Title: SPG related to the ALDH18A gene: report of two siblings.

Authors names:

MONTOURO, laura alonso matheus[1]
ROCHA, emanuelle bianchi da silva[1]
MORITA, maria da penha ananias [2]
COELHO, erica nogueira [2]
ESTEPHAN, eduardo de paula [2]

[1] Resident at the Department of Neurology at the Faculty of Medicine of São José do Rio Preto, São José do Rio Preto-São Paulo.
[2] Assistant Physician at the Department of Neurology at the Faculty of Medicine of São José do Rio Preto, São José do Rio Preto-São Paulo.

Introduction: Hereditary spastic paraparesis (SPG) related to *ALDH18A1* can be caused by pathogenic mono (SPG9A) or bi-allelic (SPG9B) variants, with these variants tending to have a more severe phenotype. We report two siblings with *ALDH18A1*-related SPG. Case1: 62-year-old, female, presents with delayed psychomotor neurodevelopment, characterized by gait difficulty and intellectual deficit since childhood. She presented a progressive evolution, with muscle atrophy and bone deformities, and worsening of motor and cognitive symptoms after pregnancy. Case 2: 65-year-old, male, (case 1's brother) developed pure spastic paraparesis (SP) at 39 years-old, progressively, and currently requires a wheelchair. There is a history of consanguinity between the paternal grandparents. Both cases have two heterozygous variants in the ALDH18A1 gene - a missense variant c.1322G>A (p.Arg441Gln - absent in population bases, highly conserved region) and an intronic splice donor site variant (c.1152+1G>A). Propedeutics: Both have SP in lower limbs with signs of pyramidal release, but case 1 also has short stature, tremors and memory impairment. Results: SPG related to ALDH18A1 gene has been previously prescribed with intronic and missense variants. SPG9B tends to be more severe and with a complex phenotype. Onset or worsening of symptoms during or after pregnancy appears to be common in these conditions. Conclusions: the conditions related to ALDH18A1 must be understood in our medical circle, whether in recessive or dominant SPG. Our work illustrates a SPG9B case, reporting the first Brazilian family with this disease.

Key words: SPG9B; SPG9A; ALDH18A1; HSP; SPG