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THERMAL DYSREGULATION IN A SUGAR WITH PRADER-WILLI SYNDROME - CASE PRESENTATION –

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ABSTRACT

Prader-Willi Syndrome (PWS) is a complex genetic syndrome characterized by a multitude of entities, including diminished fetal activity, obesity, severe muscular hypotonia, mental retardation, low stature, discrete cranio-facial dysmorphia, dental problems, hypogonadism and acromicria. In this paper, we presented the clinical features of a 5 months old female infant diagnosed with PWS and lack of hypothalamic functionality that led to thermoregulatory disorders. Disorder of thermoregulation may be part of the clinical spectrum in children with Prader-Willi syndrome and should be closely monitored, considering the severe complications with potentially fatal. In the case of the PWS thermoregulatory disorder, which manifests itself through fever spikes without a proven infectious substrate, the physical methods of combating fever have proven effective in achieving a normalization of body temperature.

Key words: Prader-Willi Syndrome, disorder of thermoregulation, infant

INTRODUCTION

Prader-Willi Syndrome (PWS) is a complex genetic syndrome characterized by a multitude of entities, including diminished fetal activity, obesity, severe muscular hypotonia, mental retardation, low stature, discrete cranio-facial dysmorphia, hypogonadism and acromicria. PWS is an autosomal dominant pathology and is caused by the absence of expression of paternal genes on the long arm of chromosome 15 (15q11-q13) (1). The life expectancy of children with PWS is low, being in line with intellectual disability and due, primarily, to hyperphagia and complications related to obesity. Among the most common causes of death in children with PWS are respiratory diseases and febrile syndrome, and in adults the fatal picture is marked by the presence of cardiovascular and digestive problems.

The thermoregulatory disorder is a known complication of Prader-Willi syndrome. This is, in most cases, benign, but can sometimes lead to hyperpyrexia and subsequently to multiple organ failure and exitus if not treated properly (2). Although it has long been believed that the clinical picture of PWS can be largely explained by hypothalamic dysfunction, no hypothalamic structural defect has been identified so far to justify these assumptions. The thermoregulatory disorders in PWS patients have been

mentioned in a few publications, being associated concomitantly with hypothalamic dysfunction, but the pathophysiological details of this mechanism have remained unknown. (2)

This case illustrates the presence of persistent hyperpyrexia in a 5-month-old infant for whom the thermoregulatory disorder in Prader-Willi Syndrome was the main etiological factor.

CASE PRESENTATION

We present the case of a 5 months old female infant, weighing 5800 grams, admitted in our clinic, being received from a hospital in the territory, with the diagnoses: in observation septic status, interstitial persistent pneumonia, acute respiratory failure and generalized hypotonia. The stationary clinical condition and the persistence of fever spikes despite the territorial treatment for 5 days led to the transfer of the patient to our clinic.

His comorbidities included grade I weight dystrophy and severe neuromotor retardation, and the treatment until admission to our clinic consisted of cefuroxime, ceftazidime, levofloxacin, ibuprofen and paracetamol. In the territory, the nasal exudate was found positive for *Staphylococcus aureus*, without other modification in lab tests.

At the admission, the patient presented a relatively good general condition, cranio-facial dystrophy (sutured sutures, narrow biparietal diameter, almond shaped eyes), hands and feet with acromicria (Fig. 1), normal cardio-pulmonary examination findings, with marked generalized hypotonia.

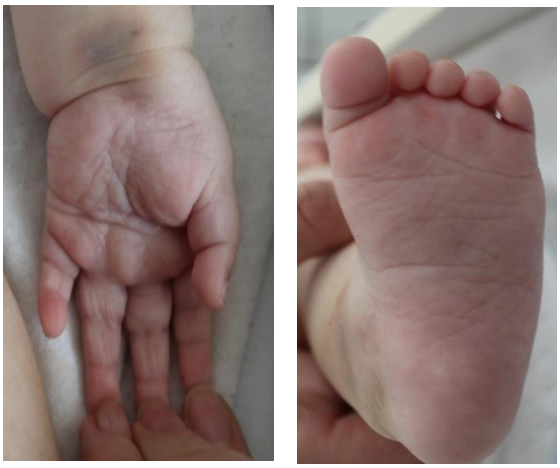

Figure 1. Clinical appearance of the patient: hands and feet (acromicria)

Laboratory tests highlights: thrombocytopenia, absent inflammatory syndrome, IgA deficiency, mild hyperammonemia, low FT4 and no other pathological changes were detected. Pharyngeal exudate, blood culture at 48 hours and anti-Cytomegalovirus, Epstein Barr, Toxoplasma antibodies were negative. Chest radiography revealed the presence of bilateral perihilar interstitial infiltrate that improved significantly with intravenous administration of antibiotics.

Despite these aspects, the patient continued to have fever spikes with a maximum temperature of approximately 38.5 °C.

In this context, the suspicion of Prader-Willi syndrome was raised and a genetic consultation was requested, which described the presence of generalized hypotonia, cranio-

facial dysmorphia with narrowed biparietal diameter, almond palpebral slits and acromicria. MLPA analysis: P245 Microdeletion Syndromes-1 identified the heterozygous deletion at the level of 15q11.2 corresponding to the Prader Willi region, confirming the high hypothesis.

Paraclinical explorations were continued by performing abdominal ultrasound that did not identify pathological aspects, and on the cranial ultrasonography a discrete increase of the bilateral subarachnoid space was revealed. The multidisciplinary evaluation was carried out by cardiological consultation and ENT examination, which did not detect anomalies. With a negative septic picture, the etiology of fever still had unknown origin. The inflammatory markers remained normal, the urinary and coproparasitological samples did not detect the presence of any infectious agent, and the viral serology was negative. In this context, the cause of prolonged febrile syndrome secondary to Prader-Willi syndrome has been established as a cause.

The patient initially benefited from antipyretics and later resorted only to physical methods of combating fever and intravenous hyperhydration with a subsequent favorable evolution. The temperature entered, in a row, within normal limits, while the inflammatory samples remained negative, and the complete blood count was normalized. The patient also underwent intense physiotherapy to regain her mobility and was discharged with good general condition and afebrile at 12 days after admission to the department.

DISCUSSIONS

Prader-Willi syndrome is a rare genetic disorder characterized by a developmental disorder associated with hypothalamic-pituitary dysfunction. It manifests itself through neonatal hypotonia with sucking-swallowing disorders, early obesity with hyperphagia and lack of satiety, endocrine disorders, cognitive disorders, behavioral and social disorders and, in some cases, psychiatric disorders (3). Hypothalamic dysfunction can disrupt thermoregulation either by maintaining it within normal limits within an infection or, conversely, by having febrile episodes in the absence of infection (4). Preventive measures should therefore consider the fact that the temperature may be normal in case of infection (5). PWS is associated with a series of endocrinopathies, developmental and behavioral problems that should be evaluated and treated, preferably, in a multidisciplinary center familiar with the problems involved with this syndrome (6).

The differential diagnosis was made with the following entities: malignant hyperthermia or neuroleptic malignant syndrome, but which in the absence of a family history or exposure to certain drugs or toxins could not be confirmed; pneumonia associated with healthcare, which could not be justified in the absence of increased inflammatory markers and negative cultures; spinal muscular atrophy (AMS) that was denied during the same genetic examination (MLPA analysis negative for AMS).

In children with PWS, hypotonia may explain the low clenching function (7). This affects the quality of speech and proper nutrition. It is limited sucking, chewing and swallowing. Subsequently, the hyperphagia in these children, result in a higher consumption of carbohydrates. A variety of oral diseases are found in patients with PWS: caries, hypoplasia of enamel, periodontal disease, dental erosion, oral microsomia, dental malocclusion, candidiasis, erythematous lesions of the oral mucosa, gingivitis, angular cheilitis, dry mouth, dentoalveolar abscess, hypotonic tongue, delayed tooth eruption (8).

Hyperpyrexia refers to a high temperature value that can lead to peripheral vasodilation and hypovolemia by increasing insensitive fluid losses, resulting in hypotension. Not

verified and corrected, this can lead to renal hypoperfusion, rhabdomyolysis, cerebral edema, encephalopathy, hepatic impairment and the development of disseminated intravascular coagulation. Therefore, it is necessary that the management of hyperpyrexia should be performed promptly, aggressively, with physical methods to combat the fever and, in the case of failure, to resort to additional methods such as myorelaxant agents and hemofiltration (9). Specific cooling measures should be in accordance with the etiology of hyperpyrexia. When an infection is proven, the hypothalamic temperature threshold is high. This can be counteracted using antipyretic agents such as paracetamol and non-steroidal anti-inflammatories. These drugs function by inhibiting prostaglandin formation within the hypothalamus, thus normalizing the homeostatic threshold (10, 11). In the case of the PWS thermoregulatory disorder, which manifests itself through fever spikes without a proven infectious substrate, the physical methods of combating fever have proven effective in achieving a normalization of body temperature (12).

Although there are several publications that mention problems of thermoregulation within the PWS, it has not yet been possible to highlight the pathophysiology of this situation. However, it has been observed that, for example, a respiratory pathology increases the patient's already high body temperature and that with the resolution of the infectious process, the temperature returns to optimal values. In the presented clinical case, the febrile syndrome could not be justified by any other paraclinical examination performed and was therefore considered an integral part of the PWS picture. In this case, the physical methods of fighting the fever were enough to reach and maintain a normal value of body temperature.

CONCLUSIONS

The importance of the subject lies in the fact that hyperthermia can lead to life-threatening situations, in the literature being described as a factor that can lead to the sudden death of the baby. Thus, when identified, it should be kept constantly under control to avoid the potentially fatal complications it may have.

In the case of the PWS thermoregulatory disorder, which manifests itself through fever spikes without a proven infectious substrate, the physical methods of combating fever have proven effective in achieving a normalization of body temperature.

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