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RESEARCH ARTICLE

HIGH BLOOD PRESSURE IN PATIENTS WITH PRADER WILLI SYNDROME : CASE REPORT AND REVIEW OF THE LITERATURE

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Prader Willi Syndrome, Complex Genetic Syndrome, Hypertension, Cardiovascular morbi-mortality.We Report the Case of a Patient Seen in Cardiology, Endocrinology consultation for diabetes 2 with obesity

Abstract

Prader-Willi syndrome (PWS), the most common genetic cause of obesity, is characterized by elevated morbi-mortality in all ages. In this context, non-obese PWS patients showed low frequency of metabolic syndrome (MetS), while a high prevalence of hypertension was observed in obese PWS and obese controls. The aim of this report was to estimate the occurrence of high blood pressure and its components in a large group of PWS adults. An association of this syndrome with elevated cardiovascular morbi-mortality was observed, but the underlying mechanisms are not fully known.

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Introduction:-

Prader–Willi syndrome (PWS) is a multi-system disorder that is estimated to occur in 1/10,000–1/29,000 people (Cassidy, Schwartz, Miller, & Driscoll, 2011; Yearwood, McCulloch, Tucker, & Riley, 2011). It is a rare complex genetic syndrome , characterized by neonatal hypotonia with failure to thrive, hypogonadism, impaired growth hormone secretion. Hyperphagia present in early childhood can gradually lead to morbid obesity if not controlled. Additional features include typical cranio-facial features with cognitive, behavioral, neurological, endocrine,and psychiatric disturbances(Cassidy et al., 2011)(1)(3)(4).PWS is caused by the non-expression of the paternal alleles of the chromosome 15q11–13 or by maternal uniparental disomy (2)(5).Mortality in patients with PWS is 3% per year. In nearly half of the patients, the cause of death is of cardiopulmonary origin.

Prevention, diagnosis and treatment of cardiovascular (CV) disease in PWS adults is complicated by the behavioral phenotype, reduced ability to express physical complaints, high pain threshold and obesity.

The aim of this study was to estimate the frequency of hypertension and the cardiovascular phenotype of PWS patients .

Case Report:

A 21 year- old -man with a past medical history of diabetes 2 under insulin therapy, obesity since childhood and confirmed Prader willi syndrome, admitted to the department of cardiology-endocrinology consultation for follow up . The patient has no clinical presentation of dyspnea or chest pain and his physical exam found a BMI: 36 kg/m2 and BP: 160/100 mmHg with no other physical signs ,transthoracic echocardiography (TTE) was ordered, but the patient was lost to follow-up.

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Discussion:-

Factors that determine the high rate of death seen in PWS are not fully clarified. In the general population, metabolic syndrome is believed to represent a strong risk factor for the subsequent development of atherosclerotic cardiovascular disease . (6)

Mortality in patients with PWS is as high as 3% per year (7, 8). In nearly half of the patients, the cause of death is of cardiopulmonary origin and three-quarters of deaths are unexpected (7, 9). Cardiovascular (CV) abnormalities can occur early in life (10) and patients with PWS have an increased risk to develop CV disease at a young age. (7, 11–12)

Causes of death are reported for both children and adults diagnosed with PWS (Butler, Manzardo, Heinemann, Loker, & Loker, 2017). Respiratory illness and sudden death associated with dysregulation of temperature are noted causes of death in children, whereas obesity related complications, including cardiovascular problems, diabetes, hypertension, and sleep apnea, are noted in adults with PWS (Schrander-Stumpel et al., 2004; Tauber, Diene, Molinas, & Hébert, 2008; Vogels et al., 2003).(1)

Apart from the complex etiology, the diagnostic trajectory of CV disease in adults with PWS is also complicated.

Recent research has shown that patients with PWS display distinct cardiovascular characteristics including higher nocturnal BP and BP variability (13). In support of this theory, a study conducted by Benedicte et al report that high prevalence of hypertension and type 2 diabetes was seen in the group with PWS and abdominal obesity was prevalent in all groups of study and was associated with an increased risk of hypertension and metabolic syndrome(14) .

PWS is associated with high ghrelin levels and an elevated acylated ghrelin/unacylated ghrelin (AG/UAG) ratio (15) which could cause weight gain and glucose intolerance (16) .

This study adds further evidence to the hypothesis that increased body fat eventually leads to an increased prevalence of CV risk factors like type 2 diabetes mellitus (DM2), hypertension, hypercholesterolemia and sleep apnea (17–18) . The theory was also illustrated by the data conducted by G. Grugni et al (19) who has confirmed that Obese PWS showed higher glucose and systolic BP than both non-obese PWS and obese controls ; and by P. Brambilla et al **(**Non-obese PWS showed significantly lower frequency of hypertension (12%) than obese PWS (32%) and obese controls (35%)(**p** = 0.003))(20).

In addition to the obesity-related increase in CV risk, patients with PWS have an additional risk due to decreased microvascular function that is associated with the syndrome (21) .

Conclusion:-

A mortality rate of 3% a year across all ages and about 7% a year in those over 30 years of age has been reported in patients with PWS. Complications associated with obesity are recognized as the main risk factors for death during the life-span of patients with PWS.Nevertheless, the factors determining the evolution to cardiovascular disease and metabolic complications remains to be still elucidated .

Therefore a multidisciplinary approach is needed. A pediatric, endocrinologist, specialized dietitian, physiotherapist and, if needed, a behavioral expert or psychologist should work together. Diagnosis and treatment can be complicated by PWS-specific behavior, non-compliance to salt and water restriction, and refusal of medication. Therefore, preventive measures, diagnostics and treatment of CV disease should preferably be guided by a multidisciplinary team.

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