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Severe respiratory failure in Prader-Willi syndrome

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Abstract: Objective: The case report described aims to demonstrate the particularities of Prader-Willi syndrome and highlight the health problems caused by such impairment, in addition to highlighting the importance of early diagnosis for targeted follow-up in order to avoid the morbidity and mortality associated with PWS. **Case report**: This is a descriptive report about the diagnostic challenges and the adequate management of Prader-Willi syndrome, seeking to avoid unfavorable outcomes in primary health care. **Results:** Given the above, this article has highlighted the importance of early diagnosis, especially in the early stages of life and in view of the initial manifestations of Prader-Willi syndrome. Such measures are necessary to prevent excessive obesity and control morbidities related to it. In addition to controlling behavior disorders.
Keywords: Childhood respiratory disorders, childhood obesity, Prader-Willi syndrome.

INTRODUCTION

Prader-Willi syndrome (PWS) is a rare neurobehavioral disorder that can affect children of both sexes, race or socioeconomic status, representing a genetic disorder characterized by hypotonia, mental retardation, hyperphagia and binge eating due to hypothalamic disorder (Gonzaga, et. al., 2004).

Individuals affected by this syndrome present deletion of the proximal portion of the long arm of the paternal chromosome 15 (15 q11-13) or, more rarely, translocations, maternal disomy of chromosome 15 or chromosomal imprinting abnormalities, for reasons still unknown, the genes from this region of the mother's chromosome 15 have no functional expression. These chromosomal alterations mainly affect hypothalamic functioning (Andrade, et. al., 2011).

Clinical manifestations are initially presented by APGAR below normal birth standards,

respiratory disorders, moderate to severe mental retardation, learning disorders, short stature due to growth hormone deficiency, hypogonadism that predisposes to incomplete sexual development, behavioral problems, muscle hypotonism that appears primarily as difficulty in sucking and swallowing in the first months of life and hyperphagia from the age of 2 years. Obesity represents an important consequence of hyperphagia, responsible in the long term for premature cardiovascular events and impairments in living conditions and increased morbidity and mortality (Gonzaga, et. al., 2004).

The diagnosis of Prader-Willi syndrome (SPW) relies on genetic tests which identify the presence of the functional region: 15q11-q13 and therefore, non-turned off, called MS-HRM (methylation test), has been effective in detecting most cases, regardless of the genetic alterations involved. Later, more detailed analyzes can be used to clarify which specific defect occurred in each individual, using complementary techniques such as FISH, MS-MLPA or Microsatellite Analysis. (Andrade, et. al., 2011).

The case report described aims to demonstrate the particularities of Prader-Willi syndrome and highlight the problems caused by such impairment, in addition to highlighting the importance of early diagnosis for targeted follow-up in order to avoid the morbidity and mortality associated with PWS.

CASE REPORT

This article is a case report based on activities carried out by medical students, through curricular internships integrated in the teaching plan of the medical internship. Students performed care at basic health units in the city of Ipuã – São Paulo, in the countryside of São Paulo.

The patient MHPB, 2 years and 1 month, attended the consultation accompanied by his mother, who requested evaluation and laboratory tests to investigate the increase in the child's weight, he brought with him a report from the Hospital das Clinicas de Ribeirão Preto, which contained data that characterized the newborn as preterm, adequate for gestational age (AGA), son of a diabetic and hypertensive mother, having presented postpartum complications such as heart rate lower than 100 bpm, requiring the use of positive pressure ventilation after birth. The mother had the result of the heel prick test with no identified alterations.

In the detailed questioning about the child's health condition and development, the mother denied relevant changes in the various systems, reported that the child started walking at 1 year and three months, denied neuropsychomotor development disorders, reported irregular sleep routine with several awakenings and night snoring associated with apnea, the child presented with daytime sleepiness. Furthermore, irregular eating habits were identified, with the child being administered a large amount of milk with sugar in bottles to the detriment of the solid diet recommended for their age. The vaccines were up to date and she was using vitamin supplementation in addition to ferrous sulfate. In addition, investigating the family history, it was found that the child had a brother diagnosed with diabetes insipitus and adrenal insufficiency.

In the consultation in question, the child was in good general condition, weight 25.6 kg, height 90 cm and BMI: 31,6 kg/m², had difficulty walking and poorly responsive to stimuli in the investigation of neuropsychomotor development. Cavum radiography was requested, which is used to analyze the size of the adenoid tissue of the pharynx and palatine tonsils, and later an adenoid hypertrophy was found, under which the child underwent a surgical procedure at 2 years of age to resolve the condition.

M.H.P.B continued to follow up at UBS with approaches aimed at increasing weight, preventing injuries and childcare. At the age of 3, the mother attends the consultation, demonstrating that she is being followed up at Hospital das Clínicas of Ribeirão Preto after being diagnosed with Prader-Willi Syndrome after recurrent hospitalizations due to respiratory problems and accelerated weight gain, reporting an increase of 16 kg in 6 months. She reported that the child had recurrent dry cough, episodes of apnea having been diagnosed with recurrent bronchiolitis. At the time of the consultation, she was using Fluoxetine, Aerolim, Clenil, Prednisolone, Ritalin, in addition to Dramim and Ranitidine due to recurrent vomiting. The child was under follow-up with a physiotherapist and pulmonologist due to respiratory difficulties, in addition to endocrinological follow-up and with the genetics department of the HC of Ribeirão Preto.

M.H.P.B at 5 years of age progresses with worsening of the respiratory condition, being admitted with severe conditions of decompensated asthma and presenting an episode of admission to the Intensive Care Unit due to cardiorespiratory arrest after an intense asthma crisis, in which he remained for 8 days. Having evolved with the need for tracheostomy and use of CPAP during sleep. The child had intense school difficulties, being prevented from performing intense physical activities, remained in constant hospitalizations due to restrictive respiratory disorders and uncontrolled asthma attacks, progressing to death later on.

RESULTS AND DISCUSSION

Prader-Willi syndrome It can manifest at different times, in the first phase it is characterized by different degrees of neonatal hypotonia and in infancy, by weak crying, temperature variations due to hypothalamic dysfunction, weak suction and genital hypoplasia. These children may contain growth restriction due to difficulty in breastfeeding, however hypotonia tends to improve between 8 and 11 months, causing the child to gain weight and become more alert (Andrade, et. al., 2011).

In a second moment, there may be psychomotor delays perceived in the delay in crawling and walking, in addition to the appearance of obesity, hyperphagia and binge eating. Other characteristics present are mental deficiency, short stature, small hands and feet, hypogonadism, characteristic facies with reduced bifrontal diameter and triangular mouth. Personality and behavior disorders tend to appear between 3 and 5 years of age, there are outbursts of rage, stubbornness, depression, especially when food is denied. Morbid obesity can lead to sleep apnea and cor pulmonale and represents the most relevant complication of the syndrome, becoming a risk factor for the development of glucose intolerance, cardiovascular and respiratory diseases, reducing life expectancy and quality of life (Andrade, et. al., 2011).

SPW mainly occurs from three genetic errors. Approximately 70% of cases have a deletion in the paternal chromosome 15. About 25% have maternal uniparental disomy: two maternal 15 chromosomes and no paternal 15 chromosome. And 2% to 5% have an error in the "imprinting" process, which makes the paternal contribution non-functional; these imprinting defects can rarely be inherited. (Cassidy, et. al., 2009).

Children who have certain potential traits for SPW must be investigated with genetic testing, DNA methylation analysis confirms the diagnosis of SPW (Other DNA analysis techniques of FISH can identify the specific genetic cause and the possible risks of recurrence in the same family), among them there are reduced fetal movements (lethargic baby, with weak crying), difficulty in sucking and

little weight gain in the first months of life, Weight gain fast or excessive between 1 and 6 years of age; central obesity if no intervention, hypogonadism, global developmental delay before 6 years of age; mild to moderate cognitive impairment or learning problems in older children. In addition to hyperphagia, sleep disorders, especially daytime sleepiness and sleep apnea, among others (Cassidy, et. al., 2009).

Some criteria can be used to facilitate the recognition of the syndrome's characteristics, among them the diagnostic criteria established by Holm stand out, being, for children under 3 years old, a total of five points (three necessarily major criteria) and for children older than 3 years old. 3 years, the sum of eight points (four major criteria). Among the major criteria are central hypotonia, feeding difficulties, early obesity, characteristic face, hypogonadism and mental retardation. And among the minors decreased fetal movement, typical behavioral disorder, sleep apnea, short stature, hypopigmentation, small hands and feet, exotropia, myopia, thick saliva, speech articulation problems, skin pinching habit. Support criteria can be used, but not pontoon and are high threshold to pain and vomiting, thermal instability, scoliosis and/or kyphosis, early adrenarche, osteoporosis, special puzzle skill, normal neuromuscular studies (Holm, et. al.,1993).

The main cause of mortality in individuals with PWS is represented by respiratory failure or cardiorespiratory failure. Sometimes death can be triggered by acute pulmonary infections, contributing to the clinical worsening of the decrease in respiratory effort and compensatory reflexes, due to the hypotony characteristic of the syndrome. In relation to individuals with neuropsychomotor development delay or obesity due to other causes, the relative risk of death is six times higher (Kim CA, et. al., 2010).

Patients with PWS have relevant respiratory disorders, including central and obstructive sleep apnea, abnormal response to hypercapnia, as well as excessive daytime sleepiness, which can be explained most often by central hypoventilation and may progress to pulmonary hypertension. This complication may be due to decreased muscle tone, obesity and reduced neural activity for breathing. The case reported here demonstrates several clinical characteristics that support the diagnostic hypothesis of PWS, in addition to the pulmonary repercussions and cause of death consistent with the complications of the syndrome (Kuo JY, et. al., 2007).

Obstructive apnea is common in Prader Willi Syndrome, affecting around 50 to 100% of patients, these individuals usually have noisy breathing and snoring associated with periods of calm, where no air circulation is noticed and if left untreated it can and have serious complications, including death. Given the above, it is clear that the pathogenesis of respiratory repercussions in PWS has a multifactorial origin, going beyond muscle hypotonia, also contributing to the disorder and change in respiratory control, with low response to CO2 elevation, kyphoscoliosis (15%) and the reduced diameter of the upper airways, causing obstruction, whether due to facial dysmorphism and/or tonsillar hyperplasia, among others (Fridman, et. al., 2000).

Furthermore, we can emphasize that there are no medications or surgical forms of effective treatments for disorders, especially respiratory, generated by SPW, with the main form of control and prevention of complications being the control of obesity with strict dietary measures and early practice of physical activity (Eiholzer U, et. al. 2006). Due to concerns about early death due to worsening respiratory obstruction, early in growth after hormonal treatment with GH, it was proposed by Eiholzer (Eiholzer U, 2005) that poly-

somnography and evaluation for tonsil and adenoid hypertrophy be performed previously and after 6 to 12 weeks of its onset (Eiholzer U, et. al. 2006).

Given the great complexity of the various factors involved in Prader-Willi Syndrome, from physical, mental and psychological, a multidisciplinary follow-up must be recommended, aiming at the well-being of the patient and their families. Together, immunization programs must be included in order to minimize the appearance and recurrence of complications caused by respiratory infections. In addition to endocrine-metabolic monitoring, preventing obesity and comorbidities associated with it.

CONCLUSION

According to what was showed previously, this article has highlighted the importance of early diagnosis, especially in the early stages of life and in view of the initial manifestations of Prader-Willi syndrome. Such measures are necessary to prevent excessive obesity and control morbidities related to it. In addition to controlling behavior disorders.

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