**Gastrointestinal symptoms, signs and associated iron-deficiency anaemia in the Jervell and Lange-Nielsen Syndrome - Clinical Phenotype Beyond the SurdoCardiac Syndrome**

Winbo A. (1), Sandström O. (1), Palmqvist R. (2), Rydberg A. (1)
Department of Clinical Sciences, Pediatrics, Umeå University, Umeå, Sweden (1); Department of Medical Biosciences, Pathology, Umeå University, Umeå, Sweden (2)

Introduction: The KCNQ1 gene is essential for gastric acid secretion. The Jervell and Lange-Nielsen Syndrome (JLNS), originally described as a surdocardiac syndrome, is characterized by impaired KCNQ1 function. Here we investigate possible symptoms and signs related to loss of gastric acid secretion in genotyped JLNS cases with KCNQ1 mutations.

Methods: We investigated 14 genotype-ascertained JLNS cases with KCNQ1 mutations (age 31±24 years, range 4-87, whereof 9 females), initially by personal interview and medical record review. Current testing for iron-deficiency anaemia and gastrointestinal function/inflammation (fasting levels of gastrin and pepsinogen, and faecal calprotectin) was performed.

Results: Previous anaemia (12/13 tested cases), subjective gastrointestinal symptoms (13/14 cases) and a previous positive faecal haemoglobin test (n=4) was revealed. Endoscopy had been performed in 5 cases revealing no case of coeliac- or inflammatory bowel disease but 2 cases of mucosal hyperplasia and one ventricular tumour. One sibling with JLNS had died from gastric carcinoma. At current testing signs of iron-deficiency anaemia or iron-substitution was present in 9/12 tested cases. Elevated levels of gastrin (in 7/9 cases, mean 379±426 pmol/L, range 22-1285, normal<60), pepsinogen (in 6/7 cases, mean 366±332 µg/L, range 121-892, normal<130) and faecal calprotectin (in 9/9 cases, mean 322±195 mg/kg, range 77-641, normal<50) were present. A significant correlation between elevated gastrin levels and current anaemia was found (p=0.028), and in no case was anaemia present without elevated gastrointestinal markers.

Conclusion: We propose that JLNS phenotypically includes iron-deficiency anaemia and gastrointestinal symptoms/signs, secondary to hypochlorhydra on the basis of KCNQ1 mutations. The resultant hypergastrinaemia is a risk factor for gastrointestinal cancer. Further studies are needed to elucidate the importance of hypochlorhydra, hypergastrinaemia and gastrointestinal inflammation in JLNS. Monitoring of JLNS cases with regards to developing anaemia and gastrointestinal cancer should be considered.