**Cardiovascular abnormalities in children with Congenital Central Hypoventilation Syndrome**

Joana Marinho1, Núria Madureira2, Teresa Silva2, Miguel Félix2, Maria Helena Estêvão2 [estevao.mh@gmail.com](mailto:estevao.mh@gmail.com)

1Serviço de Cardiologia Pediátrica, 2Laboratório de Sono e Ventilação

Hospital Pediátrico de Coimbra (HPC), Centro Hospitalar e Universitário de Coimbra, Portugal

**Introduction**: Congenital Central Hypoventilation Syndrome (CCHS) is a rare disturbance of autonomic nervous system regulation. The inadequate central control of ventilation with decreased sensitivity to hypoxia and hypercapnia.may be associated to cardiac rhythm disturbances and pulmonary hypertension. Identification of the gene related to this disease has been followed by an increasing interest in genotype-fenotype correlation for its different manifestations, including cardiovascular abnormalities.

**Objective**: To characterize cardiovascular abnormalities in CCHS children followed in HPC and to establish genotype-fenotype correlation in these manifestations.

**Methods**: Retrospective analysis of the clinical records of the CCHS children who have been followed in HPC. Cardiovascular evaluation included regular echocardiogram, 48 hours Holter recordings and analysis of heart rate variability response to hypoxia in polysomnography (PSG).

**Results:** Since 1994, eleven children were followed (5 males/6 females). Four died (2 suddenly at home) and the other seven are currently between 3 and 12 years old. PHOX2B genetic testing revealed heterozygotous mutations in 9 children - 20/26 (5), 20/27(2), delection 722-759 38nt (1), mutation on exon 1c.23dupA.pY8X (1); and in another, homozygotous PHOX2B mutation with 4 polyalanine repeat expansion (20/24). One child died before genetic testing. The child with the delection 722-759 38nt presented a very severe form and died at 3 months old. The child with a mutation of exon 1c.23dupA.pY8X had a late-onset CCHS (9 months). Nine children performed PSG and all but one (mutation of exon 1c.23dupA.pY8X) had reduced heart rate variability. The most frequent finding on echocardiogram was pulmonary hypertension (8/11). Forty eight-hour Holter recordings were performed in 10 children and abnormalities were found in 5: second degree heart block, sinus bradycardia, sinus pauses (1.351 to 4.8 sec). The child (homozigotous PHOX2B 20/24) with prolonged sinus pauses received a cardiac pacemaker. There was no correlation between the size of the polyalanine repeat expansion and the severity of the cardiovascular abnormalities.

**Conclusions**: Published data point to a direct association between the size of the polyalanine repeat expansion and the severity of the cardiovascular abnormalities. Inversely, in our group of children, the most severe bradyarrhythmia was found in the child who had an homozygotous mutation with an inferior number of polyalanine repeat expansion (20/24). In the late-onset case (mutation on exon 1c.23dupA.pY8X) diminished heart variability was not noted and may mean a less severe case. In the other ones there was no evident genotype-fenotype correlation. More detailed studies with large numbers of children are needed to better establish an association between cardiovascular abnormalities and genotype.

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