósticos menos frequentes que exigem tratamento específico, como a miastenia congênita.

Palavras-chave: evento com aparente risco de vida infantil; miastenia gravis; hipotonia muscular; apneia; lactente.

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RESUMEN

Objetivo: Alertar a los pediatras sobre la necesidad de investigar criteriosamente la etiología de eventos con aparente riesgo de muerte recorrente. No se encontraron relatos asociando tales eventos a la miastenia congénita.

Descripción del caso: Lactante de siete meses presentando historia de eventos con aparente riesgo de muerte recorrente fue internado para investigación. Durante la internación, presentó cianosis y disnea progresiva, con necesidad de ventilación mecánica por tres días. Después de la mejora clínica, y habiendo sido rechazadas las hipótesis de enfermedad del reflujo gastroesofágico y aspiración pulmonar como desencadenantes, se notó ptosis palpebral bilateral, hipotonía apendicular y lloro débil, que condujeron a la sospecha clínica de miastenia congénita. Después de la confirmación del diagnóstico, se mantuvo el tratamiento ambulatorial con piridostigmina, con recuperación nutricional y neurológica, sin nuevos eventos con aparente riesgo de muerte en los tres años siguientes.

Comentarios: La investigación minuciosa de las causas de eventos con aparente riesgo de muerte puede llevar a diagnósticos menos frecuentes que exigen tratamiento específico, como la miastenia congénita.

Palabras clave: evento con aparente riesgo de vida infantil; miastenia gravis; hipotonía muscular; apnea; lactante.

Introduction

Apparent life-threatening events (ALTE) are defined as frightening episodes to the observer, characterized by a combination of apnea (central or obstructive), change in skin color (cyanotic or pallid), change in the muscle tone (hypotonia), choke, or gag reflex^(1,2).

The occurrence of an ALTE in healthy infants is not an infrequent fact, usually as a single event, with short time duration and with complete and spontaneous resolution^(2,3). However, although most of the events have no pathological meaning and have benign course, the ALTE may be associated with a variety of underlying diseases⁽²⁻¹⁰⁾. Some infants exhibit recurrence of the signs and symptoms of ALTE, with progressively more severe clinical presentation compared to the initial event, which raises the risk of subsequent morbidity and mortality associated with the event itself or with the disease that caused it⁽³⁻⁹⁾.

This report aimed to describe the case of an infant suffering from congenital myasthenic syndrome who had recurrent episodes of ALTE as the initial manifestation of the disease. The publication of these data was approved by the Research Ethics Committee of the Faculty of Medical Sciences/UNICAMP (144/2011).

Case report

A seven-month-old female infant was referred for investigation of recurrent episodes of ALTE. She was a full term infant with adequate weight for gestational age (birth weight: 3,260g), and Apgar scores of 8 and 9, in the 1st and 5th minutes. The patient received exclusive breastfeeding during the first month of life and infant formula from the second, with poor weight gain. In the third month, she had daily episodes of ALTE – cyanosis associated with nausea and vomiting. Esophagus, stomach and duodenum contrast examination were conducted, which showed aspiration by the presence of contrast in the bronchial tree. The video-fluoroscopy showed swallowing disorder, with completion by the contrast of the hypo and nasopharynx, as well as the larynx, with several episodes of aspiration of contrast. Since then, she received exclusive nasogastric tube feeding associated with postural anti-reflux therapy and prokinetic drugs (ranitidine, domperidone and erythromycin). At the age of 5 months, the infant had a new episode of ALTE, characterized by pallor followed by cyanosis, that occurred with elevated head during the exchange of a nasogastric tube, requiring mechanical ventilation for 3 days. Aspirative pneumonia was diagnosed as the cause of the event.

At 7 months, in the first outpatient visit at this service, the infant was admitted for investigation. After 12 hours of admission, there was a new episode of ALTE in supine position during venipuncture procedure, characterized by generalized cyanosis and progressive respiratory distress, coursing with apnea and need of mechanical ventilation for 3 days. In this period there was no evidence of any signs of aspiration pneumonia. The results of high endoscopy and skull computed tomography showed no esophagogastric or encephalic anatomical abnormalities. The following blood tests were performed: serum free thyroxine (T4): 1.09ng/dL (0.9 to 1.8), Thyroid-stimulating hormone (TSH): 1.20UUI/mL (0.41 to 4.5), creatine kinase (CK): 62U/L (<145), lactate: 1.0mmol/L (0.5 to 1.6) and lactate dehydrogenase (LDH): 734U/L (<1,100).

After discharge from the Pediatric Intensive Care Unit, still during hospitalization at the Pediatric Ward, the following symptoms were noticed: bilateral and floating mild eyelid ptosis, constant weak cry, and mild appendicular hypotonia, so then the hypothesis of congenital myasthenic syndrome was considered. Thus, a therapeutic trial with pyridostigmine was conducted, which resulted in eye opening, strong cry, and overall muscle tone improvement in few seconds, characterizing positive response to the trial. The EMG examination performed later showed neuromuscular junction dysfunction, which confirmed the diagnosis of congenital myasthenic syndrome,

so a continuous treatment with pyridostigmine was conducted. After adjusting the dosage of medication, it was possible to reassume oral feeding, with removal of nasogastric tube and without recurrence of ALTE since then.

Currently, the child is receiving outpatient treatment for over 3 years, with good weight gain and neuropsychomotor development progression to normality in continuous use of pyridostigmine.

Discussion

No other case reporting association between ALTE and congenital myasthenic syndrome were found in the analyzed literature, regardless of the known fact that the initial presentation of the myasthenic syndrome may course with as eating disorders, leading to apnea, often attributed to gastroesophageal reflux disease⁽¹¹⁾. Although the patient had had frequent medical follow-up from birth, especially after the onset of symptoms, the clinical suspicion of congenital myasthenic syndrome occurred only at the age of 7 months, when the eyelid ptosis, the weak cry, and the appendicular hypotonia became apparent.

This syndrome is a rare and chronic disease, characterized by rapid fatigue of the striated skeletal muscles, especially the extrinsic ocular, swallowing, phonation, and respiratory muscles, as in the case described^(12,13). The most frequent cause is immune-mediated blockage of the neuromuscular junction, i.e., the release of acetylcholine in the synaptic cleft is normal, however, the postsynaptic membrane responds unsatisfactorily to the stimulus⁽¹¹⁻¹⁵⁾.

In young infants, as in the described case, the main clinical manifestation of myasthenia is feeding difficulty^(11,12,14). Cervical hypotonia and poor control of head movement are

also common, as well as appendicular muscle hypotonia^(11,12,14). The eyelid ptosis is uncommon in young infants^(11,12). Episodic apnea and swallowing difficulty are common in infants with congenital myasthenic syndrome, which explains the numerous episodes of ALTE described in this case report⁽¹¹⁻¹³⁾.

Electromyography, which is the indicated test for confirming the clinical suspicion, showed decrease in the pattern of response to repetitive muscle stimulation, with reduction in the amplitude of the waves, culminating in the absence of response to stimuli. This pattern is reversible by the use of cholinesterase inhibitors^(12,14). Although the test can be inconclusive in infants, when positive it supports the diagnosis, as in the case described^(12,14,15). Serum antibodies anticholinesterase measurements can be performed, and high results confirm the diagnosis. However, a negative result does not exclude the diagnosis, since changes in infants with congenital myasthenic syndrome are rarely found^(11,14). This test was not performed in the patient described.

A therapeutic trial with short-acting cholinesterase inhibitors (prostigmine methylsulfate) is recommended for diagnosis confirmation^(11,13). The positive response is a rapid and fleeting improvement of ptosis, ocular plegia, and speech muscles, as seen in the present case report^(11,13). Maintenance treatment must be performed with cholinesterase inhibitors of long duration, such as pyridostigmine⁽¹¹⁻¹⁴⁾.

The authors are aware of the rarity of congenital myasthenic syndrome diagnosis. Therefore, this should not be considered as the most likely diagnosis for infants with ALTE; however, it cannot be discharged when clinic and evolution are compatible, especially with severe and recurrent events, after the most frequent etiologies have been excluded, such as esophageal reflux disease and respiratory diseases.

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